

## **Decision of Technical Board of Appeal 3.3.8 dated 14 October 2004**

### **T 890/02 - 3.3.8**

(Translation)

Composition of the board:

Chairman: F. L. Davison-Brunel

Members: P. Julià

S. C. Perryman

**Applicant: Bayer CropScience S.A.**

**Headword: Chimeric gene/Bayer**

**Article: 54, 56, 83, 112(1) EPC**

**Keyword: "Main request - novelty (no)" - "Auxiliary request - novelty (yes) - inventive step (yes) - sufficient disclosure (yes)" - "Question referred to the Enlarged Board of Appeal - no" - "Substantial procedural violation - (no)"**

*Headnote*

*Whilst not being stricto sensu encyclopaedias or handbooks, databases (a) which are known to the skilled person as an adequate source for obtaining the required information, (b) from which this information may be retrieved without undue burden and (c) which provide it in a straightforward and unambiguous manner without any need for supplementary searches represent the common general knowledge of the skilled person as defined in the case law (see reasons, point 9), and can be taken into account as such in deciding whether the teaching of a document which prima facie destroys novelty is sufficient to be reproducible.*

#### **Summary of facts and submissions**

I. European patent application No. 96 920 888.3, with international publication No. WO 96/38567 and entitled "DNA sequence of a gene of hydroxy-phenyl pyruvate dioxygenase and production of plants containing a gene of hydroxy-phenyl pyruvate dioxygenase, which plants are tolerant to certain herbicides" was refused by the examining division under Article 97(1) EPC.

II. The main request filed on 12 October 1999, with amended claim 1 filed on 28 September 2001, was considered not to be novel (Article 54 EPC). A first auxiliary request filed on 10 October 2001 at the oral proceedings before the examining division was found not to fulfil the requirements of Article 82 EPC and Rule 30 EPC. The applicant did not approve the text on which the examining division intended to grant a patent, which was based on a second auxiliary request also filed on 10 October 2001 at the oral proceedings.

III. An appeal against the decision of the examining division was lodged by the applicant (appellant). The main request refused by the examining division and the second auxiliary request before the examining division were maintained in the appeal proceedings as main and auxiliary request respectively.

IV. Claim 1 of the main request read as follows:

"1. A chimeric gene comprising, in the direction of transcription:

- at least one promoter regulatory sequence from a gene naturally expressed in plants,
- a heterologous coding sequence,
- at least one regulatory termination or polyadenylation sequence,

characterised in that the heterologous coding sequence is the coding sequence of a gene expressing a hydroxyphenylpyruvate dioxygenase (HPPD)."

V. Claim 1 of the auxiliary request read as follows:

"1. A chimeric gene comprising, in the direction of transcription:

- at least one promoter regulatory sequence from a gene naturally expressed in plants,
- a sequence for a transit peptide of a plant gene coding for an enzyme located in a plastid, between the promoter regulatory sequence and the coding sequence,
- a heterologous coding sequence,
- at least one regulatory termination or polyadenylation sequence,

characterised in that the heterologous coding sequence is the coding sequence of a gene expressing a hydroxyphenylpyruvate dioxygenase (HPPD)."

Claims 2 to 15 related to further characteristics of the chimeric gene of claim 1. Claims 16 and 17 were directed, respectively, to a vector for transformation of plants and to plant cells comprising a chimeric gene of one of claims 1 to 15. Claims 18 to 21 were concerned with plants regenerated from the cells of claim 17 or having in their genomes a chimeric gene of one of claims 1 to 15. Claims 22 to 24 related to methods for transformation of plants to render them tolerant to inhibitors of the HPPD enzyme, and claim 25 related to a method for transformation of plants using the chimeric gene of one of claims 1 to 15 as selective marker. Claims 26 to 30 were concerned with methods of herbicide treatment of transformed plants comprising cells of claim 17.

VI. In a communication under Article 11(1) of the Rules of Procedure of the Boards of Appeal (RPBA), the Board informed the appellant of its preliminary, non-binding opinion.

VII. With a letter dated 6 September 2004, the appellant submitted further observations in reply to the Board's communication and filed complete and clean copies of the main and auxiliary requests.

VIII. Oral proceedings took place on 14 October 2004.

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

D4: C.D. Denoya et al., J. Bacteriol., September 1994, Vol. 176(17), pages 5312 to 5319;

D10: EP 0 652 286, published on 10 May 1995;

D12: A. Schulz et al., FEBS Letters, March 1993, Vol. 318(2), pages 162 to 166;

D13: J. Secor, Plant Physiol., 1994, Vol. 106, pages 1429 to 1433;

D18: G.M. Kishore and D.M. Shah, Ann Rev. Biochem., 1988, Vol. 57, pages 627 to 663;

D29: S. Lindstedt et al., *Biochemistry*, 1977, Vol. 16(15), pages 3369 to 3377.

X. The reasons given by the examining division for refusing the main request can be summarised as follows:

Document D10 disclosed chimeric genes comprising regulatory sequences (promoters) of maize alpha tubulin genes and heterologous coding sequences. A gene coding for the HPPD enzyme (identified as HPPO) was explicitly described as a heterologous gene. An HPPD gene had already been cloned (document D4) before the publication date of document D10. Since an HPPD gene was already known at the priority date of the application, document D10 provided enough information to allow the skilled person to achieve a chimeric construct with a heterologous sequence encoding the HPPD enzyme, as well as the above-mentioned regulatory sequences. Document D10 thus disclosed the subject-matter of claim 1 of the main request.

XI. The appellant's arguments in writing and during oral proceedings, in so far as they are relevant to the present decision, may be summarised as follows:

*Main request*

*Article 54 EPC*

*The relevant prior art and the definition of "common general knowledge of the skilled person" in the case law*

Document D18, a review of herbicide tolerant plants, showed that at the priority date the strategies known to the skilled person for successfully achieving herbicide tolerant plants were the overexpression of mutated targeted enzymes or the expression of detoxification enzymes. None of these strategies was followed in the present application, wherein the expressed HPPD enzymes were not mutated. In fact, documents on file referring to the HPPD enzyme and genes thereof belonged to technical fields that were remote from that of the present application and with no relation to herbicide resistant plants. As for document D10 which the examining division considered as destroying novelty, this merely mentioned the enzyme HPPD without giving any information on it. Because of the distance between the technical fields relating respectively to HPPD and herbicides, the reference to HPPD was ambiguous and not credible, unlike in the case of the reference to the EPSP synthase enzyme or the acetolactate synthase which had been known for a long time to be involved in herbicide resistance (cf. document D18).

Moreover, these references did not allow the skilled person to obtain a chimeric construct comprising the gene coding for the enzyme HPPD because the nucleotide sequence of such a gene was not described. In order to overcome this failure the skilled person had to combine document D10 with other prior art disclosing this nucleotide sequence, such as document D4. However, according to the established case law, it was possible to combine two documents for the purpose of novelty only in exceptional cases, such as for example, where a clear and unambiguous cross-reference existed in each to the other.

In reasoning concerning novelty it was also possible to take into account the common general knowledge of the person skilled in the art. This common general knowledge was, however, defined in the established case law as being what one could find in handbooks and encyclopaedias and such knowledge was clearly distinct from the whole state of the art. Thus, accessible information which was part of the state of the art was not necessarily part of common general knowledge. It only met the definition of "common general knowledge and was taken up into general or specialised handbooks or into encyclopaedias after being accepted, integrated and shared by the scientific community. The skilled person was not expected to know anything more than this common general knowledge.

*The "common general knowledge" in the present case*

The EMBL/GenBank databases were not common general knowledge in the sense defined in the case law. They represented the complete state of the art for nucleotide sequences (genes) and proteins and they were comparable to the Chemical Abstracts database. A complete search in these databases for overcoming an insufficiency in a document of the prior art represented a search in the complete state of the art. This type of search was very remote from the normal definition of common general knowledge.

The EMBL/GenBank databases did not correspond to the definition of encyclopaedia or handbook as accepted in the case law. The fact that the data therein were easily accessible using a computer with appropriate software did not make them comparable to the information found in a handbook or encyclopaedia. The information in an encyclopaedia was not only exhaustive; it was also elaborated and reasoned, providing a critical synthesis of all the knowledge on a certain subject. In other words, an encyclopaedia was a methodical or alphabetic exposition intended to summarise the complete knowledge on a certain subject so as to make it available for educational purposes. In fact, it was this elaboration and reasoned character of the stored information that differentiated the data contained in a database from an encyclopaedia.

Contrary to the information in an encyclopaedia, which was well-known, widely accepted and generally shared by the whole scientific community, the data present in the EMBL/GenBank databases were at first submitted to these databases as unverified, raw or crude information prone to contain numerous and major errors; the data was thus rendered accessible to the scientific community. It was only afterwards that this information was adopted and integrated into the common general knowledge of the scientific community.

Knowing where desired information could be found (for example, in an encyclopaedia or handbook representing the common general knowledge) was a very different thing from knowing where one could look for this information (EMBL/GenBank representing the whole state of the art). Whereas in the first case the skilled person already knew that the desired information existed, this was not true in the latter case, which thus could not be treated as a case of referring to common general knowledge.

Therefore, in so far as a nucleotide sequence of a gene encoding an HPPD enzyme was not part of the common general knowledge of the skilled person and document D10 did not refer to any document disclosing an HPPD nucleotide sequence, the claimed subject-matter - a chimeric gene comprising an HPPD sequence - was novel (Article 54 EPC), any assessment of the combination of document D10 with other prior art being possible only under Article 56 EPC.

However, in the event of the Board's arriving at a different conclusion with regard to the character of the EMBL/GenBank databases and/or the definition of "common general knowledge" as established in the case law, relevant questions of law were put forward for referral to the Enlarged Board of Appeal (cf. section XII infra).

#### *Auxiliary request*

##### *Articles 54 and 56 EPC*

Document D10 did not anticipate a chimeric gene comprising the specific combination of an HPPD gene and a sequence encoding a plastid transit peptide. The references in this document to the HPPD enzyme were ambiguous and not credible. Moreover, whereas at the priority date, the sub-cellular plastid localisation of the exemplified EPSPS was already known, the distribution of the HPPD enzyme was unknown. Therefore, there was no reason to target the HPPD enzyme into plastids using a transit peptide sequence. The subject-matter of claim 1 was also inventive.

##### *Article 83 EPC*

Evidence was provided by the appellant during the appeal proceedings showing that herbicide resistance was achieved with a chimeric construct comprising a sequence encoding an HPPD enzyme derived from a plant (*Arabidopsis*). Further, the HPPD enzyme derived from *Pseudomonas* (exemplified in the application) had kinetic properties similar to those of other HPPD enzymes derived from mammals and plants. Therefore, genes encoding these other (plant) enzymes were equally suited as part of a chimeric construct such as claimed. The claimed subject-matter was thus reproducible over its whole breadth.

*Reimbursement of the appeal fee*

During the examination proceedings, the examining division refused to consider the question of what represented the common general knowledge of the person skilled in the art. Contrary to the established case law and the explicit indications set out in the Guidelines for Examination, the examining division in denying novelty referred only to ambiguous references in document D10 or to their combination, with a document belonging to a completely unrelated technical field to the one of the application. Its decision went against the normal standard of proof and the established practice that it was not possible when examining novelty to combine several documents. Moreover, it failed to adopt the accepted practice of deciding in the appellant's favour in a case of doubt. Thus, the examining division committed a substantial procedural violation and the reimbursement of the appeal fee was justified.

XII. The appellant's question to the Enlarged Board of Appeal read as follows:

"Question to the Enlarged Board of Appeal:

Decision T 206/83 states that databases such as Chemical Abstracts cannot be representative of the knowledge of the skilled person, as they represent the whole state of the art.

Thus to require that the skilled person carry out a search in Chemical Abstracts to remedy insufficiencies in the description in a patent application would be unacceptable, as this would effectively require that the skilled person have, as common general knowledge, an exhaustive knowledge of the state of the art.

In T 890/02, Board of Appeal 3.3.8 concludes that the main request lacks novelty on the ground that document D10 described the claimed subject-matter by reference to another document D4, the contents of which would be known to the skilled person.

The reasoning in the decision is based on the fact that the contents of D4 were stored in the GenBank database, which is representative of the common general knowledge of the skilled person.

The questions posed are as follows:

1. Are databases of the GenBank type different from Chemical Abstracts, and if so, in what way?
2. Are these differences sufficient to establish that, in contrast to Chemical Abstracts, databases of the GenBank type do not represent the whole state of the art?
3. Are these differences sufficient to establish that, in the field of biotechnology, databases of the GenBank type are representative of the common general knowledge of the skilled person?

A reply in the affirmative to the last question could lead to different legal treatment depending on the technical field of the invention.

There would be differences in the interpretation of the EPC, depending on whether the invention concerned was in the field of chemistry (Chemical Abstracts) or biotechnology (GenBank). This difference in the application of the law, according to the technical field concerned, calls for a decision of the Enlarged Board of Appeal pursuant to Article 112(1) EPC."

XIII. The appellant requested that the decision under appeal be set aside, and the grant of a patent on the basis of the main request of 6 September 2004; in the alternative, the referral of a question to the Enlarged Board of Appeal; auxiliarily, the grant of a patent on the basis of the auxiliary request filed on 6 September 2004; and, in all events, the reimbursement of the appeal fee by reason of a substantial procedural violation.

**Reasons for the decision***Main request**Article 54 EPC**The prior art document D10*

1. Document D10 discloses the upstream, or 5' regulatory regions of maize alpha tubulin genes (Tub $\alpha$ 1, SEQ ID No.: 1; Tub $\alpha$ 2, SEQ ID No.: 2 and Tub $\alpha$ 3, SEQ ID No.: 3), as well as fragments thereof, capable of controlling specific gene expression in plant pollen, roots, meristems or immature plant embryos (cf. page 3, line 14 to page 4, line 6). The document further refers to chimeric plant genes comprising functional fragments of these regulatory regions (promoters) operably linked to heterologous genes encoding polypeptides which provide advantageous agronomic properties, in particular "*resistance to insects, nematodes, fungi and preferably to herbicides*" (cf. page 4, lines 47 to 56 and page 5, lines 30 to 37). In this context, reference is made to "polypeptides conferring resistance to glyphosate and to the related inhibitors of the enzymes 5-enolpyruvylshikimic acid 3-phosphate synthase (EPSPS), sulphonylureas, imidazolinones and the inhibitors of acetoxyhydroxy acid synthetase (AHAS), and 4-hydroxyphenyl pyruvate dioxygenase (HPPD)" (identified by the term HPPD in the present application) (cf. page 5, lines 37 to 40). For efficient expression of these heterologous genes, polyadenylation sequences are said to be required (cf. page 5, lines 52 to 53). Methods for producing herbicide resistant plants comprising the transformation of plant cells with a vector containing these chimeric genes are also disclosed which indicates, as preferred heterologous sequences, genes coding for "*the EPSP, the acetolactase synthase or the 4 hydroxyphenyl pyruvate dioxygenase*" (cf. page 7, lines 40 to 43). Vectors comprising the *aroA* gene - coding for the EPSPS - are further exemplified (pRPA-RD-65 and pRPA-RD-88) (cf. page 7, lines 44 to 47) and used to produce herbicide resistant tobacco plants (cf. page 15, example 4). There is, however, no actual example of chimeric genes with heterologous genes coding for the other two preferred enzymes - ALS and HPPD - and there is no information concerning the nucleotide sequence of these genes nor a bibliographic reference to where the skilled person could retrieve this information. Thus, although disclosing chimeric genes comprising the same technical features as the ones of claim 1 of the main request, prima facie document D10 does not allow the chimeric gene to be reproduced. Nevertheless, it would destroy novelty if at the priority date of the present application the nucleotide sequence of the HPPD gene was part of the common general knowledge of the skilled person.

*Definition of "common general knowledge" in the case law*

2. The common general knowledge of the person skilled in the art has been defined by the Boards of Appeal as being normally represented by the content of encyclopaedias, handbooks and dictionaries on the subject in question (cf. in particular T 766/91 of 29 September 1993, point 8.2, T 206/83 OJ EPO, 1987, 5, point 5 and T 234/93 of 15 May 1997, point 4). In several cases, however, and by way of exception, patent specifications and scientific publications have also been considered as forming part of the common general knowledge (cf. "Case Law of the Boards of Appeal of the European Patent Office", 4<sup>th</sup> Edition, 2001, II.A.2(a), page 145). In particular, special considerations prevail when a field of research is so new that technical knowledge is not yet available from textbooks (cf. T 51/87 OJ EPO, 1991, 177, point 9 and T 772/89 of 18 October 1991, point 3.3).

3. In all these cases, the Boards have acknowledged that the skilled person does not necessarily have knowledge of the whole technology, and they have identified three important aspects – common to all cases - for correctly assessing the common general knowledge of the person skilled in the art.

(a) Firstly, the skills of such a person include not only basic general knowledge of a particular field of technology, but also the ability to look up such knowledge in encyclopaedias and handbooks as well as, in exceptional cases, in a series of relevant studies (cf. T 676/94 of 6 February 1996, point 10), or in a scientific publication or a patent specification (cf. T 51/87 OJ EPO 1991, 177, point 9 and T 772/89 of 18 October 1991, point 3.3).

(b) Secondly, it cannot be expected that, in order to identify this common general knowledge, the skilled person will carry out a comprehensive search of the literature covering virtually the whole state of the art. No undue effort in the way of such a search can be required from the person skilled in the art (cf. T 171/84 OJ EPO 1986, 95, point 12, T 206/83 supra, point 4 and T 676/94 supra, point 10).

(c) Thirdly, the information found must be unambiguous and usable in a direct and straightforward manner without doubts or further research work (cf. T 206/83 supra, point 5).

These three aspects actually correspond to the classical steps of (a) picking an **adequate** reference book (handbook, encyclopaedia, etc.) from the bookshelf in the library, (b) identifying the **appropriate** section(s) without this requiring any significant effort and (c) getting the **correct** information or unambiguous data that can be used without further research work.

4. It follows from the foregoing that for each case the common general knowledge of the skilled person working in a particular technical field must be decided on its own merits, based on the facts and evidence of that particular case.

*The "common general knowledge" in the present case*

5. As the application relates to the expression of heterologous genes, in particular, genes encoding enzymes for the production of herbicide resistant plants, the skilled person is understood as one working in the field of plant herbicides with a general knowledge of current molecular biology as well as basic enzymology.

6. There are no doubts, and it has not been contested, that at the priority date of the present application, the skilled person wanting to find the nucleotide sequence of the HPPD gene mentioned in document D10 would have looked for and found this information in either of two different databases, namely the ENZYME and the EMBL Nucleotide Sequence databases. At the priority date of the application, both databases were well-known and accessible – distribution by mag tape, CD ROM or network (Intranet) - to any person working in the field of enzymology and molecular biology.

7. The EMBL Nucleotide Sequence database is a very comprehensive and large database which is accessible, in particular, from the EMBL file server (set up in 1988). This server also provided a large collection of free molecular biology software, including a software package (Wisconsin GCG Package) for homology and keyword search. For each nucleotide sequence, the information provided comprises, in particular, an accession number (AC), keyword (KW) and descriptor (DE) fields as well as the nucleotide sequence (SQ) of the searched for DNA sequence. Thus, the EMBL database may be seen as a comprehensive **handbook** disclosing the structure of different biological products (gene or fragments thereof), just as a handbook of chemistry discloses the chemical formulae of different chemical products.

8. The ENZYME database relates to enzymes and is available on the ExPASy World Wide Web (WWW) molecular biology server. For each enzyme, the entries in the database comprise the Enzyme Commission (EC) number (ID), the official name (DE), alternative names (AN), the reaction catalysed (CA) and the cofactors (CF). As from 1994, the server had hypertext links to the SWISS PROT database (DR) and from there to the EMBL database. Thus, from the official name of an enzyme (4-hydroxyphenyl pyruvate dioxygenase, DE) or the corresponding EC number (EC 1.13.11.27, ID), the skilled person could retrieve the complete information on properties as well as the amino acid sequences (SWISS PROT) and the nucleotide sequences of the corresponding genes (EMBL) derived from different organisms. In this sense, the information closely corresponds to the definition of **encyclopaedia** referred to by the appellant as a "*document de synthèse présenté dans l'ordre alphabétique ou systématique et qui fait le point des connaissances acquises sur tous les sujets ou sur un groupe de sujets connexes*" (<http://www.granddictionnaire.com>). It also closely corresponds to the definition of an encyclopaedia in the English language; "*a work that contains information on all branches of knowledge or treats comprehensively a particular branch of knowledge usually in articles arranged alphabetically often by subject*" (Merriam Webster OnLine).

9. Thus, whilst not being stricto sensu encyclopaedias or handbooks, the ENZYME and the EMBL databases nonetheless answer to the definition of, respectively, an encyclopaedia or a handbook. Furthermore, they fulfil the three criteria set out in the case law when defining the common general knowledge (cf. point 3 supra), namely (a) they are known by the skilled person to be an appropriate source for obtaining the desired information, (b) looking for this information requires no undue effort, since no search strategy is needed but only the EC number or the enzyme name (in the present case the enzyme name is known from document D10 itself), and (c) the information retrieved (for example, the nucleotide sequence) does not need any further research work, ie it is unambiguous and straightforward. For these reasons, in the Board's judgment, the information in these databases ENZYME and EMBL meets the definition of common general knowledge given in the case law.

10. Several arguments were put forward by the appellant to challenge the conclusion that the ENZYME and EMBL databases could be assimilated to an encyclopaedia or a handbook. They will be discussed in detail hereafter.

11. First of all, a search in the EMBL database was equated to a search in the Chemical Abstracts database, which, as acknowledged in the case law, embraces virtually the complete prior art and represents much more than what the skilled person is supposed to have as common general knowledge (cf. T 206/83, supra, point 6) (cf. section XII supra).

12. It is, however, evident from the content of the EMBL database (cf. point 7 supra), that this database is different from the Chemical Abstracts database or other bibliographic databases such as Biological Abstracts, EMBASE, etc. These bibliographic databases aim to summarise the complete disclosure of a scientific publication, conference, etc. by providing an abstract and several searchable fields. Owing to the amount and the quality of the information they contain, finding the desired data usually requires a sophisticated search strategy. It is not generally sufficient to query a bibliographic database with an enzyme name or an EC number alone, as the number of results obtained would be too great to look at. On the contrary it is necessary to restrict the search to improve the relevance of its results. Moreover, the kind of information retrieved – the content of the abstract – cannot be anticipated before the search has actually been made and it is usually, by its nature, incomplete or insufficient so as to require the consultation of the original publication. Thus, contrary to the EMBL database, in which a straight query (enzyme name or EC number) usually produces a reasonable number of results with clear information (nucleotide sequences), in the bibliographic databases neither the required search strategy nor the results obtained are clear and straightforward. Finally, the bibliographic databases are of no use for a straight comparison of different biological products, which the EMBL database readily allows (homology comparison), precisely because of its property of being conceived as a handbook.

13. Secondly, it was argued that the information present in the ENZYME and EMBL databases is introduced into these databases as raw information, whereas the information taken up in an encyclopaedia has been worked up and is shared by the scientific community; ie it appears in these works of reference because it is already part of the common knowledge of the skilled person (cf. T 766/91, supra, point 8.2) (cf. section XI supra).

14. The Board agrees that the information taken up in an encyclopaedia has been worked up on the basis of knowledge derived from a variety of scientific documents. But this is also the case with the information found in the ENZYME database. For any given enzyme, the information on, for example, the enzymatic reaction or the amino acid sequence will have been “harvested” from different scientific papers. Similarly, the gene sequences of corresponding genes in different organisms will have been established in the course of time by different scientific groups. The database is thus conceptually identical to an encyclopaedia.

15. The EMBL database is, as mentioned above, rather to be considered as a handbook than an encyclopaedia. The information it contains is as raw as the information contained in a handbook, in so far as, in both cases it does not comprise comprehensive data relating to everything which is known on a given compound; ie in both cases, the information provided is not worked up starting from the common general knowledge of the scientific community at large.

16. It is true, however, that whereas for a standard handbook or encyclopaedia the time elapsing between successive editions might be considerable, the time elapsing between successive database releases is usually much shorter. Nevertheless, as was accepted at the oral proceedings, this fact only results from the type of support used (Internet) and it has no bearing on the nature of the information itself. Moreover, it is this very support that allows a much wider and less expensive diffusion of the information which thus is more easily shared by and accessible to the scientific community.

17. Thirdly, it has been argued that knowing where to find the desired information was a different thing from knowing where to search for this information. In the former case the skilled person knows that the relevant information already exists before actually looking for it, whereas in the latter case it is not known whether this information exists at all (cf section XI supra).

18. This may well be true, but it does not seem to be relevant to the question of whether or not a piece of information is common general knowledge. The existence of a piece of information is an intrinsic property of this information, irrespective of when it might be looked for and/or found. Obviously, if, for example, the sequence of the HPPD gene is known to exist, it will be found in the encyclopaedia/handbook as well as in the ENZYME/EMBL databases, since



the purpose of all these is to put this information at the disposal of the public. And if there is doubt that it exists at all, there will be just as much, or as little, chance of finding it in any of them, depending solely on whether or not it exists. Here again, there does not seem to be a difference between databases such as ENZYME and EMBL and encyclopaedias/handbooks.

19. Moreover, in the present case, the reference to the HPPD gene in document D10 is found in connection with the known genes encoding the EPSP synthase and the acetolactase synthase (cf. page 7, lines 42 to 44). There is nothing to suggest that the HPPD gene is unknown. In the light of the facts and evidence of document D10, the skilled person has no reason to expect any particular difference in the availability of all these three genes. In fact, there are documents on file showing that HPPD sequences have been available and known to the skilled person for a long time (cf inter alia documents D12 and D13). Thus, in the present case, it is also reasonable to assume that the skilled person knew that the information referred to in document D10 already existed.

#### *Novelty of Claim 1*

20. It follows from the foregoing that document D10, which, as mentioned in point 1 *supra*, discloses chimeric genes comprising a regulatory promoter sequence derived from a gene naturally expressed in plants, a polyadenylation sequence and the HPPD gene, the structure of which is part of the common general knowledge being available from the ENZYME and EMBL databases (cf points 5 to 9 *supra*), is enabling without undue burden with regard to isolating said chimeric gene.

21. Thus document D10 destroys the novelty of the subject-matter of claim 1. The requirements of Article 54 EPC not being fulfilled, the main request is rejected.

#### *Auxiliary request*

##### *Article 54 EPC*

22. Claim 1 of this request differs from claim 1 of the main request by requiring in the chimeric gene the presence of a sequence encoding a transit peptide located between the promoter and the heterologous HPPD coding sequence, which transit peptide is derived from a plant gene encoding an enzyme located in a plastid (cf. section V *supra*). Document D10 discloses a particular optimised transit peptide in the construction of a chimeric gene comprising the EPSPS gene (cf inter alia page 4, line 23, page 7, lines 44 to 47 and page 15, example 4). However, there is no disclosure of a chimeric gene comprising the specific combination of a plant promoter, a sequence encoding the said plastid transit peptide and the HPPD gene.

23. Thus, the subject-matter of claim 1 is not anticipated by document D10. Since all other claims are directly or indirectly dependent on this subject matter, the auxiliary request fulfils the requirements of Article 54 EPC.

##### *Article 56 EPC*

24. The closest prior art for the subject matter of Claim 1 is document D10, which discloses a chimeric construct comprising in particular a promoter and a gene coding for an enzyme whose expression results in resistance to herbicides. Document D10 itself refers to the possibility of having other elements in the chimeric construct, including sequences encoding transit peptides (cf page 2, lines 49 to 53). In fact, document D10 explicitly provides a specific transit peptide of a plant gene encoding an enzyme active in a plastid, which is suitable for the expression of plant enzymes known to be of plastid sub-cellular localisation. A chimeric construction comprising the DNA coding for such a peptide in association with the gene coding for EPSP synthase (cf example 4), which is known to have a plastid sub-cellular localisation, is described.

25. Starting from this document, the technical problem to be solved can be defined as providing an alternative chimeric construct. The solution is provided in Claim 1 by the introduction of a sequence encoding a transit peptide - of a plant gene encoding an enzyme of plastid location - between the promoter and the sequence encoding the HPPD enzyme.

26. For assessing inventive step, the question is whether at the priority date of the present application the sub-cellular localisation of the enzyme HPPD was known. Thus if the sub-cellular distribution of the HPPD enzyme was known to be in plastids, then it would be obvious to apply the teachings of document D10 and isolate a chimeric construct carrying the HPPD encoding gene (corresponding to the gene encoding EPSPS) and a DNA encoding a plastid transit peptide.

27. Document D12 identifies the HPPD enzyme as a key enzyme in the biosynthesis of plastoquinones. This document refers to the possible relationship between quinone biosynthesis and phytoene desaturation, the latter being known as a complex redox reaction taking place in plant chloroplasts (plastids) (cf. page 162). However, neither document D12, nor any other document on file in the state of the art before the priority date of the application contained any information suggesting that the biosynthesis of plastoquinones (and hence implicitly HPPD) took place in the same location as the phytoene desaturation (in other words in the plastids). For this reason, the skilled person would have had no motivation to use a plastid transit peptide, such as that exemplified in document D10, so as to target the expression of the HPPD enzyme into plant plastids. Similarly, there is no reason to expect that targeting the HPPD enzyme into plastids would result in a successful expression of a functional HPPD enzyme.

28. Thus, the subject-matter of claim 1 is considered not to be obvious. Since all other claims are directly or indirectly dependent on this subject matter, the auxiliary request fulfils the requirements of Article 56 EPC.

#### *Article 83 EPC*

29. Document D13 (cf. page 1432, left-hand column, last full paragraph) identifies differences between the kinetic properties – the apparent Michaelis constant ( $K_m$ ) for the substrate 4-hydroxyphenylpyruvic acid (HPPA) - of the HPPD enzymes from different organisms ( $K_m$ : 4.3 to 50  $\mu\text{M}$ ) and that of the *Pseudomonas* HPPD enzyme ( $K_m$ : 30  $\text{mM}$ ). For this reason the Board in its preliminary opinion had raised doubts as to the suitability of these HPPD enzymes other than for *Pseudomonas* (exemplified in the application) for obtaining the desired herbicide resistance. However, a document has been submitted during the oral proceedings showing that the Michaelis constant for the substrate HPPA of the *Pseudomonas* HPPD enzyme is of the same order as those shown for mammalian enzymes (document D29). Moreover, there is also evidence on file showing that when a particular chimeric construct comprising DNA coding for the HPPD enzyme from Arabidopsis is transformed in tobacco plants, these become resistant to herbicides.

30. In agreement with the established case law, which requires that for an objection of insufficiency of disclosure to be successful there must be serious doubts, substantiated by verifiable facts (cf. "Case Law", supra, II.A.3, pages 147 to 148), and in the light of the evidence provided, it is concluded that the conditions of Article 83 EPC are met by the auxiliary request directed to the presence in the chimeric gene of genes coding for HPPD enzymes in general.

#### *Questions to be referred to the Enlarged Board of Appeal pursuant to Article 112(1) EPC*

31. The first question for which the appellant requested referral to the Enlarged Board of Appeal is whether Chemical Abstracts and databases such as GenBank are of the same type or different. This is a question of fact to be assessed by this Board, and not a question for referral to the Enlarged Board of Appeal.

32. The other two questions relate to matters of assessment of the sufficiency of the evidence, which are prima facie to be assessed by this Board. The Board sees no questions of law arising here which would justify or necessitate a referral to the Enlarged Board of Appeal.

33. For these reasons, the request for referral of questions to the Enlarged Board of Appeal is refused.

#### *Reimbursement of the appeal fee*

34. According to Rule 67 EPC, the reimbursement of appeal fees is to be ordered if such reimbursement is equitable by reason of a substantial procedural violation. The fact that the examining division failed to substantiate – to the appellant's satisfaction - the reasons which led it to consider the HPPD genes as forming part of the common

general knowledge of the skilled person might constitute, if anything, a deficiency in the examination, but not a procedural violation, let alone a substantial one.

35. Thus, in the absence of a substantial procedural violation, the reimbursement of the appeal fees is refused.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The request for referral to the Enlarged Board of Appeal is refused.
3. The case is remitted to the department of first instance for further prosecution on the basis of the set of claims 1 - 30 of the auxiliary request filed on 6 September 2004.
4. The request for reimbursement of the appeal fee is refused.