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Datasheet for the decision of 9 March 2017

Case Number: T 1669/15 - 3.3.04

Application Number: 07802565.7

Publication Number: 2190999

IPC: C12N15/82, A01H5/00

Language of the proceedings: EN

Title of invention:
Promotor sequence and gene construct for increasing crop yield in tomato

Patent Proprietor:
Enza Zaden Beheer B.V.

Opponent:
Nederlandsch Octrooibureau N.V.

Headword:
SP3D promoter sequences/ENZA ZADEN

Relevant legal provisions:
EPC Art. 100(c)

Keyword:
Grounds for opposition - subject-matter extends beyond content of earlier application (yes)

Decisions cited:

Catchword:

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Case Number: T 1669/15 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 9 March 2017

Appellant: (Patent Proprietor)	Enza Zaden Beheer B.V. Haling 1E 1602 DB Enkhuizen (NL)
Representative:	van Kooij, Adriaan Arnold & Siedsma Bezuidenhoutseweg 57 2594 AC The Hague (NL)
Respondent: (Opponent)	Nederlandsch Octrooibureau N.V. J.W. Frisolaan 13 2517 JS Den Haag (NL)
Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 22 June 2015 revoking European patent No. 2190999 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	M. Montrone
	L. Bühler

Summary of Facts and Submissions

I. An appeal was lodged by the patent proprietor (hereinafter the "appellant") against the decision of the opposition division to revoke European patent No. 2 190 999. The patent is based on European patent application No. 07802565.7, which was filed as an international application and published as WO 2009/021545 (hereinafter "the application as filed") with the title "*Promotor sequence and gene construct for increasing crop yield in tomato*".

II. The patent was opposed under Article 100(a) EPC on the grounds of exceptions to patentability (Article 53(b) EPC), lack of novelty (Article 54 EPC) and of inventive step (Article 56 EPC) and under Articles 100(b) and 100(c) EPC.

III. In the impugned decision the opposition division held that the subject-matter of claim 1 as granted extended beyond the content of the application as filed.

IV. With its statement of grounds of appeal the appellant submitted arguments as to why the opposition division had erred in its decision that claim 1 as granted contained added subject-matter.

Claim 1 as granted reads:

"1. SP3D promotor sequence, capable of directing transcription of a downstream SP3D gene that is operably linked to said promotor sequence, wherein the promotor sequence is derived from a species of the Solanaceae family having a sympodial index of 2, for reducing sympodial index in plants having a sympodial index of 3 or more, wherein said promotor

sequence comprises a nucleotide sequence having at least 95% identity, preferably at least 99% identity with nucleotides 1251 to 1874 of the nucleotide sequence as shown in Figure 2 and wherein said promotor sequence comprises a CA motif at a position 62-61 nucleotides upstream of the start codon of said SP3D gene."

V. In reply to the statement of grounds of appeal, the opponent (hereinafter the "respondent") submitted arguments as to why claim 1 as granted contained added subject-matter.

VI. The appellant in two further replies to the respondent's submissions filed *inter alia* document D5 (B. Lewin, Genes IV, Oxford University Press, 1990, page 551).

VII. Oral proceedings before the board were held on 9 March 2017. At the end of the oral proceedings the chairwoman announced the board's decision.

VIII. The appellant's arguments may be summarised as follows:

Extension beyond the content of the application as filed (Article 100(c) EPC)

In the following, the references are to passages and figures in the application as filed.

The feature "*nucleotides 1251 to 1874 of the nucleotide sequence as shown in Figure 2*" of the SP3D promoter sequences according to claim 1 as granted, i.e. the feature at issue in the present case, was not explicitly disclosed in the application. It defined the

length and position of the promoter sequence within the nucleic acid sequence disclosed in Figure 2.

Although the application reported consistently and explicitly only that the SP3D promoter sequences as claimed comprised nucleotides 1 to 624 of the sequence shown in Figure 2 (e.g. page 7, lines 12 to 15), the feature at issue was however implicitly derivable from the disclosure in the application.

This was so because the CA motif - as an essential element of the promoter - was located at positions -62 and -61 upstream of the translation start codon of the SP3D gene (e.g. page 4, lines 26 to 29), which corresponded to positions 1813 and 1814 of the sequence shown in Figure 2. Thus, the CA motif was not contained in the nucleotide sequence 1 to 624 disclosed in Figure 2, contrary to the explicit disclosure of the application that this motif "*should be present*" in the claimed promoter sequences (page 7, lines 31 to 33). It was therefore clear to the skilled person that the nucleotide sequence 1 to 624 did not constitute promoter sequences.

The feature at issue implied, however, that the length of the claimed promoter sequences was 624 nucleotides (1874 minus 1250). This was also derivable from the disclosure in the application that the promoter sequence "*is derived from S. Pennellii and consists of the nucleotide sequence of nucleotides 1 to 624 of SEQ ID NO: 1" (*page 8, lines 1 to 3) and from the disclosure on page 8, lines 31 to 33, that "*the SP3D gene is the SP3D gene of S. pennellii, SP3Dpen, having a genomic nucleotide sequence consisting of nucleotides 625 to 7307 of SEQ ID NO: 1*".

The location of the feature at issue at nucleotides 1251 to 1874 of the sequence shown in Figure 2 was derivable from the disclosure of the SP3D gene comprising "*nucleotides 625 to 7307 of SEQ ID NO: 1*" (page 8, lines 31 to 33) and from the legend of Figure 2 reading that the figure "*shows the nucleotide sequence of SEQ ID NO: 1, i.e. the genomic nucleotide sequence of the SP3Dpen gene including the promotor sequence (nucleotides 1-624)*" (page 12, lines 27 to 29). The skilled person would have derived from these two passages that the SP3D promoter sequence was located immediately adjacent to and upstream of the SP3D gene. Figure 2 further disclosed that the start codon "*ATG*", identifying the beginning of the coding sequence of the SP3D gene, was at positions 1875 to 1877. This necessarily meant that the last nucleotide of the promoter sequence was located at position 1874, since promoter and gene were adjacent. Moreover, since the claimed promoter sequences had a length of 624 nucleotides, the first nucleotide of the promoter sequence had to be located at nucleotide 1251 (1874 minus 623).

The location of the promoter at nucleotides 1251 to 1874 in the sequence disclosed in Figure 2 was also derivable from the legend of Figure 4 on page 13, lines 6 and 7, which reported an "*SP3Dpen promotor region of nucleotides 544-580*" in combination with the nucleotide sequence of "*S. pennellii*" disclosed in Figure 4 reading "*TCTT GTGTTGTGTT TTAGCACACA AATACACAAA AG*". An alignment of this sequence with that disclosed in Figure 2, assuming further that the promoters had a length of 624 nucleotides and stopped at the nucleotide immediately before the "*ATG*" start codon of the SP3D gene, necessarily led to disclosure of nucleotides 1251 to 1874 of the feature at issue.

Although the numbering "*544-580*" of the nucleotides reported on page 13, line 7, was inconsistent with the "*barely legible*" numbering 597 to 632 of the aligned promoter sequences disclosed in Figure 4, the skilled person would not have relied on the latter numbering, since this would have resulted in promoters partially overlapping with the coding region of the SP3D gene, which made no sense in technical terms. The skilled person would for the same reason not have relied on the numbering 1 to about 675 of the aligned promoter sequences disclosed in Figure 5.

Document D5 disclosed the genomic organisation of a gene and a promoter, including the numbering used in the art to denote the location of the promoter relative to a gene. Figure 29.5 disclosed in this context that the transcription start (start point) of a gene was identified as position +1 while the numbering in the upstream direction of this point belonging accordingly to the promoter started with number -1. The skilled person, taking his common general knowledge into account, would therefore have inferred from the disclosure in the application, for example on page 7, line 15, that the promoter sequence comprising *"nucleotides 1 to 624 of SEQ ID NO: 1 (Fig. 2)"* was in fact meant to read "*-1 to -624*", i.e. nucleotides "*1251 to 1874*" as referred to in claim 1, since the adenosine of the "*ATG*" start codon was at position +1, i.e. at nucleotide 1875.

Thus, the subject-matter of claim 1 was directly and unambiguously derivable from the disclosure of the application as filed.

IX. The respondent's arguments may be summarised as follows:

Extension beyond the content of the application as filed (Article 100(c) EPC)

The feature "*nucleotides 1251 to 1874 of the nucleotide sequence as shown in Figure 2*" of the SP3D promoter sequences according to claim 1 as granted, i.e. the feature at issue in the present case, was not explicitly disclosed in the application.

It was also not implicitly derivable from the disclosure in the application, which consistently disclosed that the SP3D promoter sequences comprised nucleotides 1 to 624 of the sequence shown in Figure 2. Due to the "comprising" language, this meant that the promoter could start at nucleotide 1 of Figure 2 and extend until somewhere after the CA motif at nucleotides 1814 and 1815 and could therefore be longer than the 624 nucleotides. Moreover, promoters with scattered functional regions, thereby not necessitating a contiguous nucleotide sequence, were also commonly known in the art (document D5).

Furthermore, the skilled person would not necessarily have derived from the disclosure in the application that the SP3D promoter comprised "*nucleotides 1 to 624 of SEQ ID NO: 1*" and that the SP3D gene comprised "*nucleotides 625 to 7307 of SEQ ID NO: 1*", implying their adjacent location, and thus that the promoter was in fact located at positions 1251 to 1874, merely because the start codon "*ATG*" of the SP3D gene was located at nucleotides 1875 to 1877 of the sequence disclosed in Figure 2. The "*ATG*" start codon identified the translation start point in the nucleic acid

sequence of the SP3D gene, i.e. the beginning of the coding sequence of the gene which was translated into a corresponding protein sequence. The "*ATG*" start codon, however, did not define the beginning of the SP3D gene. It was common general knowledge that the term "*gene*" related not only to the coding sequence but also to further nucleotide sequences which were transcribed into mRNA but not translated into a protein and which were located on both sides of the coding sequence, i.e. upstream and downstream thereof. This meant that the start points for transcription and translation of a gene were not identical. The skilled person further knew from his common general knowledge that promoters were located at the transcription start point to initiate the transcription of a gene, and not its translation (see document D5, Figure 29.5). Also, the application disclosed on page 4, lines 19 to 21, that the invention concerned "*providing a SP3D promotor sequence, which is capable of directing transcription of a downstream SP3D gene that is operably linked to said promotor sequence*". However, the application was silent about the position of the transcription start point of the SP3D gene. Thus, it was not immediately apparent to the skilled person that in the present case the translation start point was identical to the transcription start point and that the terminal nucleotide of the claimed promoter sequences was thus to be located at position 1874, i.e. the nucleotide immediately preceding the start codon "*ATG*" of the SP3D gene.

The feature "*nucleotides 1251 and 1824 of the nucleotide sequence as shown in Figure 2*" as referred to in claim 1 was also not implicitly derivable from the "*SP3Dpen promotor region of nucleotides 544-580*" disclosed on page 13, lines 6 and 7, or the "*SP3Dpen*

promotor region 1-624" disclosed on page 13, lines 11 and 12, since neither passage referred to SEQ ID NO: 1 or Figure 2 and therefore potentially meant a promoter region different from the one disclosed by nucleotides 1 to 624 in Figure 2. Moreover, Figures 4 and 5 both disclosed that the CA motif was located at nucleotides 615 and 616. Thus the numbering of the aligned nucleotide sequences was inconsistent with "*544-580*" as disclosed on page 13 of the application. Accordingly, even assuming that the promoter length was 624 nucleotides and that the regions disclosed in Figures 4 and 5 were indeed the claimed promoter sequences (for which a direct and unambiguous disclosure in the application was contested), the alignment of the sequences disclosed in Figure 4 with that of Figure 2 did not necessarily result in the feature at issue as referred to in claim 1.

X. The appellant requested that the decision under appeal be set aside and that the case be remitted to the opposition division for further prosecution ("Assessment of Articles 100(a) and (b) EPC").

The respondent requested that the appeal be dismissed.

Reasons for the Decision

Introduction to the invention

1. The invention concerns SP3D promoter sequences directing the transcription of a downstream SP3D gene (SP3Dpen) from *Solanum pennellii* (*S. pennellii)* (page 5 of the application, lines 1 to 4), which belongs to the so-called centroradialis (CETS) gene family (page 2 of the application, lines 16 to 17).

2. The CA motif in the SP3D promoter of the invention causes a reduction of the sympodial index (spi) of tomato plants from three to two, which means that the number of leaves between the trusses is reduced from three to two (page 3, line 31, to page 4, line 7). This reduction in leaf number leads to increases in the yield of tomato fruits by about 10% compared to tomato plants containing SP3D promoters lacking the CA motif (page 3, lines 17 to 30).

Extension beyond the content of the application as filed (Article 100(c) EPC)

3. In the following, the references are to passages and figures in the application as filed.

4. Article 100(c) EPC provides that a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

5. Any amendment to the parts of a European patent application or of a European patent (description, claims and drawings) can only be made within the limits of what a skilled person would derive directly and unambiguously, either explicitly or implicitly, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the document as filed. An implicit disclosure in this context is what the person skilled in the art would consider as necessarily implied by the disclosure of the document as a whole (Case Law of the Boards of Appeal, 8th edition 2016, II.E.1.2.1 and II.E.1.2.2).

6. The feature at issue in the present case is "*nucleotides 1251 to 1874 of the nucleotide sequence as shown in Figure 2*" as referred to in claim 1 as granted.

7. It was common ground between the parties that the application as filed did not contain an explicit disclosure of this feature.

8. With regard to the implicit disclosure, the appellant indicated page 4, lines 26 to 29, in conjunction with page 7, lines 31 to 33, page 8, lines 1 to 3 and 31 to 33, the nucleotide sequence shown in Figure 2 and the alignment of the sequences disclosed in Figure 4 of *S. pennellii* with that of Figure 2 in conjunction with the legend of Figure 4 on page 13, lines 6 and 7, as a basis for the feature at issue (see point 6 above). Furthermore, the appellant referred to the disclosure of document D5 in support of how the skilled person at the time of filing of the application would have understood the genomic structure of a promoter and a gene.

9. The application reports on page 7, lines 12 to 20, that the promoter sequences of the invention comprise "*nucleotides 1 to 624 of SEQ ID NO: 1 (Fig. 2)*", which according to page 4, lines 26 to 29, comprise "*a CA motif at a position 62-61 nucleotides upstream (i.e. at positions -62 and -61 nt) of the start codon of said SP3D gene*". That the CA motif forms part of the claimed SP3D promoter sequences is also derivable from the disclosure on page 7, lines 31 to 33, which reads: "*It should be understood that in all cases the CA motif should be present and the promotor should have promotor activity*". It is further disclosed on page 8, lines 31 to 33, that "*the SP3D gene is the SP3D gene of S.*

pennellii, SP3Dpen, having a genomic nucleotide sequence consisting of nucleotides 625 to 7307 of SEQ ID NO: 1". The application furthermore discloses on page 12, lines 27 to 31, that "*Figure 2 shows the nucleotide sequence of SEQ ID NO: 1, i.e. the genomic sequence of the SP3Dpen gene including the promotor sequence (nucleotides 1-624). The CA motif has been indicated in bold and underlined; the grey boxes and double underlined region indicates the SP3D codon [...]*" (see also the sequence disclosed in Figure 2).

10. In the board's view, the application thus discloses to the skilled person in the passages indicated in point 9 above that the claimed SP3D promoters are (i) located at position 1 to 624 of the nucleotide sequence shown in Figure 2, which (ii) implies that they have a minimum length of 624 nucleotides, due to the use of the "comprising" language in the application. They further disclose that (iii) the CA motif is part of the SP3D promoter sequences which (iv) is located at nucleotides 62 and 61 upstream of the "*ATG*" start codon of the SP3D gene. The sequence in Figure 2 shows that the "*ATG*" is located at nucleotides 1875 to 1877, which means that the CA motif is located at nucleotides 1813 and 1814 (1875 minus 62 or 61). It was common ground between the parties that the skilled person would have inferred from the disclosure of the start codon "*ATG*" in Figure 2 that (v) this unambiguously identifies the start point of the coding sequence of the SP3D gene, *i.e.* that part of the gene which is translated into a protein sequence. The passages further disclose that (vi) the SP3D promoter and the SP3Dpen gene are located at nucleotides 1 to 624 and 625 to 7307 of the sequence shown in Figure 2, *i.e.* that the two sequences are located immediately adjacent to each other.

11. The appellant argued that, since the "*ATG*" start codon identified the beginning of the SP3D gene and was located at nucleotides 1875 to 1877 of the sequence shown in Figure 2, the skilled person would necessarily have derived from the disclosure that the SP3D promoter and the gene were located at nucleotides 1 to 624 and 625 to 7307 of the sequence shown in Figure 2, *i.e.* immediately adjacent to each other, that the terminal nucleotide of the promoter was in fact the nucleotide immediately preceding the "*ATG*" start codon and therefore to be located at position 1874.

11.1 The board notes that the nucleotides at position 625 to 627 of the sequence disclosed in Figure 2 read "*ACC*" and therefore not "*ATG*", which as start codon of the SP3D gene translation is located further downstream of the sequence at nucleotides 1875 to 1877. The application further discloses on page 4, lines 19 to 21, that the object of the invention "*is achieved by providing a SP3D promotor sequence, which is capable of directing transcription of a downstream SP3D gene that is operably linked to said promotor sequence*" (emphasis added). The skilled person would have derived from this passage that the claimed SP3D promoter sequences initiate the transcription of the genomic DNA of the SP3D gene into messenger RNA (mRNA), and not the translation of the mRNA into the corresponding protein sequence. This is also consistent with the disclosure in document D5, which as a standard textbook in the field of genetics reflects the common general knowledge of the skilled person with regard to promoters at the filing date of the application. Document D5 discloses that "*The upstream elements may make the initial contacts that start the assembly of the transcription apparatus at the promoter. These regions therefore determine the efficiency of assembly, and thus the rate*

at which transcription is initiated" (see page 551, column 1, first paragraph; emphasis added). Document D5 further discloses that promoters are located immediately adjacent to and upstream of the transcription start point of a gene, which is implied by the disclosed position of "*+1*" for the start point of transcription and the disclosed positions "*-10*", "*-30*", "*-60*", "*-80*" or "*-100*" for various promoter motifs located upstream thereof (see Figure 29.5). However, the transcription start point of the SP3D gene is not disclosed in the application.

11.2 Moreover, the term "gene" is commonly understood to describe the coding sequence (see point 10, item (v) above) and genomic nucleic acid sequences upstream and downstream thereof which are transcribed into mRNA, but not translated into a protein. This was not contested by the appellant.

11.3 It follows from this that the transcribed nucleic acid sequence of a gene may be longer than that part of the sequence which is actually translated into a corresponding protein sequence. This also means that the start point of transcription of a gene is not necessarily identical to the start point of translation, *i.e.* the "*ATG*" start codon, since the transcription of a gene may start earlier. It further follows that the start codon "*ATG*" does not necessarily define the beginning of a gene. Therefore in the board's view, the skilled person would not necessarily have derived from the disclosed adjacent location of the SP3D promoter and SP3D gene sequences at positions "*1 to 624*" and "*625 to 7307*" of the sequence shown in Figure 2 that the last nucleotide of the SP3D promoter is in fact the nucleotide which immediately precedes the start codon "*ATG*" at nucleotides 1875 to 1877, *i.e.*

the nucleotide at position 1874. Accordingly, the same applies to nucleotide 1251 of the feature at issue (see point 6 above), since this position of the nucleotide depends on that of the nucleotide at position 1874, assuming that the length of the disclosed promoter is 624 nucleotides (1874 minus 623). Thus, this argument of the appellant must fail.

12. Furthermore, the location of the "*nucleotides 1251 to 1874*" of the feature at issue (see point 6 above) can also not be derived from the sequence disclosed in Figure 4 in conjunction with the disclosed promoter region of "*nucleotides 544-580*" on page 13, lines 6 and 7, as argued by the appellant, even if the board in the appellant's favour assumes that the sequences disclosed in Figure 4 in fact mean the SP3D promoter nucleotides "*1 to 624*" as disclosed in Figure 2. This is so because the disclosed SP3D promoter sequences in Figure 4 consist of 36 nucleotides, which when aligned to the sequence disclosed in Figure 2 are located at nucleotides 1795 to 1830 in the latter sequence. Thus, the nucleotide sequences disclosed in Figure 4 are different from "*nucleotides 1251 to 1874*" as referred to in claim 1. Moreover, for the reasons set out in points 11.1 to 11.3 above, the disclosure in the application does not necessarily imply that the terminal nucleotide of the promoter sequences disclosed in Figure 4 is to be located at the nucleotide immediately preceding the "*ATG*" start codon disclosed in Figure 2, because the translation start point of the SP3D gene is not necessarily identical to the transcription start point. Accordingly, this argument of the appellant is likewise not convincing.

13. Lastly, the appellant argued that the skilled person, taking account of his common general knowledge that

promoters were commonly denoted by a negative numbering relative to the transcription start point of the gene (see document D5, page 511, Figure 29.5 and Figure 29.6), would have interpreted the disclosed positions of the SP3D promoter nucleotides "*1 to 624*" in Figure 2 to mean in fact "*-1 to -624*", *i.e.* nucleotides "*1251 to 1874*" as referred to in claim 1, since the start codon "*ATG*" was located at position 1875.

13.1 The board notes that the application as filed does not disclose the transcription start point of the SP3D gene but only the translation start point, *i.e.* the "*ATG*". Moreover, since the translation start point is not necessarily identical to the transcription start point for the reasons set out in points 11.1 to 11.3 above, this argument of the appellant must also fail.

14. The board therefore concludes that the feature "*nucleotides 1251 to 1874 of the nucleotide sequence as shown in Figure 2*" referred to in claim 1 as granted is not directly and unambiguously disclosed in the application as filed. Consequently, the subject-matter of claim 1 as granted extends beyond the content of the application as filed (Article 100(c) EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated