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D E C I S I O N
of 15 January 2003

Case Number: T 0149/98 - 3.3.4

Application Number: 90401427.1

Publication Number: 0408403

IPC: C12N 15/32

Language of the proceedings: EN

Title of invention:
Prevention of resistance development against Bacillus thuringiensis insecticidal crystal protein

Patentee:
Bayer BioScience N.V.

Opponent:
SYNGENTA PARTICIPATIONS AG

Headword:
Resistance development/BAYER

Relevant legal provisions:
EPC Art. 53(b), 83, 56

Keyword:
"Plant varieties - (no)"
"Sufficiency of disclosure - (yes)"
"Inventive step - (yes)"

Decisions cited:
G 0009/91, G 0010/91, G 0001/98, T 0688/91

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0149/98 **-** 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 15 January 2003

Appellant I: (Proprietor of the patent)
Bayer BioScience N.V.
Jozef Plateaustraat 22
BE-9000 Gent (BE)

Representative:
Almond-Martin, Carol
Ernest Gutmann - Yves Plasseraud S.A.
62 rue de Bonnel
F-69448 Lyon Cedex 03 (FR)

Appellant II: (Opponent)
SYNGENTA PARTICIPATIONS AG
Schwarzwaldallee 215
CH-4058 Basel (CH)

Representative:
Fisher, Adrian John
CARPMAELS & RANSFORD
43 Bloomsbury Square
London WC1A 2RA (GB)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 17 November 1997 concerning maintenance of European patent No. 0408403 in amended form.**

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: A. L. L. Marie
S. G. Perryman

Summary of Facts and Submissions

I. European Patent EP-0 408 403 was granted on the basis of a set of 20 claims, claims 1, 16, 17 and 19 of which read:

"1. Cells of a plant, characterized by: at least two B. thurigiensis Insecticidal Crystal Protein genes stably inserted into the genome of said plant; said genes being under the control of the same or distinct promoter and each of said genes encoding a different non-competitively binding Insecticidal Crystal Protein for the same insect species; whereby at least two different Insecticidal Crystal Proteins can be produced in cells of said plant."

"16. A plant, consisting of the plant cells of any one of claims 1 to 12."

"17. Brassica, tomato, potato, tobacco, cotton or lettuce consisting of the plant cells of any one of claims 1 to 12, wherein said Insecticidal Crystal Protein genes comprise one of the following pairs of genes: bt2 and bt18 or bt73 and bt15 or bt2 and bt18 or bt2 and bt14 or bt2 and bt4 or bt15 and bt18 or bt14 and bt15 or bt4 and bt15 or bt13 and bt21 or bt21 and bt22 or bt13 and bt22."

"19. A plant characterized by: at least two B. thurigiensis Insecticidal Crystal Protein genes stably inserted into the genome of said plant; said genes being under the control of the same or

distinct promoter and each of said genes encoding a different non-competitively binding Insecticidal Crystal Protein for the same insect species; whereby at least two different Insecticidal Crystal Proteins can be produced in cells of said plant."

Claims 2 to 12 and claim 20 defined further embodiments of the claimed cells of a plant. Claim 13 was directed to a vector for transforming said cells of a plant. Claims 14 and 18 respectively referred to a process for producing a plant with improved insect resistance and to a method for rendering a plant resistant to insects. Claim 15 was directed to a plant cell culture.

II. The patent was opposed on the grounds of Article 100(a) EPC (for lack of inventive step (Article 56 EPC)) and Article 100(b) EPC (for insufficiency of disclosure (Article 83 EPC)). The opposition division, making use of the power conferred by Article 114(1) EPC, raised an objection against the granted claims 16, 17 and 19 under Article 53(b) EPC. The patent was maintained pursuant to Article 102(3) EPC on the basis of the 18 claims of the first auxiliary request, corresponding to the claims as granted, from which claims 16 and 19 had been deleted and claim 17 amended by introduction of the word "*cells*" after "*Brassica, tomato, potato, tobacco, cotton or lettuce*" in order to overcome the objection raised by the opposition division under Article 53(b) EPC.

III. Appeals were filed against the decision of the opposition division by both the patentee (appellant I) and the opponent (appellant II).

IV. The Board issued a communication pursuant to Article 11(2) of the rules of procedure of the boards of appeal giving a preliminary opinion on the patentability of the subject-matter of claims 16, 17 and 19 as granted in view of the decision G 1/98 (OJ EPO 2000, 111).

V. Oral proceedings were held on 15 January 2003.

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

(1) W.H. McGaughey, Agriculture, Ecosystems and Environment, 1994, Vol. 49, pages 95 to 102

(3)* C. Hofmann, Dissertation ETH No. 8498, "The binding of Bacillus thurigiensis delta-endotoxin to cultured insect cells and to brush border membrane vesicles", Zürich, Switzerland, 1988

(4) C.C. Payne, Med. Fac. Landbouww. Rijksuniv. Gent, 1987, Vol. 52(2a), pages 113 to 123

(5) H. van Mellaert et al., XXI Annual Meeting of the Society for Invertebrate Pathology, University of California, San Diego at La Jolla, August 14-18, 1988

(6) EP-0 305 275

(7) M.G. Koziel et al., Biotechnol. Genet. Eng. Rev., 1993, Vol. 11, pages 171 to 228

(8) T.B. Stone et al., Journal of Invertebrate Pathology, 1989, Vol. 53, pages 228 to 234

(18) T.B. Stone et al., Biotechnology for Biological Control of Pests and Vectors, 1991, pages 53 to 66

(19) J. Ferre et al., Proceedings of the National Academy of Sciences USA, 1991, Vol. 88, pages 5119 to 5123

(22) W.H. McGaughey and D.E. Johnson, Journal of Economic Entomology, 1992, Vol. 85, pages 1594 to 1600

(25) Abstract book for document (5), back cover

(26)* C. Hoffmann et al., Proceedings of the National Academy of Sciences USA, 1988, Vol. 85, pages 7844 to 7848

(28) V.A. Hilder et al., Nature, 1987, Vol. 300, pages 160 to 163

*: documents (3) and (26) are a Doctor thesis and the corresponding scientific publication, respectively. They have a similar content, so that, unless otherwise specified, they are cited as document (3)/(26).

VII. The arguments submitted by Appellant II may be summarized as follows:

Article 83 EPC:

- objection was raised against the extrapolation from results obtained on a laboratory scale with feeding experiments to an "in field" situation.

Article 54 EPC:

- if the feature "non-competitively binding" was disregarded (cf infra, under "Article 56 EPC"), then the cells and the plant of claims 1 and 19 were only characterized by the fact that they contained the genes coding for two different Bt. ICPs. Document (4) was in this case novelty-destroying.

Article 56 EPC:

- although not a ground for opposition, clarity of the claims was relevant to the assessment of inventive step. The feature "non-competitively binding" used in claims 1 and 19 was rendered obscure by the definitions given in the patent in suit for "competitivity", "high saturability" and "receptor" (page 5, lines 7 to 15) and because of the absence in the patent in suit of a method to measure the affinity of a *Bacillus thurigiensis* Insecticidal Crystal Protein (Bt. ICP) for a particular subset of receptors among a plurality of distinct populations of receptors. The feature "non-competitively binding" was further defined on page 5 (lines 3 to 7) of the patent in suit in relation to the expression "for at least one target insect species" and requested the skilled

person to conduct binding experiments on every insect species before knowing whether a given pair of Bt. ICPs was falling within the scope of claims 1 and 19 of the patent in suit. This feature was hence an indeterminate feature unsuitable for defining the scope of claims 1 and 19 and had to be disregarded. Furthermore, the complete saturation of a receptor or the complete displacement of a Bt. ICP by another competitively-binding one were not possible, because these were processes tending asymptotically to a value which was never reached. There was also a certain extent of unspecific binding of a given Bt. ICP to a given receptor.

- document (4), the closest prior art, identified the expected development of resistance to Bt. ICP in insects due to the selection pressure caused by the constitutive expression of Bt. ICP in transformed plant cells as the problem to be solved and suggested as a solution, at the end of a paragraph on Bt. ICPs, to insert several genes each coding for a "*different insecticidal molecule*", an expression meaning "*another Bt. ICP*". The combination of document (4) with document (3)/(26), which described a couple of Bt. ICPs showing a non-competitive binding in *P. Brassicae*, led in an obvious manner to the subject-matter of the claims under consideration.

- as an alternative closest prior art, document (8) described the appearance of resistance in tobacco budworm to a Bt. ICP expressed by transgenic *P. fluorescens* and suggested the use of more than one

"*B.thurigiensis* variety or other insecticidal proteins", an expression meaning "*another Bt. ICP*" and the combination with document (3)/(26) led in an obvious manner to the subject-matter of the claims of the patent in suit.

- document (6), as a third possible closest prior art, described a plant cell transformed with two different Bt. ICPs genes in order to broaden its insecticidal spectrum. The problem to be solved was the expression of another advantageous combination of Bt. ICP genes in plant cells. The obvious solution was here also given by a combination with document (3)/(26). The skilled person being led to this obvious solution by the knowledge of the problem caused by the appearance of resistance to Bt. ICPs in insects as described in documents (4) or (5).

- as a fourth possible closest prior art, document (5) described the binding of different Bt. ICPs to different receptors of the midgut brush border membrane vesicles. The technical problem was to put into practice this teaching in the context of plants.

VIII. The arguments of Appellant I may be summarized as follows:

Article 83 EPC:

- re-introduction of this ground at this stage of the procedure was not allowable, since appellant

II withdrew his objection during the oral proceedings before the opposition division.

Article 54 EPC:

- novelty was never a ground of opposition against the patent in suit and, according to decisions G 9/91 (OJ EPO 1993, 408) and G 10/91 (OJ EPO 1993, 420), no consent was given to introduce this new ground into the procedure.

Article *56 EPC*:

- clarity was not a ground for opposition.

- the patent in suit did not use the adjective "*high*" in relation to saturability and gave on page 5 (lines 7 to 16) a precise definition of the terms "receptors", "saturability", "affinity" and the "*non competitively binding*" feature (page 5, lines 3 to 7) and indicated means for the determination of the binding properties of a sub-set of receptors (page 6, lines 19 to 35).

- appellant II's interpretation of documents (4) and (8) was incorrect. The expression "different insecticidal molecule" in document (4) did not mean "*another Bt. ICP*", let alone "*another non-competitively binding Bt. ICPs*". Had the author of document (4) meant a "*non-competitively binding Bt. ICP*", he would have explicitly said so. Furthermore, document (28) showed that at the priority date of the patent in suit the gene of another insecticidal molecule was known. Document

(8), as far as it referred to transgenic plants, only mentioned the possibility of either a tissue- or a development stage-specific expression of the cloned Bt. ICP gene and the use of more than one Bt. variety or other insecticidal proteins was put in parallel to the mixing of commercial pesticides spread over the plants.

- document (5) was, as shown by document (25), no Article 54(2) EPC prior art document, because of a secrecy condition.

- document (6) was not concerned with the problem of delay/prevention of the appearance of resistance in insects, but aimed at broadening the insecticidal spectrum of transgenic plants and was thus inappropriate as a closest prior art.

- Examples 7 and 8 of the patent in suit showed that the use of two non-competitively binding Bt. ICPs resulted in an improvement in delay/prevention of the occurrence of resistance to Bt. ICP in insects.

IX. Appellant I requested that the decision under appeal be set aside and the patent be maintained as granted.

X. Appellant II requested that the decision under appeal be set aside and the patent be revoked.

Reasons for the decision.

Article 53(b) EPC

1. Claims 16, 17 and 19 as granted relate to transgenic plants, without mentioning individual plant varieties. The Board, following the view expressed in decision G 1/98 (cf supra section IV) that a claim wherein specific plant varieties are not individually claimed is not excluded from patentability, even though it may embrace plant varieties, concludes that claims 16, 17 and 19 meet the requirements of Article 53(b) EPC.

Article 83 EPC

2. The withdrawal of the Article 83 EPC objection against claims 14 to 18 as granted during the oral proceedings before the opposition division was not absolute but merely conditional, since it was made dependent on the positive conclusion reached by the opposition division on the fulfilment of the requirements of Article 56 EPC by claim 1 as granted (see decision of the opposition division, page 2, last paragraph and page 3, first two lines).

3. Due to the function of the appeal proceedings and the suspensive character of the appeal (cf Case Law of the Boards of Appeal of the European Patent Office, 4th edition, 2001, pages 504 and 505), the conclusions of the first instance on the grounds of opposition are in appeal submitted to re-consideration. Since Appellant II is on appeal challenging inventive step in relation to claim 1, on its own logic the conditional withdrawal of its objection under Article 83 EPC to claims 14 to

18 cannot debar it from arguing the point on appeal. While the Board is unable quite to follow the logic why one objection was coupled to the outcome of another, the Board sees no good reason for refusing to consider the Article 83 EPC objection.

4. The patent in suit describes in Examples 7, 11 and 12 "feeding experiments" carried out on a laboratory scale, but does not indicate that "in field" experiments using transgenic plants as claimed in claims 14 to 18 as granted have been carried out.

5. Appellant II considered doubtful whether such laboratory scale experiments are appropriate to draw reliable conclusions both on the occurrence of a resistance problem to Bt. ICPs still unknown up to the priority date and on its cure. In this context, documents (1)(pages 99 and 101) and (7)(page 215) were cited.

6. As far as the occurrence of resistance to Bt. ICP is concerned, post-published document (19) shows on page 5119 (bridging paragraph between the left and the right column) that resistance development to ***B. thurigiensis*** formulations **in the field** had already occurred in the Philippines and mentions therefor "reference 11", which was published in 1988, ie before the priority date of the patent in suit. Therefore, the appearance of resistance to Bt. ICP in the field is not a theoretical or academical problem, but a real one.

7. Laboratory scale feeding experiments are considered by the scientific community to "mimic" in a satisfactory manner the conditions leading to occurrence of

resistance and to give valuable information on the toxic action of Bt. ICPs on insects.

8. For instance, document (18), cited as an expert opinion, states on page 57 (fourth full paragraph) that said laboratory experiments may be used "*as models for understanding the potential development, the mechanisms of resistance, and developing strategies for delaying or preventing the occurrence of resistance to B. thurigiensis*".

9. Document (19), cited as an expert opinion, shows on page 5122 (heading "Discussion"), using feeding experiments, that the mechanisms of resistance and the susceptibility to *B. thurigiensis* are the same in a laboratory strain and in a field population.

10. Document (7), cited as an expert opinion, although suggesting a cautious attitude when extrapolating to field resistance, states on page 207 (heading "Field and laboratory occurrence") that laboratory-scale experiments can provide important information on how a species can adapt to the stress caused by the addition of Bt. ICP to its diet.

11. Documents (8)(page 229, right column, heading "Selection procedure") and (22)(page 1595, right column, first full paragraph), the latter document being cited as an expert opinion, make use of feeding experiments on a laboratory scale. Document (3) states on page 99 (second paragraph) that no major differences between *in vivo* and *in vitro* toxicity of lepidopteran Bt. ICP were seen.

12. Thus, despite the absence of reported field experiments in the patent in suit, the Board has no reason to believe that the invention as claimed cannot be put into practice. Claims 14 to 18 as granted meet the requirements of Article 83 EPC.

Availability to the public of document (5)

13. According to appellant I document (5) was not available to the public, because of a secrecy condition as shown by document (25), the back cover of the book containing the abstracts of the XXI annual meeting of the Society for Invertebrate Pathology, which stated that "...These abstracts should not be considered as publications and therefore, should not be cited without the author's permission". In the Board's opinion, document (25) does not state that there was a secrecy agreement, but only that the abstract should not be considered as a citable publication attributable to a named author, the information content of the abstract was however made available to the public. Therefore, document (5) is, in the Board's opinion, a prior art document in the sense of Article 54(2) EPC.

Technical features

14. An objection to the claims must relate to a provision of the EPC under which in opposition proceedings an objection may be based. An objection under Article 84 EPC concerning clarity or lack of support of a claim cannot be made in opposition proceedings against a claim as granted. It would only be in very rare cases, that a feature would be so unclear, or technically meaningless, that it would have to be disregarded

completely when determining the validity of a granted claim. An objection that a claim is "indeterminate" does not exist under the EPC, though it might be possible to argue that a claim is so broad, that its subject matter is not novel or can be derived in an obvious manner from the state of the art (ie objections of lack of novelty under Article 54 EPC or lack of inventive step under Article 56 EPC), or that the skilled person would be unable to put into practice some of the subject matter claimed, because he or she would not know what to do (an objection under Article 100(b)/83 EPC). However, an objection under Article 100(b)/83 EPC must relate to some subject matter under the claim which a practical skilled person would wish to put into practice, and not merely to something which could in theory be argued to be covered by the claim, but which would be of no practical utility. It must be assumed that the skilled person wishes to achieve some useful result.

15. For the purpose of assessing novelty or inventive step the Board first has to determine what are the technical features of the claims.

16. Appellant II raised objections in this context against the "non-competitively binding" feature of claims 1 and 19 in relation to the definition of the terms "receptor", "saturability" and "affinity" (page 5, lines 7 to 15 of the patent in suit) and the expression "*at least one target insect species*" (page 5, lines 3 to 6 of the patent in suit), which was understood by appellant II as requesting the skilled person to test a given pair of Bt. ICP in each and every insect before knowing whether it falls within the scope of claim 1.

They further concern the absence in the patent in suit of a method for determining the affinity of a subset of receptors and the fact that the total saturation of a receptor by a Bt. ICP can theoretically not be achieved, since said total saturation represents an asymptotic limit to which the binding tends, but cannot reach, that a first ICP cannot completely be displaced by a competitively-binding second one, and that there may be some extent of unspecific binding or some degree of unspecific displacement of a Bt. ICP by another non-competitively binding one.

17. However, in the Board's opinion, the terms "affinity" and "saturability", even in connection with the unclear adjective "high", are commonly used in the field of receptor/ligand binding, as shown by document (26)(cf abstract; page 7844, left column; page 7846, right column), document (3)(page 20, last line; page 89, lines 10 and 14; page 94, lines 3 and 13) and document (5).

18. The patent in suit further teaches the skilled person how to draw a so-called "homologous binding/displacement curve", as shown in Figures 1 to 12 and explained on page 5, lines 7 to 15 and page 6, lines 19 to 31 of the patent in suit, which results in a sigmoidal curve with a plateau at each extremity, said plateaux being assumed to respectively represent a total saturation and a total displacement, ie a 100% and a 0% saturation of the given receptor by the given Bt. ICP. Every subsequent experiment to determine the possibly competitive character of another Bt. ICP with the first one will not be carried out "in absolute", but in relation to this reference curve, which thus

sets the skilled person free from the hypothetical considerations of appellant II on saturation and unspecific displacement or binding. The Board is convinced that this teaching of the patent in suit enables the skilled person to determine whether two Bt. ICPs are fully-, partially- or non-competitive to each other for the binding to a given receptor.

19. The patent in suit (page 23, line 14) teaches that the determination of the affinity of a given Bt. ICP for a subset of receptors is made using the so-called Scatchard plot, which has been published in 1949. Further, on page 13, lines 19 to 23 the binding data are said to be analysed using the LIGAND computer programm which calculates the dissociation constant K_d and the binding site concentration, said LIGAND programm having been the object of a publication in 1980 (page 14, lines 12 to 15 of the patent in suit). This teaching is corroborated by document (3), which in view of the limitations of the Scatchard plot, suggests in the paragraph bridging pages 103 and 104 another method published in 1986, ie before the priority date of the patent in suit. Therefore, the patent in suit at the priority date, as well as the prior art, provided the skilled person with means to titrate a subset of Bt. ICP receptors among a plurality of Bt. ICP receptors.

20. As far as appellant II, making reference to the definition of the "non-competitively binding ICPs" given on page 5, lines 3 to 6 of the patent in suit, further argues that this is an indeterminate feature, inappropriate to distinguish the subject-matter of claims 1 and 19 from the prior art and has thus to be disregarded, because, when used in combination with the

term "*at least one target insect species*", it compels the skilled person to determine the competitive or non-competitive character of 2 Bt. ICPs **in each and every insect species**, the Board considers that there appears here to be a confusion between the notions of "clarity" and "breadth of the claims". However, as stated in decision T 688/91 (21 April 1993), breadth is not to be equated to absence of clarity. First of all, the claims read alone or in the light of the description (ie with consideration of the incriminated expression "*at least one target insect*"), provide the skilled person with a clear and technically understandable teaching. Further, document (7), cited here as an expert opinion, indicates on page 171 (fourth sentence) that Bt. ICPs have "*a narrow spectrum of insect targets*" and, on page 180 (last paragraph), that "*the spectrum of insecticidal activity in an individual endotoxin tends to be quite narrow, with a given endotoxin being active against only a few (known) insects.*". This teaching is also corroborated by document (28) which states on page 161 (left column) that "*Bt. toxins are very specific*". Therefore, the skilled person, interpreting the "non-competitively binding" feature of claims 1 and 19 in the light of the expression "*at least one target insect*" given in the patent in suit on page 5, lines 3 to 6, would not have an unduly large number of insects to test. Moreover, as stated on pages 173 (last paragraph) and 182 (second and third lines) of document (7) only a few pests (ie insects) are of commercial importance, which further reduces the number of insects to be tested.

21. The Board is thus convinced that the claims are clear and technically understandable and that the term "non-competitively binding" as used in claims 1 and 19 is a meaningful technical feature.

Article 54 EPC

22. As a consequence, the "non-competitively binding" feature of claims 1 and 19 cannot be disregarded, but serves to distinguish the subject-matter of claims 1 and 19 from that of document (4) considered by appellant II to disclose the transformation of plant cells with two Bt. ICPs. Document (4) is hence not detrimental for the novelty (Article 54 EPC) of claims 1 and 19 of the patent in suit.

Article 56 EPC

23. The closest prior art is defined in the established case law (Case Law of the Boards of Appeal of the European Patent Office, 4th edition, 2001, pages 102 to 106) as being directed to the same purpose or effect as the invention.

24. The purpose of the patent in suit is the preparation of cells of plants genetically engineered in order to delay or prevent the appearance of resistance against Bt. ICPs in insects being parasitic to said plants, of plants consisting of said cells of plants, of vectors and methods for transforming said cells of plants or for rendering plants resistant to an insect species.

25. Document (5) is not concerned with the problem of the patent in suit as defined above, but with the binding of Bt. ICPs on receptor sites of the brush border membrane from lepidopteran insects.

26. Document (6) does concern the transformation of plants with two genes coding for Bt. ICPs. However, this is done to broaden the insecticidal spectrum of said plants and not to delay or prevent the appearance of resistance in insects against Bt. ICPs and, thus, serves quite a different purpose than the claims under consideration.

27. Document (8) is primarily directed to the resistance of tobacco budworm against a *P. fluorescens* transformed with a gene coding for Bt. ICP. In the last, speculative and future-oriented paragraph, a sentence states that in transgenic plants a tissue- or growth stage-specific expression of the Bt. ICP gene may be envisaged to limit the occurrence of a resistance in insects. The next sentence suggests that "*more than one B. thurigiensis* ***variety****, or other insecticidal proteins, may also be combined as in the mixing of commercial pesticides*". The Board is, first of all, not convinced that this sentence should be read in combination with the preceding one on the transgenic plants to suggest the transformation of plant cells with two genes coding for Bt. ICPs. This sentence is furthermore ambiguous. Through the reference to "*commercial pesticides*" which are usually spread over the plants and preferably use whole bacteria rather than proteins, which can more readily be inactivated, the term "*B. thurigiensis* ***variety***" could mean "*the whole bacterium*". On the other hand, because of the parallel to "*other insecticidal*

proteins", Bt. ICP as a protein could also be meant. However, this is still no indication that two Bt. ICPs genes have to be introduced into the transgenic plants, since the Bt. ICPs could be spread over the plants as are the commercial pesticides mentioned in this sentence.

28. Therefore, having regard to the purpose of the patent in suit, documents (5), (6) and (8) are not considered by the Board to be the closest prior art.

29. Rather, in the Board's view, and in accordance with appellant II, document (4) is the closest prior art. It is a review article on the current uses and future prospects of microbial pest control agents. Under the heading "Introduction" on page 113, it mentions the general problem of the development of resistance in some insects against insecticides. A long paragraph (pages 115 and 116) is dedicated to bacteria in general as biocontrol agents, but in fact only considers the case of Bt. ICPs and teaches on page 116 (second paragraph) that crop plants (especially tobacco) have been transformed with Bt. ICP genes to render them immune to insect attack. Document (4) envisages, as a consequence of the potentially high selection pressure imposed to the insects due to the constitutive expression of Bt. ICP in the transformed plants, the occurrence of a resistance to Bt. ICPs in the insects. The last sentence of this paragraph suggests that "*...the insertion of several genes, each coding for a* ***different insecticidal molecule*** *would be a better long-term approach*" to avoid the occurrence of said resistance.

30. The technical problem which can thus be derived from document (4) is the provision of a plant, already expressing **one** Bt. ICP gene, able to delay or prevent the occurrence of resistance to Bt. ICP in insects.

31. The solution proposed in the patent in suit is to transform a cell of a plant with at least two genes, each gene coding for a different, non-competitively binding Bt. ICP toxic for the same insect species. This solution is reflected in the claims under consideration directed to such transformed cells of plant, transformed plants, vectors for said transformation, methods and processes for rendering a plant resistant to an insect species or having improved insect resistance.

32. In view of Examples 7 to 12 of the patent in suit (cf supra, points 4 to 12), the Board is satisfied that this solution has successfully been performed. In particular, Examples 7 and 8 of the patent in suit show the advantages related to the use of at least two non-competitively binding Bt. ICPs in the delay/prevention of the resistance. Example 7 shows that the decrease in sensitivity (ie the occurrence of resistance) of *M. sexta* fed for several generations on a diet containing the non-competitively binding Bt. ICPs Bt2 and Bt18, either isolated from each other or combined, is about 100 times slower when Bt2 and Bt18 are combined together in the diet. Example 8 shows that the high level of resistance which had occurred in *P. Xylostella* against Dipel, a commercially available pesticide containing 3 competitively binding Bt. ICPs (Bt2, Bt3 and Bt73), involves an alteration of the binding site for Bt2. However, when tested with Bt15, another Bt.

ICP non-contained in Dipel and non-competitively binding with the Bt. ICPs of Dipel, the *P. Xylostella* strain resistant to Dipel is still sensitive to Bt15, showing that the alteration of the receptor site for a given Bt. ICP is without influence on the sensitivity for another, non-competitively binding ICP, for which the strain still remains sensitive. The solution proposed in the patent in suit, ie the use of at least two non-competitively binding Bt. ICPs reflected in its various aspects in the claims under consideration, is hence an improvement over the existing prior art relating to pesticides containing either a single Bt. ICP, as in document (4), or several competitively binding Bt. ICPs, as in Dipel.

33. Nevertheless, the relevant question for the assessment of inventive step is whether the skilled person would have come to the solution proposed in the patent in suit in an obvious manner by considering the teaching of document (4) alone or in combination with other prior art documents and/or the common general knowledge. The answer to this question *de facto* depends on whether the skilled person would have understood the expression "*different insecticidal molecule*" used in document (4) as meaning "*another Bt. ICP*" and, if this was the case, whether he/she would have considered that the two Bt. ICPs must be non-competitively binding for the same insect species.

34. To answer this question the purpose of document (4) has to be considered, as well as the formulation of this expression and its place of occurrence in document (4). The purpose of document (4), as a review article, is to summarize the knowledge of the skilled person at a

given time in a given field, and, based on this knowledge, to envisage on a broad basis future developments as demonstrated by the title of document (4) itself: "Current uses and future prospects for microbial pest control agents". Therefore, document (4) is not only concerned with Bt. ICPs, but also deals with several other pest control agents, such as baculovirus, fungi, protozoa and nematodes. Further, the expression "*different insecticidal molecule*" is found at the end of a long paragraph about Bt. ICP. If this expression had been supposed to mean "*a second Bt. ICP*", the author could have explicitly said it, as suggested by appellant I, or would have simply used the expression "*different/another Bt. ICP molecule*" solely putting thereby the accent on the molecular difference between the two Bt. ICPs. On the contrary, the term "*different insecticidal*" in this expression stresses, in the Board's view, the fact that the second molecule is different on the insecticidal (ie on the functional) level and hence has a mode of action different from that of the Bt. ICP already present in the cells of a plant and belongs to another "*insecticidal family*". Therefore, this expression excludes the possibility of using a second Bt. ICP. Insofar, the combination suggested by appellant II of document (4) with document (3/26) disclosing a pair of B.t. ICPs showing a non-competitive binding in *P. brassicae* can only be the result of an *ex post facto* analysis.

35. The skilled person was well able to put this embodiment of document (4) into practice at the priority date of the patent in suit, since document (28) describes such an insecticidal molecule with a mode of action different from that of Bt. ICP: the cowpea trypsin

inhibitor, which, when transferred to tobacco, enhances the resistance to this species' own herbivorous insect pests (page 161, left column). Document (28) also mentions (page 161, left column) the use of Bt. ICPs as pest control agents, but favours for this function the cowpea trypsin inhibitor, which is said to have "*a number of attractive features*" for the purpose of controlling insects development and, in particular, to be active against a wide range of insects, contrary to the Bt. ICPs which have a narrow specificity. Document (28), seen in combination with document (4) hence does not lead the skilled person to the use of a second Bt. ICP, ie to the solution of the claims of the patent in suit.

36. Furthermore, even if for the sake of argumentation it was considered that document (4) did suggest the use of two Bt. ICPs, then there would, nevertheless, be no indication for the skilled person to use two non-competitively binding Bt. ICPs, a feature which was found to be technically meaningful (cf supra, point 21) and to result in an improvement over the insecticidal formulations of the prior art (cf supra, point 32). Here again, the skilled person would not be brought to the idea of combining the teaching of document (4) with that of document (3/26).

37. In view of the foregoing, the Board considers that the solution of the patent in suit, ie the use of at least two non-competitively binding Bt. ICPs, the various aspect of which are reflected in claims 1 to 12, 15 to 17, 19 and 20 (cells of a plant, plant cell culture, plants), claim 13 (vector for transforming the cells of a plant), claims 14 and 18 (process and method for

rendering a plant resistant to an insect species or to improve the resistance of said plant to said insect species), is an improvement over the prior art and cannot be derived in an obvious manner from the cited prior art. Therefore, an inventive step is acknowledged for the subject-matter of claims 1 to 20 as granted, which meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is maintained as granted.

The Registrar: The Chairwoman:

P. Cremona U. Kinkeldey