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D E C I S I O N
of 25 January 2005

Case Number: T 1050/99 - 3.3.8

Application Number: 87303761.8

Publication Number: 0251446

IPC: C12N 15/00

Language of the proceedings: EN

Title of invention:

Non-human Carbonyl hydrolase mutants, DNA sequences and vectors encoding same and hosts transformed with said vectors

Patentee:

GENENCOR INTERNATIONAL, INC.

Opponent:

NOVOZYMES A/S

Headword:

Carbonyl hydrolases/GENENCOR

Relevant legal provisions:

EPC Art. 123(2)

Keyword:

"Allowability of disclaimer - accidental anticipation - no"

Decisions cited:

G 0001/93, G 0001/03

Catchword:

-



Case Number: T 1050/99 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 25 January 2005

Appellant: NOVOZYMES A/S
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
20 September 1999 concerning maintenance of
European patent No. 0251446 in amended form.

Composition of the Board:

Chairman: L. Galligani
Members: F. L. Davison-Brunel
C. Rennie-Smith

Summary of Facts and Submissions

- I. European patent No. 0 251 446 with the title "Non-human Carbonyl hydrolase mutants, DNA sequences and vectors encoding same and hosts transformed with said vectors" was granted with 9 claims for all designated Contracting States on the basis of European patent application No. 87 303 761.8.

Granted claim 1 read as follows:

"1. A subtilisin mutant derived by the substitution of at least one amino acid residue of a precursor subtilisin with a different amino acid, so that the subtilisin mutant has at least one property which is different from the same property of the precursor subtilisin, characterised by the substitution at one or more of Tyr21, Thr22, Ser24, Asp36, Ala45, Gly46, Ala48, Ser49, Met50, Asn77, Ser87, Lys94, Val95, Leu96, Ile107, Gly110, Met124, Lys170, Tyr171, Pro172, Asp197, Met199, Ser204, Lys213, His67, Leu135, Gly97, Ser101, Gly102, Glu103, Gly127, Gly128, Pro129, Tyr214, and Gly215 of Bacillus amyloliquefaciens subtilisin and equivalent amino acid residues in other precursor subtilisins."

- II. An opposition was filed pursuant to Article 100(a) and (b) EPC for lack of novelty, lack of inventive step and lack of sufficient disclosure. The opposition division decided to maintain the patent in amended form pursuant to Article 102(3) EPC on the basis of the first subsidiary claim request then on file.

Claim 1 of the request accepted by the opposition division read as follows:

"1. A subtilisin mutant, other than a wild type subtilisin, derived by modification of the DNA sequence of a precursor subtilisin so as to result in the substitution of at least one amino acid residue of the precursor subtilisin with a different amino acid, so that the subtilisin mutant has at least one property which is different from the same property of the precursor subtilisin, characterised by the substitution at one or more of Tyr21, Thr22, Ser24, Asp36, Ala45, Gly46, Ala48, Ser49, Met50, Asn77, Ser87, Lys94, Val95, Leu96, Ile107, Gly110, Met124, Lys170, Tyr171, Pro172, Asp197, Met199, Ser204, Lys213, His67, Leu135, Gly97, Ser101, Gly102, Gln103, Gly127, Gly128, Pro129, Tyr214, and Gly215 of Bacillus amyloliquefaciens subtilisin and equivalent amino acid residues in other precursor subtilisins; with the proviso that when Gly110 is substituted by a different amino acid, there is additionally substitution at a position other than 219; **and with the exclusion of the subtilisin mutants Cys24/Cys27 and Cys199/Cys178.**" (emphasis added by the board)

- III. The appellant (opponent) filed an appeal, paid the appeal fee and submitted a statement of grounds of appeal.
- IV. The respondent (patent proprietor) answered the grounds of appeal and, in addition to the main request corresponding to that allowed by the opposition division, proposed two auxiliary requests with an amended disclaimer in claim 1.

V. In view of the referrals to the Enlarged Board of Appeal then pending under the references G 1/03 and G 2/03, the board informed the parties in a short communication dated 15 September 2003 that it intended to suspend these appeal proceedings until the Enlarged Board decision was issued. After that decision was issued, the board sent a communication dated 13 July 2004 pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal. The respondent's attention was drawn, in particular, to the fact that disclaimers such as found in claim 1 of all claim requests did not seem to fulfil the criteria to be applied when assessing allowability of disclaimers, listed in the Enlarged Board of Appeal decision G 1/03 (OJ EPO 2004, 413).

VI. The parties each sent further submissions. The respondent's submissions of 23 December 2004 were accompanied by a new main request and seven auxiliary requests which replaced all previous requests. Claim 1 of all the requests contained disclaimers.

VII. Oral proceedings took place on 25 January 2005. The respondent filed a new main request and thirteen auxiliary requests which replaced all its earlier requests.

Claim 1 of the **main request** read as follows:

"1. A subtilisin mutant derived by the modification of the DNA sequence of a precursor subtilisin so as to result in the substitution of at least one amino acid residue of a precursor subtilisin with a different

amino acid, so that the subtilisin mutant has at least one property which is different from the same property of the precursor subtilisin, characterised by the substitution at one or more of Tyr21, Thr22, Ser24, Asp36, Ala45, Gly46, Ala48, Ser49, Met50, Asn77, Ser87, Lys94, Val 95, Leu96, Ile107, Gly110, Met124, Lys170, Tyr171, Pro172, Asp197, Met199, Ser204, Lys213, His67, Leu135, Gly97, Ser101, Gly102, Gln103, Gly127, Gly128, Pro129, Tyr214, and Gly215 of Bacillus amyloliquefaciens subtilisin and equivalent amino acid residues in other precursor subtilisins; with the proviso that when Gly110 is substituted by a different amino acid, there is additionally substitution at a position other than 219; **and with the exclusion of mutations which comprise double mutants in which two cysteine residues have been substituted at amino acid residue positions forming a disulphide bridge between the two substituted cysteine residues.** (emphasis added by the board)

The feature "and with the exclusion of..." was found in claim 1 of auxiliary requests 1 to 6, the claim being formulated as process claim in auxiliary requests 3 and 4. The said feature was deleted in auxiliary requests 7 to 13.

VIII. The following document is referred to in the present decision:

(23) Hartley, B.S., Phil. Trans. R. Soc. Lond. A 317, pages 321-331, 1986, Proceedings of a Royal Society discussion meeting held on 5 and 6 June 1985.

IX. The appellant's submissions insofar as they are relevant to the present decision may be summarized as follows:

Main request, auxiliary requests 1 to 6

Admissibility of the feature "with the exclusion of..." in claim 1

- In the course of the proceedings, it had successively been argued by the respondent that the feature "with the exclusion of..." in claim 1 was a disclaimer to delimit the claimed subject-matter against an accidental anticipation, namely document (23), or a limitation of the protection conferred by excluding part of the subject-matter of the claimed invention in accordance with G 1/93 (OJ EPO 1994, 541). In fact, this feature was not allowable irrespective of whatever it was considered to be because:

Document (23) taught the double Cys24/Cys87 and Cys199/Cys178 mutants in the context of designing mutant subtilisins with improved properties. It was not an accidental anticipation which could be disposed of by way of a disclaimer. Even if it was considered allowable to delimit the claimed subject-matter against document (23) by way of a disclaimer, it nonetheless remained that the feature "with the exclusion of..." was not an acceptable disclaimer because its scope was wider than necessary (eg. it comprised double Cys mutants of other subtilisins than that of *B. amyloliquefaciens* disclosed in document (23)).

The excluded subject-matter did not correspond to the technical contribution in the patent in suit. By failing to mention any position where the two cysteine residues may be substituted, the exclusion covered substitutions at any positions providing that a disulphide bridge could be formed. The limitation, thus, created a technical contribution to the art which was not in the application as filed. In addition, the patent in suit disclosed that a first category of mutants was thermally and oxydatively stable, that this category comprised double Cys24/Cys87 mutants and that these mutants were indeed thermostable but only under conditions where di-sulphide bridges were formed between the two Cys (page 30, lines 16, 20 to 24 and example 11). Thus, the exact subject-matter to exclude would be Cys24/Cys87 double mutants under oxidising conditions.

Admissibility of auxiliary claim requests 7 to 13

These claim requests should be refused as being late filed. In each of them, claims were present which still contained disclaimers whereas the unsuitability of disclaimers had already been pointed out in the board's communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal. The respondent should not be allowed to tailor his requests on the spur of the moment depending on what appeared to be the board's current thinking.

- X. The respondent's submissions insofar as they are relevant to the present decision may be summarized as follows:

Main request, auxiliary requests 1 to 6

Admissibility of the feature "with the exclusion of..." in claim 1

- When attempting to meet the requirements of novelty and inventive step, it was a permissible course of action to abandon parts of the originally described invention. Amendments to that effect could be positively or negatively formulated, whichever was the clearest. Here, the subject-matter of claim 1 had been "negatively" amended by excluding from the scope of protection the first category of mutants described on page 49, lines 21 to 27 of the application as filed. What had, thus, been done did not depart from the usual way of achieving patentability.

- The amendment was in accordance with the principle laid down in the Enlarged Board decision G 1/93 (supra) that a feature which did not provide a technical contribution to the subject-matter of a claimed invention but merely limited the protection conferred by excluding part of said invention was not to be considered as subject-matter extending beyond the content of the application as filed within the meaning of Article 123(2) EPC. Indeed, giving up some of the subject-matter in the application as filed did not make a contribution to what was left.

- The amendment to the claim was so worded as to limit the invention as originally described. If it so happened that this wording was of the same kind as that used for wording disclaimers aimed at delimiting an invention against a piece of prior art, this did not mean that the limitation should be regarded as a disclaimer.

- In the Enlarged Board decision G 1/03 (supra) where criteria were established for the allowability of disclaimers under Article 123(2) EPC, the situation was clearly different since neither the disclaimer nor the disclaimed subject-matter then under consideration had a basis in the application as filed. These criteria did not apply to the present exclusion. In particular, the finding in G 1/03 that a disclaimer may be allowable to delimit the claimed subject-matter against an anticipation under Article 54(2) EPC only in the case where that anticipation was accidental was not relevant to the present case.

The abandonment of part of the invention by way of exclusion was allowable under Article 123(2) EPC.

Admissibility of auxiliary requests 7 to 13

In its communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal, the board expressed many concerns about several embodiments of, in particular, claims 1 and 2 of the main request then on file. The purpose of this communication was solely to express a preliminary opinion and, therefore, it did

not make sense for the respondent to file a great number of auxiliary claim requests in advance of the oral proceedings when it would become clearer at oral proceedings which of these concerns were definite. Furthermore, objections were raised at oral proceedings which had never been mentioned before. The respondent had to be allowed to file further requests to take the new developments into consideration.

- XI. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 0 251 446 be revoked.

The respondent (patentee) requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request or auxiliary requests 1 to 13 filed during the oral proceedings.

Reasons for the decision

Auxiliary requests 1 to 6; admissibility

1. The new main and first to sixth auxiliary requests filed by the respondent during the oral proceedings differ from the corresponding previous requests only as to the extent and exact wording of certain disclaimers. They contain nothing which could be considered to require extensive additional consideration or which took the appellant by surprise. Accordingly the Board considers them to be admissible.

Main request, Auxiliary requests 1 to 6

Article 123(2) EPC; claim 1

2. Claim 1 of the main request and of auxiliary requests 1, 2, 5 and 6 is a "product" claim directed to a subtilisin mutant made by recombinant DNA techniques, while claim 1 of auxiliary requests 3 and 4 is a "process" claim directed to a process for modifying the DNA sequence of a precursor subtilisin. In all these requests the claim contains at the end two disclaiming features which were not present in claim 1 as granted (a "product" claim), namely **i)** "with the proviso that when Gly110..." and **ii)** "with the exclusion of mutations which comprise double mutants in which two cysteine residues have been substituted at amino acid residue positions forming a disulphide bridge between the two substituted cysteine residues". Claim 1 of auxiliary requests 1 and 2 contains at the beginning a further negative feature "other than wildtype subtilisin".

3. As regards in particular the disclaiming feature **ii)**, this was introduced into claim 1 at the oral proceedings before the board in replacement of an earlier disclaimer which was aimed at excluding from protection the two specific double mutants disclosed in document (23). The replacement was done in an attempt to circumvent the objection that, since document (23), which was state of the art under Article 54(2) EPC, was not an accidental anticipation, the presence of such a disclaimer would have prejudiced the allowability of the claim under Article 123(2) EPC, in view of the ruling on disclaimers in decision G 1/03 (supra, cf in particular points 2.1 and 2.3 of the order). The

earlier disclaimer was reformulated as an "exclusion" feature on the basis of a more general teaching in the application as filed in relation to whole category of double mutants wherein two Cys residues were substituted which also covered those of document (23). The respondent argued that, as the feature in question related now to subject-matter which was "disclosed" in the application as filed, the amendment derived therefrom was to be regarded as a mere "waiver" of part of the disclosed invention rather than as a disclaimer. Consequently, in his view, the criteria applying to "undisclosed" disclaimers as set out in decision G 1/03 (supra) did not apply. He, furthermore, argued that, in view of decision G 1/93 (supra), a patentee was always allowed to abandon any part of the originally described invention as he saw fit, including by way of a negative amendment, if - as in the present case - the said exclusion did not bring any technical contribution to the claimed invention.

4. The decision G 1/93 (supra) deals with the conflicting requirements of Article 123, paragraph 2 and 3, EPC and, in this framework, it establishes that:

"A feature which has not been disclosed in the application as filed but which has been added to the application during examination and which, without providing a technical contribution to the subject-matter of the claimed invention, merely limits the protection conferred by the patent as granted by excluding protection for part of the subject-matter of the claimed invention, is not to be considered as subject-matter which extends beyond the content of the

application as filed within the meaning of Article 123(2) EPC." (cf point 2 of the order).

5. It is readily apparent that the respondent's argument (point 2, supra) only took into account half of the relevant sentence in point 2 of the order. In fact, the situation then considered was different from that in the present case in a very important aspect. Here, the exclusion feature was not added at the examination stage and, thus, was not part of the granted claims. To the contrary, it was added post-grant in order to overcome a novelty objection vis-à-vis an Article 54(2) EPC prior art document. Thus, it is not possible to transfer and apply the findings in G 1/93 to this case.

6. Furthermore, it would be wrong to interpret the quoted decision as giving the patentee the possibility to waive part of the invention at any time and under any circumstances, as long as it does not bring any technical contribution. This is quite clear from the Enlarged Board of Appeal's decision G 1/03 (point 2.5 of the reasons) which deals in particular with the exclusion from a granted claim of embodiments which were disclosed in the application as filed and later shown not to be workable, ie which do not bring any technical contribution to the claimed invention. This decision establishes that such embodiments may not be waived by an explicit exclusion in the granted claim ie by way of disclaimers.

7. In respect of the contention that the ruling on disclaimers of decision G 1/03 (supra) does not apply to the present case, the board's reasoning is as follows:

(a) The term "disclaimer" is defined, in accordance with the case law and as reported in decision G 1/03 (supra, point 2 of the reasons) as meaning:

"...an amendment to a claim resulting in the incorporation therein of a "negative" technical feature, typically excluding from a general feature specific embodiments or areas."

(b) The expression "with the exclusion of..." in the amendment to claim 1 of the requests at issue is a *negative feature*: the subject-matter which is excluded (mutations) has a technical meaning and therefore, the exclusion is a *negative technical feature*; the generically claimed subtilisin mutants correspond to a *general feature* and the double Cys mutants are a *specific embodiment* of this general feature. Thus, there is no doubt that the amendment "with the exclusion of..." answers to the definition of a disclaimer.

(c) In the application as filed, on page 49, various categories of mutants belonging to the invention are described. In particular, in lines 21 to 27: "The first category comprises double mutants in which two cysteine residues have been substituted at various amino acid residue positions within the subtilisin molecule. Formation of disulphide bridges between the two substituted cysteine residues results in mutant subtilisins with altered thermal stability and catalytic activity". Thus, there is a basis in the application for the subject-matter which is excluded in the claim. However, that subject-matter is presented as

a **part of the invention, not** as an area which should be excluded or avoided. In this sense, **the disclaimer is in fact an "undisclosed" disclaimer** because there is no disclosure in the application as filed of the disclaimer per se.

(d) In the respondent's opinion, because point 1 of the order of decision G 1/03 refers to a situation where neither the disclaimer nor the subject-matter excluded by it is disclosed in the application as filed, point 2 of said order should be understood as solely relating to such a situation, although it specifically deals with an undisclosed disclaimer - no reference at all being made to the subject-matter excluded by it. The board does not share this opinion nor, of course, its corollary that the criteria for admissibility of disclaimers should not apply in the present case. As already mentioned in point 6, supra, the Enlarged Board considered in the body of the decision, a situation such as the present where the disclaimer is not disclosed in the application as filed and the subject-matter excluded by it is (point 2.5 of the reasons).

From these observations the board concludes that the ruling of decision G 1/03 (supra), which deals with the allowability of disclaimers not disclosed in the application as filed (cf point 2 of the reasons), fully applies to the present case.

8. In point 2.6.5 of G 1/03 (supra), the Enlarged Board of Appeal states that:

*"...a disclaimer may serve **exclusively** the purpose for which it is intended and **nothing more...** In the case of*

a disclaimer concerning state of the art under Article 54(2) EPC, its purpose is to establish novelty vis-à-vis an accidental anticipation as defined in this decision... If a disclaimer has effects which go beyond its purpose as stated above, it is or becomes inadmissible."

In point 2.2.2 of the reasons, an accidental anticipation is defined as a disclosure

"...so unrelated and remote that the person skilled in the art would never have taken it into consideration when working on the invention"

In point 3 of the reasons it is further stated:

"...a disclaimer should not remove more than is necessary to restore novelty or to disclaim subject-matter excluded from patentability for non-technical reasons."

9. Based on the quoted passages of decision G 1/03, it can only be concluded that the disclaiming feature **ii)** of the requests at issue is not allowable. In fact:

(a) The feature was introduced into the claim to delimit its subject-matter from a document which is prior art for the assessment of novelty under Article 54(2) EPC. Document (23) describes a scientific contribution made to a Royal Society discussion meeting held on 5 and 6 June 1985. It is concerned, in particular, with designing and constructing novel *B. amyloliquefaciens subtilisin* mutants with improved

properties. In this framework, it discloses on page 329:

"Another obvious target for protein engineering of subtilisin is to improve stability by introducing new disulphide bridges. ... Only two candidates for isosteric internal substitutions emerged; a pair of hydrogen-bonded residues (Ser-24-Ser-77); and Met-199, whose methyl group is in contact with Gly-178."

These mutants would fall within the scope of claim 1, were it not for the disclaimer.

(b) Comparing the teaching of document (23) and the wording of the disclaiming feature **ii)**, it is readily apparent that the disclaimer **covers more than** the two specific double mutants disclosed in the prior art insofar as it comprises double substituted subtilisin mutants irrespective of the origin of the subtilisin and, also, double Cys substitutions at any pair of amino acids providing that these amino acids are close enough for the substitution to lead to the formation of a disulphide bridge. It, thus, removes from the claim more than is necessary to restore novelty and does not fulfil the criteria in point 3 of G 1/03 (supra).

(c) In the same manner, it cannot be denied that document (23) is concerned with the very same problem as the patent in suit, namely, the isolation of mutant subtilisin molecules. Its teaching, therefore, could not have been ignored by the skilled person when making the invention. Consequently, document (23) is **not an accidental anticipation**. A disclaimer is not suited to delimit the claimed subject-matter from its teaching.

10. For the above reasons, the board concludes that the disclaimer "with the exclusion of..." is not allowable under Article 123(2) EPC as it goes beyond the stated purpose of a disclaimer (cf point 8 supra).
11. The main request and auxiliary requests 1 to 6 all contain the disclaimer. They are rejected for failing to fulfil the requirements of Article 123(2) EPC. Under these circumstances, it is not necessary to examine the other outstanding issues in relation to these requests.

Auxiliary requests 7 to 13

12. The seventh to thirteenth auxiliary requests were filed by the respondent during the oral proceedings when it had become apparent that the main and first to sixth auxiliary requests, also filed during the oral proceedings (cf point 1, supra), were unlikely to be allowed. On considering the seventh to thirteenth auxiliary requests it was immediately apparent that they all contained disclaimers which, although not including that discussed in paragraphs 3 to 10 above (feature **ii**), point 2, supra), were none the less disclaimers which would have required further extensive discussion in view of the Enlarged Board of Appeal decision in G 1/03 (supra). No request avoiding the use of disclaimers was ever filed in spite of repeated warnings by the board that requests containing disclaimers posed serious problems (cf eg section V, supra).
13. The board must bear in mind that these appeal proceedings were suspended while the Enlarged Board of

Appeal was considering the referral to it of questions concerning disclaimers (the referral which gave rise to G 1/03); that this suspension was brought to the parties' attention (see paragraph V above); that, as just mentioned, after G 1/03 was published, the board sent a communication to the parties drawing particular attention to the terms of that decision and its possible consequences for the present case; and that the respondent had thereafter filed sets of requests, all of which contained disclaimers, both with its letter of 23 December 2004 and at the beginning of the oral proceedings. The respondent thus had ample opportunity to file requests which did not contain disclaimers and which met the requirements of the Enlarged Board decision. A party which ignores such opportunity cannot expect the board to exercise the discretion to admit very late-filed requests in its favour. Accordingly, the board considers the seventh to thirteenth auxiliary requests inadmissible.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:

A. Wolinski

L. Galligani