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D E C I S I O N
of 14 February 2003

Case Number: T 0345/01 - 3.3.8

Application Number: 91908986.2

Publication Number: 0531315

IPC: C12N 9/42

Language of the proceedings: EN

Title of invention:

An enzyme capable of degrading cellulose or hemicellulose

Patentee:

Novozymes A/S

Opponent:

GENENCOR INTERNATIONAL INC.,

Headword:

Cellulose degrading enzyme/NOVOZYMES

Relevant legal provisions:

EPC Art. 123(2)

Keyword:

"Main request and first auxiliary request - amendments - added subject-matter (yes)"

"Second auxiliary request - amendments - added subject-matter (no)"

Decisions cited:

T 0514/88, T 0288/92, T 0615/95, T 0684/96, T 1118/98

Catchword:

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Case Number: T 0345/01 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 14 February 2003

Appellant: Novozymes A/S
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 29 January 2001
revoking European patent No. 0 531 315 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: L. Galligani
Members: P. Julia
S. C. Perryman

whereas claim 3 as originally filed read:

"3. An enzyme according to claim 1, wherein the variations in the amino acid sequence shown in claim 1 are selected as follows
in position 1, the amino acid is Trp or Tyr;
in position 2, the amino acid is Gly or Ala;
in position 7, the amino acid is Gln, Ile or Asn;
in position 8, the amino acid is Gly or Asn;
in position 9, the amino acid is Trp, Phe or Tyr;
in position 10, the amino acid is Ser, Asn, Thr or Gln;
in position 12, the amino acid is Pro, Ala or Cys;
in position 13, the amino acid is Thr, Arg or Lys;
in position 14, the amino acid is Thr, Cys or Asn;
in position 18, the amino acid is Gly or Pro;
in position 19, the amino acid (if present) is Ser, Thr, Phe, Leu or Ala;
in position 20, the amino acid is Thr or Lys;
in position 24, the amino acid is Gln or Ile;
in position 26, the amino acid is Gln, Asp or Ala;
in position 27, the amino acid is Trp, Phe or Tyr;
in position 29, the amino acid is Ser, His or Ala;
and/or in position 32, the amino acid is Leu, Ile, Gln, Val or Thr."

Claim 4 as originally filed was dependent on claim 3 and disclosed 10 specific sequences with the amino acids defined in all positions. Independent claim 18 as originally filed concerned a carbohydrate or cellulose binding domain (CBD) homologous to a terminal A region of Trichoderma reseei cellulases, which CBD comprised an amino acid sequence defined as in claim 1 above. Claim 19 as originally filed was dependent on claim 18 defining the amino acids and the positions as in claim 3, whereas, however, in position 29, the amino

acid was Ser, His or Tyr. Claim 20 as originally filed was dependent on claim 19 and disclosed 10 specific sequences with the amino acids defined in all positions and being these 10 sequences identical to the ones disclosed in claim 4.

III. Claim 1 as granted for all the designated contracting states except ES was a combination of claims 1 and 3 as originally filed but defining the amino acids in the additional positions:

in **position 22**, the amino acid is Thr, Arg, Glu or Lys;
in **position 23**, the amino acid is Lys, Gln or Ala, or
in **positions 22 and 23**, the amino acids are Thr Lys, Arg Gln, Val Lys, Lys Lys, Arg Ala or Glu Lys;

and in positions 27 and 29 the amino acids were defined as:

in **position 27**, the amino acid is Trp or Phe;
in **position 29**, the amino acid is Ser, His, Tyr or Ala

thus, differing from the ones of originally filed claim 3 in position 27 by the deletion of Tyr and in position 29 by the addition of Tyr.

Independent claim 16 as granted concerned a CBD homologous to a terminal A region of T. reesei cellulases, which CBD comprised an amino acid sequence defined as above in claim 1 as granted.

Claims 1 to 10 for ES were in the form of method claims.

IV. The arguments of the appellant can be summarized as follows:

The introduction of preferred residues in positions 22 and 23 in claims 1 and 16 as granted fulfilled the conditions of Article 123(2) EPC. The application as originally filed was concerned with (hemi-)cellulases having a consensus sequence for a CBD. This consensus CBD sequence was defined by a broad generic formula (page 3 and claim 1, as originally filed) which was narrowed to 10 specific CBD sequences (page 5 and claim 4, as originally filed) through an intermediate generic formula (page 4 and claim 3, as originally filed) consistent with these specific CBD sequences. The specific CBD sequences of the examples, which were part of the original disclosure as a whole, were expected to represent preferred embodiments of the invention. Amended claims 1 and 16 as granted were also intermediate generic claims which, following the teaching of the application and in context with its general disclosure (page 3 lines 25 to 31 of the application as filed), had been merely narrowed to bring the consensus CBD sequence closer to these preferred examples. These amended generic claims maintained the same individual amino acids as set out in the preferred examples. These amino acids had been already individualized in each and every position of the preferred specific CBD sequences. The introduced residues were **all** taken from the examples and **only** from the examples. There was no undisclosed intermediate generalisation (such as the introduction of general aromatic residues as preferred residues), no selection of an undisclosed subgroup (**all** preferred residues were already present as individual residues in the original examples) or extension of the original disclosure (**only**

residues which were already present in the examples). Thus, the amended claims represented a mere synthesis of the individual preferred examples in accordance with the general context of the original disclosure and they fulfilled all the criteria normally used for assessing the allowability of an amendment under Article 123(2) EPC, ie they were clearly and unambiguously derivable from the application as originally filed, they could have been expected beyond any reasonable doubt and the skilled person would not have been surprised by their presence.

The appellant further relied on decisions T 615/95 (of 16 December 1997) and T 684/96 (of 24 September 1999). Both decisions were concerned with generic chemical formulae which were amended to reduce the number of possibilities in stated positions but, because the amended formulae were still very broad, no new concept was considered to be brought to the mind of the reader.

No subject matter was added by the deletion of Tyr in position 27 and the amendment in position 29 was a synthesis of two original disclosures found in claims 3 and 19 as well as in the passage bridging pages 4 and 5 of the original description.

V. The respondent (opponent) essentially argued that:

The alteration of the intermediate generic CBD sequence entirely changed its imparted technical meaning, altering the nature of the CBDs covered thereby and giving new information about preferred embodiments, particularly in positions 22, 23, 27 and 29. The existence of particular amino acid residues in certain positions of specific CBD sequences could not provide a

basis for claiming these residues in different contexts, such as the ones present in the broad range of CBD sequences encompassed by the intermediate generic CBD sequence. The intermediate generic CBD sequence was not a mere synthesis of preferred examples and it could not be redefined by arbitrary combinations with members and parts thereof. An amendment of a generic CBD sequence without a basis in the application as filed created new subject matter even if it was narrower and (the selection of) the preferred residues was obvious from the disclosure as filed. There was no proper basis in the application as filed for paired combinations of amino acids let alone for the specific ones introduced in the claims as granted. The decisions referred to by the appellant related to a different set of facts, which was not analogous to the present case (T 615/95, supra) or else the requirement for a proper basis had been exercised in addition to other assessments (T 684/96, supra).

Claim 3 as originally filed was concerned with enzymes, whereas claim 19 as originally filed was directed to CBDs. They referred to different subject matter and they were defined differently too. The preferred residues in position 29 of claims 1 and 16 as granted, being a synthesis of both formulae, represented thus added subject-matter.

VI. The board issued a communication pursuant to Article 11(2) of the Rules of Procedure of the Boards of Appeal indicating the established case law of the Boards of Appeal for amendments and its implications for the amendments introduced in the different positions.

- VII. In reply to the board's communication, the appellant filed two auxiliary requests on 10 January 2003. Auxiliary request 1 (AR1) differing from the claims as granted by the deletion in claims 1 and 16 of the paired combinations in positions 22 and 23 and auxiliary request 2 (AR2) by the deletion of claims 1 and 16 as granted.
- VIII. Oral proceedings were held on 14 February 2003. The parties essentially relied in their pleadings on the same arguments presented in writing (cf Sections IV and V above). No new requests were filed except for the set of claims for ES of the second auxiliary request.
- IX. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained as granted or, auxiliary, on the basis of auxiliary request 1 or 2 filed on 10 January 2003, and for the Contracting State ES on 14 February 2003 at the oral proceedings.
- The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

Main request

Article 123(2) EPC

1. Article 123(2) EPC requires that a European patent application or 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.

In accordance with the established case law of the Boards of Appeal, the content of an application comprises the whole disclosure that is directly and unambiguously derivable from this application including information which is **implicitly** apparent to a person skilled in the art reading the application. The gist of Article 123(2) EPC is that the public must not be taken by surprise by claims which could not directly and unambiguously have been expected on the basis of the original disclosure in the application as filed (cf *inter alia* T 514/88 OJ EPO 1992, 570, points 2.2 and 2.7, and T 1118/98 of 23 January 2002, points 2 and 8).

2. Claims 1 and 16 as granted present five differences in comparison to claims 3 and 19 of the application as originally filed, namely (i) introduction of preferred residues in **position 22**, (ii) introduction of preferred residues in **position 23**, (iii) introduction of preferred paired combination of residues in **positions 22 and 23**, (iv) in **position 27** deletion of one residue, and (v) in **position 29** introduction of one additional preferred residue (cf Section III supra).

3. No explicit basis in the application as originally filed has been indicated for the preferred residues in positions 22 and 23 and/or for the paired combination of residues in these two positions (points 2.(i) to 2.(iii) above). Thus, the question arises whether this subject-matter is (directly and unambiguously) apparent in an **implicit** manner to a person skilled in the art reading the original application as a whole.

The application as originally filed, in particular claim 1, comprises a definition of a cellulose or

hemicellulose-degrading enzyme characterized by a carbohydrate or cellulose-binding domain (CBD) which comprises a generic amino acid sequence of 33 residues, and wherein the residues are defined in 11 positions and undefined (Xaa) in the other 22 positions. The application further refers to these CBDs containing enzymes as being derivable from strains of Humicola, Fusarium or Myceliophthora and it explicitly states that some of the variations in their amino acid sequence appear to be "conservative", i.e. certain amino acids are preferred in these positions among the various CBD-containing enzymes. Preferred residues are defined in the 17 positions of claim 3 as originally filed (page 4 line 19 to page 5 line 9). The remaining 5 positions (16, 17, 22, 23 and 33) are completely undefined (Xaa) and thus, they are not expected to have any "preferred" or "conservative" residues, ie **any** possible residue out of the 20 normal residues could be expected to be found at **each and every one** of these 5 positions. There is no (implicit) reason to expect from this disclosure that any of the residues shown to be in these 5 positions by the 10 specific CBD sequences of the examples (page 5 to 6 and claim 4 as originally filed) could represent a "preferred" or "conservative" residue. These residues have to be seen as "unique" to these specific CBD sequences. Moreover, there is no (implicit) reason to single out any particular position from among all these 5 positions, ie there is no reason to expect that one or some of them could be actually different from the others and have specific properties (such as the presence of "conservative" residues) different from the other positions.

The board understands that for an amino acid sequence each position is "unique" in the sense that it defines

or specifies a "unique" position within the three-dimensional conformation of the corresponding protein or polypeptide. The presence of "preferred" or "conservative" residues in a specific position conveys to the skilled person the additional information that the (maintenance of the preferred) residue present in this position is important for achieving an appropriate folding, a suitable three-dimensional conformation and/or a functional activity of the protein or polypeptide. On the other hand, positions which do not present "preferred" or "conservative" residues will probably not be involved in any of these relevant properties.

4. It has been argued that, as the examples are always preferred embodiments, an **implicit** teaching of the application as originally filed is the narrowing of the generic CBD sequences of claims 1 or 3 by merely taking as preferred residues in each and every position of these generic CBD sequences considered in isolation the residues already present in the corresponding positions of the 10 specific CBD sequences of claim 4 as filed. The board, however, cannot follow this line of argument for the following reasons:

- (i) This alleged implicit teaching would apply to all 33 positions of the CBD sequence, including all 5 undefined positions (16, 17, 22, 23 and 33), which according to the description do not have, however, any "preferred" or "conservative" residue (with the implied lack of a structural and/or functional relevance, see point 3 above). Thus, taken at its face value this teaching already runs counter to the disclosure of the original description. Moreover,

such an implicit teaching in its **generality** cannot single out the specific positions 22 and 23 from the other three positions (16, 17 and 33). This individualisation would make these two positions different from the other three (ie having different properties), identifying a subgroup of CBD sequences which by its **particularity** goes far beyond this general implicit teaching.

- (ii) Moreover, whereas all residues of claim 3 as originally filed are residues which are found in the 10 specific CBD sequences of claim 4 as filed, there are, however, two positions with residues which are not present in any of these 10 specific CBD sequences, namely Tyr at position 1 and Lys at position 13. The selection of these two residues has not been carried out following this alleged implicit teaching (ie by taking the residues shown in claim 4 as filed). Even if, as argued by the appellant, these two residues are normal "conservative" substitutions of the residues present in the specific CBD sequences (Trp in position 1 and Arg in position 13) (and thus, within the normal expectations and/or abilities of the skilled person), the board fails to see any basis in the application as filed either for a generalisation of these "conservative" substitutions to all residues of the exemplified specific CBD sequences or else for an individualisation to specific residues other than the ones originally disclosed. The presence of these two residues shows that the selection of preferred residues is open to several possible alternatives and thus, the

alleged implicit teaching is neither direct nor unambiguous in the sense that it is not unique. If for the sake of argument, positions 22 and 23 were expected to have any "preferred" residue (which according to point 3 above is not the case), there is no implicit reason to expect that these residues would be **only and exclusively** the ones shown in claim 4 as originally filed.

(iii) In this respect too, whereas position 23 in claim 1 as granted comprises all the residues present in the corresponding position of the 10 specific CBD sequences of claim 4 as originally filed (Lys, Gln or Ala), position 22 in claim 1 as granted presents only four residues (Thr, Arg, Glu or Lys) out of five possible different residues (Thr, Arg, Glu, Lys and Val) present in these 10 specific CBD sequences. There is, however, no implicit teaching in the application as filed that could have allowed the skilled person to select in position 23 the four specific residues of claim 1 as granted from all possible five residues present in this position in the sequences of claim 4 as originally filed.

In conclusion, the skilled person could not expect (he would be surprised by) (i) that positions 22 and 23 were different from positions 16, 17 and 33 by having "preferred" or "conservative" residues and (ii) that these "preferred" or "conservative" residues were **only** the ones exemplified in the specific CBD sequences but (iii) not **all** of the residues present in these specific CBD sequences.

(iv) Furthermore, this alleged implicit teaching cannot be a basis for combining fragments (even if they are as short as paired combinations of residues) of the amino acid sequences derived from the specific examples given in claim 4 as originally filed let alone for selecting the specific paired combinations of residues 22 and 23. There is a reference in the application as originally filed to the opportunity to "shuffle" the various regions of different cellulose- or hemicellulose-degrading enzymes (paragraph bridging pages 8 to 9). However, these regions are clearly and unambiguously identified as being the CBD, R region and the catalytically active domain but not any fragment thereof.

In view of the foregoing items (i) to (iv), the board concludes that the description as originally filed does not provide any (direct and unambiguous) implicit teaching that could be seen as a valid basis for the subject matter of claims 1 and 16 as granted.

5. The appellant has also referred to decisions T 615/95 (supra) and T 684/96 (supra). According to the former decision, if there are three independent lists of sizeable length specifying distinct meanings for three residues in a generic chemical formula in a claim, then the deletion in each list of one originally disclosed meaning is allowable under Article 123(2) EPC if it does not result in singling out any hitherto not specifically mentioned individual compound or group of compounds, but maintains the remaining subject-matter as a generic group of compounds differing from the original group only by its smaller size.

The appellant has argued that the generic chemical formula of claim 3 as originally filed (implicitly) comprised positions 22 and 23 with an (implicit) list of all 20 normal possible amino acids in each position (list of sizeable length specifying distinct meanings). The deletion of 16 residues in position 22 and of 17 residues in position 23 does not result in singling out any specific group which was not already specifically mentioned in the application as originally filed as far as the remaining residues were already and explicitly mentioned in the specific examples of the application as filed.

However, as stated in points 3 and 4.(i) above, the general information conveyed to the skilled person by the presence of all 20 normal amino acids in a specific position of an amino acid sequence is different from the one conveyed by the presence of a limited number of "preferred" or "conservative" residues in this position. In the latter case, the skilled person is made aware of the possible relevance of this specific position in the conformation, structure and/or functional activity of the corresponding protein. Thus, the information conveyed to the skilled person by the deletion of some of these implicit residues and the explicit presence of "preferred" or "conservative" residues in positions 22 and 23 of claims 1 and 16 as granted is very much different from the one conveyed by the application as originally filed.

Therefore, the factual situation underlying these two decisions referred by the appellant is different from the one of the present case. Contrary to these two decisions, in the present case there is no deletion of subject matter already disclosed in the application as

originally filed but an addition of subject matter which was neither explicitly nor implicitly disclosed in the application as filed. The presence of this additional subject matter results in singling out a group of positions (and of compounds) not **specifically** mentioned in the application as originally filed.

6. Someone in possession of one or more inventions embodied in a number of closely related amino acid sequences each of which has been found to serve the same function, can when originally filing a patent application relatively freely generalize his invention and prepare a set of claims of decreasing generality ending with claims directed to the actual amino acid sequences he has found. Not even claims would be necessary where at least passages of description describe the invention at various levels of generalisation. The generalisation may be based on further experimental work, theoretical considerations or intuition. Each generalisation will amount to a different invention with a different technical content. The applicant will thus have prepared for himself fall back positions.

During prosecution of the application, or later in opposition proceedings, the applicant/patentee can restrict himself to these fall back positions without fear of violating the requirements of Article 123(2) EPC. If however the applicant wishes to restrict himself to claims based on a different generalisation not present in the fall back positions originally prepared, almost inevitably these claims will fail to meet the requirements of Article 123(2) EPC. To meet the requirements of Article 123(2) EPC it is not enough that the amended claim sought is narrower than the

broadest claim originally filed, and is consistent with the examples. The amended claim itself and all its requirements must be clearly and unambiguously derivable from the original application so that it is beyond question that it relates to an invention disclosed in the application as originally filed (cf also T 288/92 of 18 November 1993).

7. Thus, claims 1 and 16 as granted comprise subject matter which extends beyond the application as originally filed and the main request, which comprises these claims, does not fulfil the requirements of Article 123(2) EPC.

First auxiliary request

Article 123(2) EPC

8. This request differs from the main request in that the paired combinations of residues at positions 22 and 23 have been deleted. The objection raised in point 4.(iv) above for these specific paired combinations has been overcome by this request. However, the objections raised in point 3 and points 4.(i) to 4.(iii) still remain and they fully apply to this request too.

Thus, this request does not fulfil the requirements of Article 123(2) EPC.

Second auxiliary request

Article 123(2) EPC

9. Claims 1 and 2 as granted as well as claim 16 as granted have been deleted from this request. Claims 1 to 13 of this request correspond to granted claims 3 to 15 and claims 14 to 15 of this request correspond to

granted claims 17 to 18.

No objections have been raised by the respondent to the subject matter of this claim request in the two versions for all designated contracting states except ES and for ES. The board is also satisfied that the application as originally filed provides an explicit basis for this request.

Thus, the request is considered to fulfil the requirements of Article 123(2) EPC.

10. The decision to revoke the contested patent was solely based on Article 123(2) EPC. As the Opposition Division did not decide on the other grounds of opposition, the case has to be remitted to the Opposition Division for further prosecution on the basis of these claims pursuant to Article 111 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The matter is remitted to the first instance for further prosecution on the basis of the claims 1 to 15 of auxiliary request 2 submitted on 10 January 2003 for the Contracting States AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE, and claims 1 to 8 submitted at the oral proceedings on 14 February 2003 for the Contracting States ES.

The Registrar:

The Chairman:

A. Wolinski

L. Galligani