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**Datasheet for the decision
of 7 April 2016**

Case Number: T 1791/11 - 3.3.02

Application Number: 02745188.9

Publication Number: 1409659

IPC: C12N9/54, C11D3/386

Language of the proceedings: EN

Title of invention:
SUBTILASE VARIANTS

Patent Proprietor:
Novozymes A/S

Opponent:
Danisco US Inc.

Headword:
Subtilase variants/NOVOZYMES

Relevant legal provisions:
RPBA Art. 15(3)
EPC Art. 56

Keyword:
Oral proceedings - held in absence of appellant
Inventive step - (no)

Decisions cited:

T 0537/02, T 1329/04

Catchword:



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Case Number: T 1791/11 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 7 April 2016

Appellant: Novozymes A/S
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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
15 June 2011 concerning maintenance of the
European Patent No. 1409659 in amended form.**

Composition of the Board:

Chairman U. Oswald
Members: T. Sommerfeld
L. Bühler

Summary of Facts and Submissions

- I. European patent No. 1409659, based on European patent application No. 02745188.9, which was filed as an international patent application published as WO 2003/006602, was granted with 13 claims.
- II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and lack of inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).
- III. By an interlocutory decision announced at the oral proceedings on 13 April 2011 and posted on 15 June 2011, the opposition division decided that the patent was to be maintained in amended form on the basis of the fifth auxiliary request filed during oral proceedings (Articles 101(3)(a) and 106(2) EPC).

The opposition division considered that the main request, as well as the first, second and third auxiliary requests did not comply with Article 123(2) EPC, and that the fourth auxiliary request contravened Article 83 EPC.

- IV. Both the patent proprietor and the opponent lodged an appeal against that decision.

In the statement of the grounds of appeal, the appellant-patent proprietor requested that the patent be maintained on the basis of the main request or alternatively according to one of auxiliary requests 1 to 8, all filed with the grounds of appeal.

In its statement of the grounds of appeal, the appellant-opponent requested that the decision be set aside and that the patent be revoked in its entirety.

- V. A summons for oral proceedings before the board was issued, scheduling oral proceedings for 7 April 2016.
- VI. By letter dated 10 February 2016, the appellant-opponent withdrew its request for oral proceedings and stated that it would not attend oral proceedings.
- VII. By letter dated 7 March 2016, the appellant-patent proprietor replaced all requests on file by a new main request and new auxiliary requests 1 to 7.

Claim 1 of the **main request** reads:

"1. A variant of the BLSAVI subtilase, comprising the substitution V68A, where the variant has protease activity, and the position corresponds to a position of the amino acid sequence of subtilisin BPN', shown in Figure 1, wherein the variant is V68A+S106A; or V68A+V139I."

Claim 1 of **auxiliary request 1** is identical to claim 1 of the main request.

Claim 1 of **auxiliary request 2** differs from claim 1 of the main request by addition of the feature "optionally further comprising at least one modification in the positions 27, 36, 56, 76, 87, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 120, 123, 159, 167, 170, 206, 218, 222, 224, 232, 235, 236, 245, 248, 252 or 274 (BASBPN numbering)".

Auxiliary request 3 corresponds to the claims as maintained by the opposition division. Its claim 1 differs from claim 1 of the main request by the following amendments (insertions underlined, deletions struck through):

"1. A variant of the BLSAVI subtilase, ~~comprising the substitution V68A,~~ where the variant has protease activity, and the position corresponds to a position of the amino acid sequence of subtilisin BPN', shown in Figure 1, wherein the variant ~~is~~ differs from the BLSAVI subtilase only by the substitutions V68A+S106A; or V68A+V139I, optionally with at least one modification in the positions 27, 36, 56, 76, 87, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 120, 123, 159, 167, 170, 206, 218, 222, 224, 232, 235, 236, 245, 248, 252 or 274 (BASBPN numbering)."

Claim 1 of **auxiliary request 4** differs from claim 1 of the main request by the following amendments:

"1. A variant of the BLSAVI subtilase, comprising the substitution V68A, where the variant has protease activity and has improved wash performance compared to BLSAVI, and the position corresponds to a position of the amino acid sequence of subtilisin BPN', shown in Figure 1, wherein the variant is V68A+S106A; or V68A+V139I."

Claim 1 of **auxiliary request 5** is identical to claim 1 of auxiliary request 4.

Claim 1 of **auxiliary requests 6 and 7** differs from claim 1 of, respectively, auxiliary requests 2 and 3 by addition of the feature "and has improved wash

performance compared to BLSAVI" (as in auxiliary requests 4 and 5).

- VIII. Oral proceedings took place as scheduled, in the absence of the appellant-opponent. At the end of the oral proceedings, the Chairman announced the decision of the board.
- IX. The documents cited during the proceedings before the opposition division and the board of appeal include the following:
- D1 WO99/20770
 - D9 WO95/10615
 - D10 Experimental Report from 15 February 2011
- X. The submissions of the appellant-patent proprietor, in so far as relevant to the present decision, may be summarised as follows:

D1 was the closest prior art, and the technical problem was to provide alternative variants to BLSAVI that had improved wash performance compared to the parent enzyme. The solution was the subject-matter as claimed and the problem had been solved, as made plausible by the application as filed and further confirmed by D10. Unambiguous disclosure of improved wash performance could be found throughout the application as filed, for example page 1, last paragraph to page 2, line 2; page 20, last 3 lines to page 21, line 2; page 24, lines 1 to 18; page 25, third paragraph; Example 3, in particular page 57, last paragraph. Decision T 1329/04 related to a very different scenario, because, in the present case, several variants were disclosed, of which it was to be expected that some would show improvement in wash performance. D1 provided no hint or teaching to

make the substitutions V68A with S106A or V139I and no pointer that the V68A substitution was of importance; in fact, this substitution was clouded by all other substitutions present in the variants of D1. Claim 1 of D1 made clear that position 103 was important, not V68A. Thus nothing in D1 led to a focus on the V68A substitution, let alone to combining it with any of the other two substitutions as claimed. Moreover D1's V68A-comprising variants did not all show improved wash performance. None of the claimed variants were at all suggested in the prior art and thus their provision would not have been an obvious solution to the technical problem.

XI. The arguments of the appellant-opponent, in so far as relevant for the present decision, may be summarised as follows:

The application as filed contained no indication at all that the specific variants claimed improved wash performance. The combination variants of claim 1 as maintained were only set out on page 23, under "Savinase (BLSAVI)", as being "considered interesting" (second paragraph of page 23) but with no indication of why. In Example 2, the only comment about the activity of these variants was that they all exhibited proteolytic activity (page 56, first paragraph). As such, the technical problem should be the provision of further arbitrary Savinase mutants which retained some degree of protease activity, regardless of any other technical effect. Such a technical problem was trivial as it just amounted to providing arbitrary mutants regardless of effect; provision of such mutants was obvious, as confirmed in T 537/02 (Reasons, point 22). Should the patentee's version of the technical problem be followed, i.e. the

provision of variants with improved wash performance, then said problem could not be considered solved, because the only data on file (D10) should not be taken into consideration: in fact, the application did not fulfil the requirement of credibility/plausibility set out in T 1329/04 for admissibility of post-filed data. Moreover, variants of Savinase having the substitution V68A and showing improved wash performance over Savinase were known in the art at the priority date: e.g. D1 showed a number of such variants which had improved wash performance in relation to the reference Savinase variant N76D/S103A/V104I, which was itself known to have significantly improved wash performance over wild type Savinase, as illustrated in D9.

XII. The appellant-patent proprietor requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request, or, alternatively, of auxiliary requests 1 or 2, all filed with letter dated 7 March 2016, or, alternatively, that the appellant-opponent's appeal be dismissed (auxiliary request 3), or, alternatively that the patent be maintained on the basis of one of auxiliary requests 4 to 7, all filed with letter dated 7 March 2016.

The appellant-opponent requested in writing that the decision under appeal be set aside and that the European patent No. 1 409 659 be revoked.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of the appellant-opponent who had been duly summoned but decided not to attend.

The present decision is based on facts and evidence put forward during the written proceedings and on which the appellant has had an opportunity to comment.

Moreover, as stipulated by Article 15(3) RPBA the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case.

3. Main request

- 3.1 Article 123(2) EPC

- 3.1.1 Claim 1 of the main request is directed to specific variants of BLSAVI which are the variants V68A+S106A or V68A+V139I. The use of the closed language "wherein the variant is..." implies that only the two specific variants are encompassed by the claim, hence leaving no room for further mutations. Such a subject-matter finds an explicit basis in originally filed claim 6, which was directed to 30 alternative BLSAVI variants, among which the two variants now in claim 1.

- 3.1.2 The board thus comes to the conclusion that claim 1 of the main request fulfils the requirements of Article 123(2) EPC.

- 3.2 Inventive step

3.2.1 The present patent discloses "novel subtilase variants exhibiting alterations relative to the parent subtilase in one or more properties including: Wash performance, thermal stability, storage stability or catalytic activity" (application as filed: page 1, first paragraph; page 16, fourth paragraph). Specific variants of BPN' (BASBPN) and of Savinase (BLSAVI) are set out on page 23 of the application as filed as being "considered interesting". The paragraph immediately following this list of variants then states that "The wash performance of a selected variant of the invention may be tested in the "Model Detergent Wash Performance Test" disclosed in Example 3 herein". No results concerning wash performance (or any other properties) are however provided for any of the listed variants, nor is it apparent why these variants have been selected as "interesting". The only information concerning the activity of these variants in the application as filed is found on page 56, first paragraph, where it is stated that "All these variants exhibited proteolytic activity as indicated above" (apparently referring to page 50, where the proteolytic activity is further defined). It can thus be concluded that the patent aims at providing subtilase variants with improved properties, in particular with improved wash performance, and that it discloses a number of selected "interesting" variants which are however still to be tested for their performance. It is not apparent from the patent which of the selected variants - if any - do indeed display improved wash performance as compared to the parent subtilase. In fact, while it may be expected that some of the many variants disclosed by the patent may display improved wash performance, it is not rendered plausible by the patent that this property is present in any one of the specific variants.

- 3.2.2 The closest prior art is document D1. Like the patent, it discloses subtilisin variants "having a different proteolytic activity, stability, substrate specificity, pH profile and/or performance characteristic as compared to the precursor carbonyl hydrolase from which the amino acid sequence of the variant is derived" (page 23, first paragraph). In particular, D1 discloses protease variants derived from a *Bacillus subtilisin*, "more preferably" derived from *Bacillus lentus* subtilisin and/ or subtilisin 309 (D1, page 23, lines 15 to 17). Subtilisin 309 is BLSAVI, as apparent from the patent application (page 4, sixth full paragraph). Example 1 of D1 (starting on page 38), discloses the production of such variants (displayed in Table 3), a large number of which are then tested for their wash performance in Example 2 (starting on page 60). Among the variants tested are also variants that have the substitution V68A and show improved wash performance over wild type Savinase/BLSAVI (further discussed below).
- 3.2.3 The difference to claim 1 of the main request is that the specific variants claimed, i.e. the variants V68A+S106A and V68A+V139I, are not disclosed. There is however no data in the patent application or elsewhere on file which allows the performance of the claimed variants to be compared with that of the variants of D1. Accordingly, the technical problem in view of D1 has to be formulated as the provision of further variants of BLSAVI. Such problem can be considered plausibly solved by the claimed subject-matter, since the patent discloses that the claimed variants have proteolytic activity (as discussed above, section 3.2.1).

3.2.4 However, the mere provision of further subtilase variants, of which the claimed variants are just two among many possible alternative solutions, would be obvious for the skilled person, because "simply proposing a series of possible mutations without showing an effect is not considered to involve any inventive contribution over the prior art wherein a number of other mutations has already been proposed" (decision T 537/02 of 19 October 2004, Reasons 22). Claim 1 of the main request is thus considered to lack an inventive step.

For the sake of completeness, it is furthermore noted that D1 already discloses the substitution V68A as being one among a number of possible mutations that leads to variants with improved properties, and variants comprising this mutation were shown in D1 to have an improved wash performance: as can be seen in Table 4 (displaying the results for the wash performance test of Example 2), variants comprising the V68A substitution consistently show an improved wash performance in comparison with the reference protease variant N76D/S103A/V104I, at least within the detergent composition A (see tables on page 61 and 65 to 67). Improved wash performance was also shown in D1 for a specific variant which only differs from the reference variant N76D/S103A/V104I by the presence of the V68A substitution (page 65, row 14 of the Table). It should be noted that the protease variant N76D/S103A/V104I was itself known to have significantly improved wash performance over the wild type subtilase, as illustrated in D9 (table VII on page 34, 10th line of the table). It would thus not come as a surprise that mutants comprising this particular mutation (independently of the presence of other mutations)

eventually showed better wash performance than the parent Savinase/BLSAVI.

- 3.2.5 The appellant-patent proprietor formulated the technical problem differently, namely as the provision of further variants with improved wash performance in relation to the parent BLSAVI, and argued that the patent application made plausible that the claimed variants indeed solved such a problem. D10 should be taken into consideration as post-published data confirming what the patent application had already rendered plausible. The solution would furthermore be inventive because there was no pointer in D1 to the claimed mutations and no disclosure at all in the prior art of the claimed mutation combinations.
- 3.2.6 The board cannot agree with the arguments of the appellant-proprietor. As discussed above, the patent does not provide any experimental data concerning the claimed variants (or any of the many listed variants) and thus no functional characterisation of the variants by an alleged advantage should be taken into account when formulating the technical problem. Otherwise, if the technical problem was formulated to include any such advantage, then it would, in the absence of any experimental data in the patent application, not be possible to conclude that such problem had been plausibly solved: this would thus require reformulating the technical problem in a less ambitious manner, resulting in the problem as formulated by the board.
- 3.2.7 The post-published experimental data of D10, which indeed shows that the claimed variants have better wash performance than the parent BLSAVI (Table 2), could only be taken into account if it just served to confirm

what had been rendered plausible by the patent application.

In fact, according to established case law, "the definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve. Therefore, even if supplementary post-published evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve" (T 1329/04 of 28 June 2005, Catchword).

As discussed above (section 3.2.1), it is apparent from the patent application itself that it was not yet known which variants solved the problem and that a test still had to be performed to confirm the alleged advantage. The board thus comes to the conclusion that the patent does not render it plausible that the claimed subject-matter solves the technical problem as formulated by the appellant-proprietor, and the experimental post-published evidence of D10 is in fact the sole basis allowing to conclude that said problem has been plausibly solved.

4. Auxiliary request 1 - Inventive step

4.1 Claim 1 of auxiliary request 1 is identical to claim 1 of the main request and thus, for the same reasons as given above, also fails to meet the requirements of Article 56 EPC.

5. Auxiliary request 2 - Inventive step

5.1 Claim 1 of this request differs from claim 1 of the main request solely in the addition of an optional feature. Since the optional feature does not restrict the claimed subject-matter, auxiliary request 2 is also considered to lack an inventive step, for the same reasons as for the main request.

6. Auxiliary request 3 - Inventive step

6.1 The board fails to see any difference in the subject-matter covered by claim 1 of this request and claim 1 of auxiliary request 2, and the appellant-proprietor also agreed that in fact they covered the same subject-matter. As such, auxiliary request 3 also contravenes the requirements of Article 56 EPC for the reasons given for the main request.

7. Auxiliary requests 4 and 5 - Inventive step

7.1 Claim 1 of these requests differs from claim 1 of the main request in that the variants are further defined by a functional feature, namely that they have "improved wash performance compared to BLSAVI". The board notes that, since the claim is a product claim covering two specific variants, such functional features are in fact redundant as they refer to intrinsic properties of the product, which the product either possesses or not. The subject-matter claimed, namely the claimed variants, is still the same whether the intrinsic property is recited in the claim or not. As such, claim 1 of auxiliary requests 4 and 5 does not fulfil Article 56 EPC for the same reasons as for the main request.

8. Auxiliary requests 6 and 7 - Inventive step

- 8.1 Claim 1 of auxiliary request 6 only differs from claim 1 of auxiliary requests 4 and 5 in the addition of an optional feature, which does not further limit the claimed subject-matter. As such, the same considerations as for auxiliary requests 4 and 5 also apply to this request. Claim 1 of auxiliary request 7, on its turn, only differs from claim 1 of auxiliary request 6 in the use of the same language as in auxiliary request 2. As discussed above in relation to auxiliary request 2, the subject-matter covered by claim 1 of auxiliary request 7 is considered to be the same as that covered by claim 1 of auxiliary request 6.
- 8.2 Hence, auxiliary requests 6 and 7 also fail to 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 revoked.

The Registrar:

The Chairman:



N. Maslin

U. Oswald

Decision electronically authenticated