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D E C I S I O N
of 6 April 2005

Case Number: T 0179/01 - 3.3.8

Application Number: 91917090.2

Publication Number: 0546090

IPC: C12N 15/54

Language of the proceedings: EN

Title of invention:
Glyphosate tolerant 5-enolpyruvylshikimate-3-phosphate synthases

Patentee:
MONSANTO COMPANY

Opponents:
GREENPEACE DEUTSCHLAND e.V.
Syngenta Limited
Dr. Christoph Then und Thomas Schweiger

Headword:
Herbicide resistant plants/MONSANTO

Relevant legal provisions:
EPC Art. 53(b), 54, 56, 83
EPC R. 64(b), 23c(b)

Keyword:
"- exception to patentability under Article 53(b) - plant varieties - no"
"- novelty, inventive step - sufficiency of disclosure - yes"
"- referral of questions to the Enlarged Board of Appeal - no"

Decisions cited:
G 0001/98, G 0004/95, T 0081/87, T 0301/87, T 0606/89, T 0356/93, T 0277/95, T 1054/96, T 0149/98, T 0475/01, T 0315/03

Catchword:
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Case Number: T 0179/01 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 6 April 2005

Appellant I: (Proprietor of the patent)
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Representative: -

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 31 January 2001 concerning maintenance of the European patent No. 0546090 in amended form.**

Composition of the Board:

Chairman: L. Galligani
Members: F. L. Davison-Brunel
C. Rennie-Smith
T. J. H. Mennessier
M. B. Günzel

Summary of Facts and Submissions

I. European patent No. 0 546 090 with the title "Glyphosate tolerant 5-enolpyruvylshikimate-3-phosphate synthases" was granted on the basis of the European patent application No. 91917090.2 with 34 claims.

II. Three oppositions were filed on the grounds of Article 100a) to c) EPC for added subject-matter, lack of novelty and inventive step, lack of sufficiency of disclosure and also on the ground that the subject-matter of claims 25 to 28 was not patentable under Article 53(a) and (b) EPC. The patent was maintained by the opposition division on the basis of the first auxiliary request then on file.

III. Appellant I (patentee) filed an appeal against this decision as well as appellant II (opponent 01) and appellant III (opponent 02). Opponent 03 is party to the proceedings as of right. All appellants submitted statements of grounds of appeal in due time and paid the appeal fee. Appellant III's statement of grounds of appeal was accompanied by experimental data.

IV. Appellant I submitted observations on the statements of grounds of appeal filed on behalf of appellants II and III.

V. The board sent a communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal, indicating its preliminary non-binding opinion.

VI. All appellants replied to this communication. Appellant I submitted five auxiliary claim requests to

be considered in addition to the granted claims (main request) and also argued that appellant III's appeal was not admissible.

VII. At oral proceedings which took place on 6 April 2005, appellant II requested that an expert who had not previously been announced be allowed to present new arguments under Article 53(a) EPC. This request was refused. Appellant I withdrew all previous claim requests and filed a new main request which was identical to the granted claims except for the deletion of claim 2. Claims 1, 4, 7 and 24 read as follows:

"1. An isolated DNA sequence encoding a Class II EPSPS enzyme, said enzyme being an EPSPS enzyme having a K_m for phosphoenolpyruvate (PEP) between 1-150μM and a K_i(glyphosate)/K_m(PEP) ratio between 3-500, which enzyme is capable of reacting with antibodies raised against a Class II EPSPS enzyme selected from the group consisting of the enzymes of SEQ ID No:3 and SEQ ID No:5.

4. An isolated DNA sequence encoding a protein which exhibits EPSPS activity where said protein is capable of reacting with antibodies raised against a Class II EPSPS enzyme selected from the group consisting of the enzymes of SEQ ID NO:3 and SEQ ID NO:5.

7. A recombinant, double-stranded DNA molecule comprising in sequence:

a) a promoter which functions in plant cells to cause the production of an RNA sequence;

b) a structural DNA sequence that causes the production of an RNA sequence which encodes a Class II EPSPS enzyme capable of reacting with antibodies raised against a Class II EPSPS enzyme selected from the group consisting of the enzymes of SEQ ID No:3 and SEQ ID No:5; and

c) a 3' non-translated region which functions in plant cells to cause the addition of a stretch of polyadenyl nucleotides to the 3' end of the RNA sequence

where the promoter is heterologous with respect to the structural DNA sequence and adapted to cause sufficient expression of the fusion polypeptide to enhance the glyphosate tolerance of a plant cell transformed with said DNA molecule.

24. A glyphosate tolerant plant comprising plant cells of Claim 20."

Dependent claims 2, 3 and 5 respectively related to further features of the DNA sequence of claim 1 or 4. Claim 6 was directed to a DNA sequence encoding a Class II EPSPS enzyme selected from the group of SEQ ID No:3 and SEQ ID No:5. Dependent claims 8 to 13 related to further features of the DNA molecule of claim 7. Claim 14 was directed to a method of producing genetically transformed plants which were tolerant toward glyphosate herbicide and dependent claims 15 to 19 related to further features of the method of claim 14. Claim 20 was directed to a glyphosate tolerant plant cell comprising a DNA molecule according to preceding claims and claims 21 to 23 related to further features of the plant cell of claim 20.

Claim 25 to 27 related to further features of the glyphosate tolerant plant of claim 24. Claim 28 was directed to a method for selectively controlling weeds in a field and dependent claims 29 to 33 related to further features of the method of claim 28.

VIII. The following documents are mentioned in the present decision:

(1): Fischer, R.S. et al., Arch.Biochem.Biophys, Vol.256, No.1, pages 325 to 334, July 1987;

(2): Henner, D.J. et al., Gene, Vol. 49, pages 147 to 152, 1986;

(3): EP-A-0 218 571 (published on 15 April 1987);

(6): Kishore, G. et al., in "Biotechnology for Crop Protection" ACS Sympos. Series, Hedlin et al., Eds, pages 37 to 48, 1988;

(14): US-A-5 633 435 (published on 27 May 1987);

(15): Declaration of Dr. T.R. Hawkes dated from January 2000 together with experimental data;

(19): Experimental data accompanying appellant III's grounds of appeal received at the EPO on 30 May 2001;

(26): An information sheet sent by fax by appellant III on 4 April 2005 presenting a compilation of EPSPS enzymes and a kinetic data survey as at August 1991.

IX. Appellant I's arguments in writing and during oral proceedings so far as relevant to the present decision may be summarised as follows:

Admissibility of appellant III's appeal

In accordance with Rule 64(b) EPC, the notice of appeal should contain a statement identifying the extent to which amendment or cancellation of the decision under appeal was requested and Rule 65(1) EPC stated that if the appeal did not comply with Rule 64(b) EPC, the Board of Appeal shall reject it as inadmissible. Appellant III's notice of appeal did not contain a statement as mentioned in Rule 64(b) EPC. Furthermore, confusing statements were made in the grounds of appeal as to the extent to which cancellation of the first instance decision was requested. Thus, appellant III's appeal was inadmissible.

Article 53(b) EPC; claim 24

This claim was addressed to glyphosate-tolerant plants in general and not to specific plant varieties. For this reason and in accordance with the case law (G 1/98; OJ EPO 2000, 111), it was not excluded from patentability under Article 53(b) EPC.

Article 54 EPC
Novelty of the subject-matter of claims 1 and 4 over the teachings of document (2):

Document (2) disclosed a B.subtilis DNA fragment which carried three open-reading frames ORF1-ORF3. The

sequences of the three corresponding proteins were deduced on the basis of the genetic code and a comparison with the sequences of other known proteins showed that the protein encoded by ORF3 had 24% identity with the S.typhimurium aroA encoded EPSPS protein. This led the authors to suggest that ORF3 was the B.subtilis aroE gene encoding an EPSPS enzyme. However, the isolated DNA was not expressed, nor was the aroE encoded protein isolated, nor, of course, were its properties ever investigated. It was not appropriate to conclude that the DNA described in document (2) destroyed the novelty of the DNA of claims 1 or 4 on the basis of a simple guess that this DNA may encode a protein which could have the activity and property(ies) mentioned in the claims.

As for Appellant II's experimental data relating to the immunological properties of the aroE encoded protein, this was so biased by the way the experiments had been carried out as to make it meaningless.

Novelty of the subject-matter of claims 1, 4 and 7 over the teachings of document (3):

Document (3) disclosed the DNA encoding the E.coli D96A EPSPS mutant enzyme. However, the enzyme had not been isolated nor had its chemical or immunological properties been defined. Thus, for the same reasons as above mentioned in relation to the DNA disclosed in document (2), document (3) did not destroy the novelty of the claimed subject-matter. If one was to take document (6) as a disclosure of the inherent chemical properties of the E.coli D96A enzyme, it became readily apparent that its K_m fell outside the range mentioned in

claim 1. The argument to the effect that the observed difference in K_m (220 µM versus the claimed range of 1-150 µM) could be due to experimental errors was not credible. For these reasons, even reading document (3) in the light of document (6) did not affect novelty.

Article 56 EPC; inventive step of the subject-matter of claim 1:

In its reasoning on inventive step, Appellant III primarily relied on a combination of the teachings of documents (3) and (1). Document (3) related to engineering herbicide tolerance in plants and the concept which was put into practice was that of having the "glyphosate tolerant" EPSPS enzymes from E.coli or plants (expressed in the transformed plants) directed to a compartment of the transformed plant cells where the best level of herbicide tolerance would be achieved, namely the chloroplast; in contrast, document (1) was an **in vitro** study of the Bacillus subtilis EPSPS enzyme which was not even mentioned in document (3). Thus, although both documents related to EPSPS enzymes, there were no obvious reasons why they should be combined. Furthermore, in its attempt to justify why the B.subtilis enzyme should be chosen for engineering herbicide tolerance in plants, appellant III had combined no less than 14 documents - document (26) being a compilation of data from ten documents of the art. Finally, appellant III misrepresented the teachings of document (1) when alleging that the B.subtilis enzyme would be thought particularly advantageous for the intended purpose. In fact, document (1) taught that the activity of the B.subtilis EPSPS enzyme varied considerably as a function of the

ionic conditions in which the enzyme found itself and this variability was not at all a desirable property for achieving reliable herbicide tolerance in vivo.

In the light of the prior art, it had to be concluded that the skilled person would not have had any interest in obtaining the DNA encoding the B.subtilis EPSPS enzyme when attempting to engineer herbicide tolerance in plants. Inventive step had to be acknowledged.

Article 83 EPC; sufficiency of disclosure:

The isolation of three different Class II EPSPS genes was disclosed in the patent in suit and, on page 13, a full paragraph was devoted to describing methods for further isolating such genes. The introduction and expression of EPSPS genes into plants was also illustrated by several examples. Measuring K_m and K_i would be done as a matter of routine (see document (1)) and it was clear from appellant III's own data that finding out whether an EPSPS enzyme had the claimed immunological properties could be achieved without undue burden. For these reasons, the patent in suit provided a sufficient disclosure of the claimed invention.

X. Appellant II's arguments concentrated on the fact that, in its opinion, the subject-matter of claim 24 (glyphosate tolerant plants) was excluded from patentability under Article 53(b) EPC. The board should have the courage to reverse the previous case law which allowed patents to be granted for claims apparently directed to plants in general but, in fact, addressed to plant varieties because this earlier case law was

wrong. The change relating to the patentability of plants introduced by Rule 23c(b) EPC was of such significance that it could only have legitimacy if it had been introduced in the EPC itself rather than in its Implementing Regulations. Thus, the Rule should not be applied.

Claim 24 reflected the invention as described in the patent specification -encompassing many plant varieties- and, thus, was directed to plant varieties. In fact, the introduction of a gene "coding for herbicide tolerance" in the genome of the plants followed by its stable transmission to the progeny resulted in every one of these plants being an "essentially derived variety" which, like all others, was barred from patentability. Further evidence that the claim was related to plant varieties could be drawn from the fact that the herbicide tolerant plants were, of course, meant to be grown in the fields and it was a matter of common general knowledge that only plant varieties were of agricultural importance.

The patent was quite different from earlier plant patents which did not lead to the production of plant varieties, such as the patent concerned with fitting a plant promoter in front of a plant gene, or the patent which was at issue in the decision T 1054/96 of 6 December 2000 where herbicide resistant plants were to be obtained by the introduction of more than one gene into the plant genome.

In fact, the present case was similar to the case dealt with in decision T 475/01 of 15 June 2004, yet it was only clearer that plant varieties were claimed and,

therefore, that the claimed subject-matter offended the requirements of Article 53(b) EPC.

In case the board was minded to decide in favour of patentability, the following questions should be referred to the Enlarged Board of Appeal (submitted in German):

"- Sind Pflanzen patentierbar, wenn die beanspruchte Eigenschaft gleichzeitig ein sortenbestimmenden Merkmal ist?

- Sind Ansprüche gewährbar, die erkennbar abgeleitete Sorten beinhalten?

- Sind im wesentlichen abgeleitete Sorten individuell bestimmbare Sorten und damit nach Artikel 53b ausgeschlossen?"

XI. Appellant III's arguments in writing and during oral proceedings so far as relevant to the present decision may be summarised as follows:

Admissibility of the appeal

The notice of appeal contained a statement identifying the extent to which the decision of the first instance was appealed as it stated that the appeal was from the decision to maintain the patent in amended form. Furthermore, in accordance with the case law, Rule 64(b) EPC did not constitute a barrier to admissibility as long as it was possible to infer the extent of the appeal from the overall submissions which had been made. Here, the extent of the appeal was

further identified in the grounds of appeal. The fact that three alternative requests were made which were to be considered by the board in a defined order did not bring any lack of clarity as to the extent to which cancellation was requested.

Article 53(a) EPC

Appellant II's expert should not be allowed to speak as it had not been announced in advance of oral proceedings. To do otherwise would go against the right of each party to have a proper opportunity to reply to another party, which right stemmed from a fundamental principle of procedural law (G 4/95, OJ EPO 1996, 412).

Article 54 EPC
Novelty of the subject-matter of claims 1 and 4 over the teachings of document (2):

The novelty of claims 1 and 4 was affected by the disclosure in document (2) of a B.subtilis DNA fragment which carried the aroE gene identified by its sequence and by the sequence of the protein it encoded. On page 150, it was mentioned that this gene was the equivalent of the aroA gene in S.typhimurium and, thus, the aroE encoded protein was an enzyme with EPSPS activity. The properties of the enzyme were not mentioned in document (2) but evidence was on file that it had kinetic properties within the ranges defined in claim 1 (document (14)). Moreover, this appellant had provided unequivocal data to show that the aroE protein had the immunological properties mentioned in the claim (documents (15) and (19)). Thus, it was inherent in the protein encoded by the isolated DNA described in

document (2) that it had the claimed properties and, therefore, this DNA fell within the scope of claims 1 and 4 which were not novel.

Novelty of the subject-matter of claims 1, 4 and 7 over the teachings of document (3):

Document (3), example 8 disclosed a DNA encoding an E.coli mutated EPSPS enzyme. This enzyme was antigenically closer to the CP4 EPSPS enzyme of the patent in suit than the wild type E.coli enzyme because of the replacement of D by A at position 96. Thus, like the wild type E.coli enzyme (see documents (15) and (19)), it would be expected to react with anti-SEQ ID No:3 antibodies. Its chemical properties were described in document (6): both its K_i/K_m ratio (20) and its K_m (220 µM) fell within the claimed ranges, taking into account experimental variations in the case of the K_m. For these reasons, claims 1, 4 and 7 lacked novelty over the teachings of document (3).

Article 56 EPC; inventive step of the subject-matter of claim 1:

The closest prior art document was document (3) which disclosed the use of recombinant DNA encoding EPSPS from various sources to produce transgenic plants which were tolerant to the herbicide glyphosate.

The problem to be solved could be defined as providing an alternative, preferably better DNA construct for that purpose.

The claimed solution was a DNA encoding an EPSPS enzyme with a high affinity for its substrate (low K_m) and a low affinity for the glyphosate inhibitor (high K_i/K_m).

This solution was obvious in view of the teachings of document (1). This document specifically mentioned that engineering herbicide resistance into plants was a desirable goal. It taught that the B.subtilis EPSPS enzyme had a K_i/K_m ratio which was high in the presence of K^+ ions - most frequent in plant cells - while its K_m remained low under the same conditions. The skilled person would also be aware that the K_i/K_m ratio of this enzyme was the most favourable amongst the K_i/K_m ratios of the EPSPS enzymes up till then studied (document (26)). The choice of cloning the B.subtilis EPSPS gene as a first step for the intended use would, thus, be obvious and the cloning per se would be considered a matter of routine, all the more so since the gene had already been obtained in recombinant form (document (2)) and, therefore, its sequence was known. For these reasons, claim 1 lacked inventive step.

Alternatively, the combination of the teachings of documents (3) and (2) rendered the claimed subject-matter obvious as the B.subtilis EPSPS DNA was an obvious alternative DNA to use for engineering glyphosate tolerance in plants. In the same manner, starting from document (1) or (2) as closest prior art, one could define the problem to be solved as finding a use for the B.subtilis EPSPS protein/DNA described therein and in view of the teaching of document (3), the concept of transferring the DNA into plants for achieving herbicide resistance would be obvious and could be put into practice as a matter of routine.

Article 83 EPC; sufficiency of disclosure

It was very clear from document (1) that kinetic parameters such as those mentioned in the claims varied depending on the concentration of cations in the sample to be tested. Thus, in the absence of any guidance in the patent in suit as to the concentration of cations to be used, the skilled person was faced with too much burden when attempting to find out whether a given EPSPS enzyme fell within the claim.

XII. Appellant I (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed during oral proceedings. Appellant I further requested that the appeal filed by opponent 02 be declared inadmissible.

Appellant II (opponent 01) and the respondent (opponent 03) requested that the decision under appeal be set aside and that the European patent No. 0 546 090 be revoked; or as auxiliary request that the questions filed during oral proceedings be referred to the Enlarged Board of Appeal.

Appellant III (opponent 02) requested that the decision under appeal be set aside and that the European patent No 0 546 090 be revoked; or as a first auxiliary request, that the patent be maintained in a more limited amended form; or, as second auxiliary request, that the proprietor's appeal be dismissed.

Reasons for the decision:

Admissibility of Appellant III's appeal

1. Under Rule 64(b) EPC, a notice of appeal shall contain a statement identifying the decision which is impugned and the extent to which amendment or cancellation of the decision is requested. In numerous decisions of the boards of appeal (cf. Case law of the Boards of Appeal of the European Patent Office, 4th edition 2001, VII.D.7, pages 526 and 527), this requirement for the admissibility of the appeal (Rule 65(1) EPC) is considered to be fulfilled when the extent to which cancellation of the decision is requested can be determined from the totality of the appellant's submissions.

2. Appellant III's notice of appeal contains the following statement: "... I hereby give notice of appeal to the decision of the Opposition Division to maintain - in an amended form - the above identified patent", leaving no doubt as to which decision is impugned and defining in an admittedly succinct manner the request for cancellation. A detailed request is found in the statement of grounds of appeal in the form of three requests to be considered in a clearly identified order: "We request that the decision of the Opposition Division be set aside and that the patent be revoked in its entirety for all Contracting States. Failing that we request that the patent be maintained in amended form with claims more limited than those amended claims allowed by the Opposition Division. Failing that we request that the patent be maintained in the amended form allowed by the Opposition Division."

3. On this basis, the Board has no difficulty in identifying Appellant III's request and, in accordance with the case law, concludes that the appeal is admissible.

Article 53(a) EPC; claim 24 and dependent claims thereof

4. At oral proceedings, Appellant II requested that evidence be heard from a person accompanying him, allegedly under Article 53(a) EPC, on the consequences the patenting of plants may have on the sales in Europe of agricultural goods produced outside Europe. This person had not been announced in advance of oral proceedings.

5. In the decision G 4/95 (supra), the Enlarged Board of Appeal reflected on the importance of the general principle of procedural law that, in an inter partes proceeding, each party should have a proper opportunity to reply to the case which is presented by an opposing party. In particular, it was concluded (Order, point 3(iii)) that, in accordance with this principle, a request for a person accompanying the professional representative of a party to make submissions shortly before or at the oral proceedings should in the absence of exceptional circumstances be refused, unless each opposing party agrees to the making of the proposed oral submission.

6. At oral proceedings, the other parties were asked whether or not they accepted that the hitherto unannounced person should be heard and Appellant III declined to do so. The board could not see any

exceptional circumstances and accordingly, the request was rejected.

7. Appellant II's representative did not want to re-iterate those arguments filed at the first instance. In the decision under appeal, compliance with Article 53(a) EPC was accepted on the basis that there was no absolute bar to the patentability of plants under the EPC and that in the decision T 356/93 (OJ EPO 1995, 545) also relating to herbicide tolerant plants, it had been concluded that Article 53(a) EPC did not constitute such a prohibition. No evidence was brought forward on appeal which would require this finding by the opposition division to be re-considered. It is, thus, concluded for the same reasons that the subject-matter of claim 24 and dependent claims thereof is not excluded from patentability.

Article 53(b) EPC; claim 24 and dependent claims thereof

8. The Board understands Appellant II's arguments with regard to the patentability of plants to be both at the legal and at the technical levels. In its view, Rule 23c(b) EPC which entered into force on 1 September 1999: *Biotechnological inventions shall also be patentable if they concern: ... (b) plants or animals if the technical feasibility of the invention is not confined to a particular plant or animal variety;..."* was a change of such significance that it should have been made in the EPC and not in the Implementing Regulations. Furthermore, in its view, the claimed subject-matter clearly related to a great number of "essentially derived" plant varieties which were present in the claim "in disguise" under the simple

wording "plants", and, therefore, the claim was barred from patentability.

9. The board observes that such arguments have often been raised in other proceedings relating to similar subject-matter and/or circumstances. In T 315/03 of 6 July 2004, see Section 5, in particular point 5.8, to be published in OJ EPO), it was explained how the decision to legislate in the articles or in the implementing regulations of the EPC was entirely a matter for the legislator and that, as long as the board sees no conflict between a Rule and an Article (which is the case here), it has no power to prevent the operation of correctly enacted legislation. In T 475/01 (supra), where the issue was, like here, the patentability of a claim to plants having acquired tolerance to a herbicide by virtue of being transformed (a claim to plants comprising essentially derived plant varieties), the board made it abundantly clear that such a claim was not excluded from patentability under Article 53(b) EPC together with Rule 23c(b) EPC for the reasons already explained in the Enlarged Board decision G 1/98 (Section 4 of the decision, see supra). In doing so, it confirmed the earlier decisions T 1054/96 of 6 December 2000 and T 149/98 of 15 January 2003.

10. Rather than repeat once more the same reasons in answer to the same arguments, the board finds it expedient to refer to these earlier decisions as they reflect its finding on the patentability under Article 53(b) EPC of the present plant claims. Thus, it is concluded that claim 24 and dependent claims thereof are not barred from patentability under this provision of the law.

11. Appellant II requested that three questions be sent to the Enlarged Board of Appeal (see point X, supra). However, the Enlarged Board of Appeal decision, G 1 /98 (supra) already provided an answer to these three questions. In particular, the board refers to point 5.3 of that decision: *"Whether a plant variety is the result of traditional breeding techniques, or whether genetic engineering was used to obtain a distinct plant grouping, does not matter for the criteria of distinctness, homogeneity and stability ...* - implying that an essentially derived plant variety is a plant variety for the present purpose - together with point 3.10: *"It is not sufficient for the exclusion of Article 53(b) EPC to apply that one or more plant varieties are embraced or may be embraced by the claims".* There is, thus, no need for a referral to the Enlarged Board of Appeal.

Article 54 EPC
Novelty of the subject-matter of claims 1 and 4 over the teachings of document (2)

12. Document (2) is concerned with finding out the structural organisation of the B.subtilis genome downstream of the trp operon in an attempt to determine whether, as earlier state of the art suggests, a *his* gene might be present in this region. The nucleotide sequence of approximately 3 Kb of DNA distal to the operon is determined and three open-reading frames (ORF) are identified. When the sequences of the corresponding three proteins are deduced on the basis of the genetic code and compared with the sequences of other known proteins, it is found that, while the first ORF is that

of hisA, the third one encodes what appears to be the B.subtilis equivalent to the S.typhimurium EPSPS protein. However, no experiments are carried out in respect of the gene (ORF3,aroE) hypothesized to encode EPSPS. Appellant III argued that document (2) was novelty destroying to the subject-matter of claims 1 and 4 because it was an **inherent** feature of the isolated 3Kb DNA fragment that it encoded an enzyme with the claimed properties.

13. If a decision of lack of novelty is to be reached on the basis of inherency then it is necessary that inherency be proved. An inherent feature of a DNA molecule is its sequence. This sequence is "reflected" in the sequence of the protein it encodes which is, in turn, responsible for the biological properties of the protein. While the reality of this chain of events is unquestionable, it leads to the paradox that the inherent property of a DNA molecule is deducible from that of another molecule (the protein) and, thus, it leads to the concept of "indirect proof of inherency". This concept is, prima facie, at odds with the generally accepted principles for the evaluation of novelty which require that the relevant document of the state of the art provides a clear, unambiguous (albeit sometimes implicit) and enabling disclosure of the claimed subject-matter (see for example, T 81/87 OJ EPO 1990, 250 and T 301/87, OJ EPO 1990, 335). In the Board's judgment, while the uniqueness of the DNA molecule may justify that "indirect proof of inherency" be taken into account while assessing novelty, it remains nonetheless that the evidence produced in this respect in the relevant document of the state of the

art must provide a clear, unambiguous and enabling lead to the inherent properties.

14. Document (2) does not disclose the expression of any of the proteins encoded by the DNA it describes. It suggests the possibility that the ORF3-encoded protein has EPSPS activity on the basis of theoretical considerations but does not show that it is the case. Furthermore, it is wholly silent as to how to obtain said protein. It, thus, fails to provide an adequate teaching which would permit testing the "indirect proof of inherency" which lies in the properties of the protein per se (enzymatic activity, immunological and biochemical properties). Accordingly, document (2) is not even an implicitly enabling disclosure of a DNA having the property to encode an enzyme as defined in the claims.

15. Appellant III put forward post-published evidence (document (14)) that the chemical properties of the ORF3-encoded protein fell within the ranges defined in claim 1. It also filed experimental evidence to show that the protein had the immunological properties defined in claims 1 and 4 (documents (15) and (19)). However, as document (2) on its own neither points towards, nor enables any of these data, it is concluded that they do not represent the "inherent" teaching of the prior art and that, therefore, it becomes irrelevant whether or not they show that the DNA of document (2) has the inherent property of encoding a protein as is characterised in the claim.

16. In this framework, it is of interest to recall the case T 277/95 of 16 April 1999 which dealt with the issue of inherency in relation to priority rights. The then claimed subject-matter was a method for producing erythropoietin ("Epo") with a given pattern of glycosylation. What was disclosed in the priority document was a deposited cell line capable of producing Epo, the glycosylation pattern of this product being left undetermined. It was argued in that case that, as the glycosylation pattern of the Epo resulting from the claimed method would be an inherent feature of the Epo produced by the deposited cell line, priority could be acknowledged. The board held that the skilled person could derive neither the specific features of the method then claimed nor the specific Epo glycosylation pattern from a direct analysis of the deposited cell line. It concluded that priority could not be acknowledged and emphasized that inherency had "*to be established on the basis of certainty, not probability or possibility*".

17. For the reasons given above, it is concluded that the teachings of document (2) are not detrimental to the subject-matter of claims 1 and 4.

Article 54 EPC
Novelty of the subject-matter of claims 1, 4 and 7 over the teachings of document (3)

18. Document (3), example 8 discloses DNA fragments carrying a mutated derivative of the aroA gene of E.coli encoding an EPSPS enzyme with altered characteristics. On page 17, lines 3 to 5, a recombinant construct (pMON8078) is also disclosed

wherein the aroA altered gene is inserted between a promoter which is active in plants and a polyadenylation signal. Appellant III argues that these DNA fragments and recombinant construct respectively fall within the scope of claims 1, 4 and 7.

19. Claim 1 is directed to an isolated DNA sequence encoding a Class II EPSPS enzyme. Such an enzyme is defined on page 3 lines 6 to 9 as readily distinguishable "*from Class I EPSPS's by their inability to react with polyclonal antibodies prepared from Class I EPSPS enzymes under conditions where other Class I EPSPS enzymes would readily react with the Class I antibodies*". Furthermore, it is mentioned on page 6, Table II that E.coli EPSPS is a Class I enzyme. As this enzyme will, by definition, react with antibodies raised against itself ie with anti-Class I EPSPS antibodies, it does not fall within the definition of a Class II enzyme. If only for this reason, the DNA fragment encoding the E.coli EPSPS enzyme disclosed in document (3) does not destroy the novelty of the subject-matter of claim 1. The same conclusion is reached in relation to the subject-matter of claim 7 which is directed to a construct which encodes a Class II EPSPS enzyme.

20. The class of the enzyme encoded by the DNA of claim 4 is not specified, it only being mentioned that the enzyme is able to bind to antibodies raised against a Class II EPSPS enzyme selected from the group of the enzymes of SEQ ID NO:3 and SEQ ID NO:5. As these antibodies were identified for the first time in the patent in suit, they do not form part of the state of the art. This implies that document (3) does not

provide an enabling disclosure of an isolated DNA sequence encoding an enzyme having the claimed properties (see also point 13, supra). Accordingly, document (3) does not destroy the novelty of the subject-matter of claim 4.

21. The claim request fulfils the requirements of Article 54 EPC.

Article 56 EPC; inventive step of the subject-matter of claim 1

22. Documents (3), (1) and (2) were cited by Appellant III as being possible starting points for evaluating inventive step. In accordance with the case law (eg T 606/89 of 18 September 1990), the closest prior art for assessing inventive step is normally a prior art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common. Document (3) describes DNA fragments encoding EPSPS enzymes for the purpose of transforming plants to make them less sensitive to glyphosate ie herbicide resistant. Document (1) is a research study on the glyphosate sensitivity of the B.subtilis EPSPS enzyme in vitro, which mentions in its introduction the interest of identifying EPSPS genes keeping in mind the prospect of genetically engineering the marker into plants. Document (2) (see point 14, supra) is not concerned with EPSPS activity. Document (3) is, thus, the closest prior art.

23. In document (3), it is explained that EPSPS plays an essential role within the plant cell, in the

biosynthesis of three essential amino acids (tyrosine, phenylalanine and tryptophan) and that the herbicide glyphosate acts by blocking this pathway with the consequence that the plant dies. The invention then described is to transform agriculturally useful plants with an EPSPS gene in such a manner that EPSPS is preferentially expressed in the chloroplasts with the effect that the plant becomes less sensitive to glyphosate and its corollary that glyphosate may be used to eradicate weeds. The EPSPS genes used in document (3) are essentially of plant origin. Yet, it is also envisaged to use a mutated E.coli EPSPS gene as the corresponding enzyme exhibits a lower sensitivity to glyphosate than the wild-type enzyme (Example 8). However, the E.coli altered enzyme also exhibits a lower affinity for its own substrate (cf. document (6), passage bridging pages 42 and 43) which, of course, somewhat reduces its usefulness.

24. Starting from the closest prior art, the problem to be solved may be defined as providing an alternative tool for engineering glyphosate tolerance into plants.

25. The solution is a DNA fragment encoding an EPSPS enzyme which retains a high affinity for its natural substrate (low K_m) while having a lower affinity for glyphosate (high K_i; high K_i/K_m). One such DNA fragment is provided which encodes the B.subtilis EPSPS enzyme.

26. B.subtilis EPSPS was already known from the prior art: document (1) presents an in vitro study of its properties. It shows that the enzyme is activated by monovalent cations and that the state of activation strongly varies depending on the ion used (NH_4^+ being

the most efficient followed by K^+) as well as on its concentration. As for glyphosate sensitivity, it is said to be variable depending on the state of activation of the enzyme and, for a given state of activation, to be dependent on the nature of the inducing agent (it is lower with K^+ than with NH_4^+). In fact, document (1) warns against false interpretations of data, which may arise from not taking into account that the behaviour of the enzyme is the result of an interplay between these different parameters: *"Before assigning relative sensitivities to EPSPS synthase enzymes to PMG-mediated inhibition, an evaluation of possible modulation of enzyme activity by monovalent cations seems essential."*

27. In the board's judgment, the skilled person wanting to solve the above mentioned problem would not turn to an enzyme, the properties of which are strongly influenced by the conditions it is put into, all the more so that these conditions are not controllable in vivo, ie in the circumstances where it is intended to put the enzyme to use.

28. Appellant III pointed out to a number of reasons why the claimed DNA construct was, in its opinion, obvious: that the K_m and K_i/K_m values of the B.subtilis enzyme were the most favourable of all known EPSPS enzymes (document (26)), that the ion which was the most frequent in plants (K^+) was precisely the one for which the difference between the affinities of EPSPS for its substrate and for glyphosate was optimal and, finally, that the cloning of the B.subtilis EPSPS gene was obvious.

29. As already mentioned above, it is, in fact, not possible to ensure that the EPSPS enzyme will have the most advantageous K_m and K_i/K_m ratio in vivo and, besides, document (1) shows that the "advantageous" values are only obtained at the highest concentration of NH_4^+ which was tested (Tables II and III). In the same manner, nothing can be done to control the K^+ concentration in the plants. As for the cloning, it may indeed be obvious it to achieve taking into account documents (1), (2) and the common general knowledge at the effective date of the patent in suit. Yet, the cloning need not be taken into account for inventive step to be acknowledged (see point 27, supra)

30. For the reasons given in point 22 to 27, supra, it is concluded that the requirements of Article 56 EPC are fulfilled.

Sufficiency of disclosure

31. The patent in suit describes the isolation of three genes falling within the scope of the claim (pages 7 to 12). Methods for isolating further such genes are also disclosed (page 13). It is shown that the expression of the claimed DNA constructs in plants results in glyphosate tolerance. Sufficiency of disclosure is, thus, achieved in relation to the claimed subject-matter.

32. Appellant III argued that it would be too much burden for the skilled person to establish the conditions in which to measure K_m and K_i. The Board notices that the file contains numerous documents including document (1) but also all of the documents referred to in document (26) where K_m and K_i have been measured, seemingly as a matter of routine. In the absence of any evidence to the contrary, it is accepted that this is also true in the present case. In any case, the argument appears to be more an argument of lack of support - an argument under Article 84 EPC which is not a ground of opposition -, than under Article 83 EPC. Its relevance is, thus doubtful.

33. For these reasons, it is concluded that the request filed at oral proceedings on 6 April 2005 fulfils the requirements for patentability.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The request to refer questions to the Enlarged Board of Appeal is refused.

3. The case is remitted to the first instance with the order to maintain the patent on the basis of the main request filed during the oral proceedings and the description and figures as granted.

The Registrar: The Chairman:

A. Wolinski L. Galligani