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Datasheet for the decision
of 11 December 2015

Case Number: T 1484/11 - 3.3.08
Application Number: 02799344.3
Publication Number: 1465655
IPC: A61K38/46
Language of the proceedings: EN

Title of invention:
MICROBIALLY-EXPRESSED THERMOTOLERANT PHYTASE FOR ANIMAL FEED

Applicant:
AB Enzymes GmbH

Headword:
Thermotolerant phytase/AB ENZYMES

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4), 13

Keyword:
"Main request and auxiliary request I - admission into the proceedings (no)
Auxiliary request II - inventive step (no)
Decisions cited:
G 0009/91, G 0010/91, T 0923/92, T 0915/94, T 1139/08

Catchword:
Case Number: T 1484/11 - 3.3.08

DECISION
of Technical Board of Appeal 3.3.08
of 11 December 2015

Appellant: AB Enzymes GmbH
(Applicant)
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Decision under appeal: Decision of the Examining Division of the European Patent Office posted on 9 February 2011 refusing European patent application No. 02799344.3 pursuant to Article 97(2) EPC.

Composition of the Board:
Chairman M. Wieser
Members: M. R. Vega Laso
W. Ungler
Summary of Facts and Submissions

I. The appeal by the applicant (appellant) lies from a decision of an examining division of the European Patent Office under Article 97(2) EPC posted on 9 February 2011, refusing the European patent application No. 02799344.3 with the title "Microbially-expressed thermostable phytase for animal feed". The application had been filed under the Patent Cooperation Treaty (PCT) and published as WO 03/057247.

II. In the decision under appeal, the examining division found that the subject-matter of the claims according to the main request and the auxiliary request ("auxiliary request 1") then on file did not involve an inventive step within the meaning of Article 56 EPC.

III. Claim 1 of the main request read:

"1. A method to prepare a thermostable phytase, comprising:
expressing in a microbial host cell an expression cassette comprising a promoter operably linked to a nucleic acid molecule encoding a thermostable phytase wherein, the nucleic acid molecule comprises an XhoI and NotI restriction fragment of SEQ ID NO: 4."

IV. Claim 1 of the auxiliary request read:

"1. A method to prepare a thermostable phytase, comprising:
expressing in a microbial host cell an expression cassette comprising a promoter operably linked to a nucleic acid molecule encoding a thermostable phytase comprising SEQ ID No. 1."
Claims 2 to 34 of both requests were identical.

V. Together with its statement setting out the grounds of appeal, the appellant filed a set of amended claims that replaced the sets of claims underlying the decision under appeal. The appellant requested interlocutory revision according to Article 109(1) EPC or, failing that, that the board sets aside the decision under appeal and orders the grant of a patent on the basis of the amended claims or any further claims to be filed in appeal proceedings. Subsidiarily, oral proceedings were requested.

VI. The examining division did not rectify its decision and referred the case to the board of appeal (Article 109(1) EPC).

VII. The board summoned the appellant to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons, the board drew attention to Article 12(4) RPBA and indicated that the admission of the new set of claims into the proceedings would have to be discussed at the oral proceedings. The board also made observations on substantive issues relating to Articles 84 and 56 EPC.

Upon request by the appellant, the oral proceedings were postponed twice.

VIII. On 15 July 2015, the appellant replied to the board's communication and filed three sets of claims as, respectively, main request and auxiliary requests I and II which replaced the set of claims filed together with the statement of grounds of appeal.
IX. Oral proceedings were held on 11 December 2015.

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


XI. The submissions made by the appellant concerning issues relevant to this decision, were essentially as follows:

Admission of the claims according to the main request and auxiliary request I into the proceedings – Articles 12(4) and 13 RPBA

The claims filed in response to the board's communication were not characterized by a particular complexity. In fact, the claims of the main request corresponded to the claims already on file with a minor amendment to comply with the provisions of Article 84 EPC. Although claims 1 and 2 were directed to a thermostolerant phytase and a nucleic acid molecule encoding a thermostolerant phytase, the relevant issues were the same as for the claims directed to the method of preparing the phytase. The claims of auxiliary request I corresponded to the claims filed together with the statement of grounds of appeal, except that the subject-matter of claims 1 and 2 had been incorporated into claim 3, and that minor amendments had been introduced to comply with Article 84 EPC.

Since during the oral proceedings the examining division did not specify the reasons for the denial of an inventive step, it was not clear to the applicant which amendments could be introduced in order to satisfy the requirement of Article 56 EPC. Thus, the present amended claims could not have been filed in
examination proceedings. If Article 12(4) RPBA were applied restrictively, the applicant would be hindered from filing claims which, in exactly the same wording, had not already been filed with the first instance. It was hardly imaginable that this could be the intention of Article 12(4) RPBA.

**Auxiliary request II - Article 56 EPC**

Document (1), which was considered by the examining division to be the closest state of the art, described recombinant thermally stable bacterial phytases and polynucleotides encoding them, in particular a polynucleotide having a nucleotide sequence substantially identical to SEQ ID NO:7 in which specific nucleotides were modified. Specific examples were the nucleotide sequence of SEQ ID NO:9 and the corresponding amino acid sequence of SEQ ID NO:10.

The objective problem to be solved was the provision of a method for the production of an alternative thermostable phytase. The solution proposed in claim 1 was a method comprising expressing in a microbial host cell an expression cassette comprising a promoter operably linked to a nucleic acid molecule encoding a thermostolerant phytase comprising SEQ ID NO:1.

The thermostolerant phytase described in the passage on page 68, lines 24 and 25 of document (1) differed from the thermostolerant phytase with SEQ ID NO:1 of the present application in one mutation (R180Y vs. R181Y). The amino acid sequence in SEQ ID NO:10 and Figure 8 of document (1) was two amino acids shorter than the sequence of the thermostolerant phytase of the present application, because the amino acid arginine at position 169 and the amino acid leucine at position 278
were missing. The examining division had not duly taken into account these differences.

The thermotolerant phytase having SEQ ID NO:1 of the present application was not derivable from document (1) in an obvious manner. The prior art document described a wide variety of sequences which could be obtained by variation of the wild-type E. coli phytase sequence. Specifically picking out SEQ ID NO:10 could only be made with the benefit of hindsight having knowledge of the present invention. No reason was apparent why a person skilled in the art should specifically have chosen SEQ ID NO:10 as a starting point for designing further phytase variants.

The examining division’s assumption that a person skilled in the art reading document (1) would have recognised that SEQ ID NO:10 was erroneous and would have corrected the error in position 180/181, was based on hindsight. Even if the skilled person would have noticed that position 180 in the E. coli wild-type sequences had not been changed, he would have had no reason to assume that SEQ ID NO:10 needed correction and what the correction should be.

Moreover, the examining division had failed to take into account the fact that SEQ ID NO:10 in document (1) was shorter by two amino acids than SEQ ID NO:1 of the application. In view of the statements on page 23, last paragraph of document (1) defining a substantially identical amino acid sequence as one comprising one or more deletions, the skilled person would not hit upon the idea that SEQ ID NO:10 should be two amino acids longer.
The thermostable phytase of SEQ ID NO:1 was not to be regarded as an arbitrary choice among all possible phytase variants described in document (1). Since amino acid deletions or substitutions might have functional consequences, it was surprising and could not have been predicted in view of the content of document (1) that, in spite of the different amino acid sequence, the phytase with the amino acid sequence in SEQ ID NO:1 had the same activity as that of SEQ ID NO:10 in document (1).

XII. The appellant (applicant) requested that the decision under appeal be set aside and a patent be granted on the basis of the claims of the main request, or on either of auxiliary request I or II, all filed under cover of a letter dated 15 July 2015.

Reasons for the Decision

Admission of the claims according to the main request and auxiliary request I into the proceedings - Articles 12(4) and 13 RPBA

1. The main function of the appeal proceedings is to give a judicial decision upon the correctness of an earlier decision taken by a department of first instance on a case (see decisions G 9/91 and G 10/91, OJ 1993, 408, 420). Albeit a party to appeal proceedings can, in principle, amend its case either at the outset or during the proceedings, the right to do so is subject to limitations specified in the Rules of Procedure of the Boards of Appeal (RPBA), in particular Article 12(4) RPBA - as regards amendments introduced with the statement of grounds of appeal or the reply.
thereto - and Article 13 RPBA - for amendments introduced at a later stage of the appeal proceedings.

2. In the present case, the appellant replaced at the outset of the appeal proceedings the sets of claims according to the main and auxiliary request underlying the decision under appeal (see sections III and IV above) by a new set of claims consisting of 14 claims. Claims 1 and 2 of the new set of claims were product claims directed to, respectively, a thermostable phytase having SEQ ID NO:1 and a nucleic acid molecule encoding a thermostable phytase and comprising an XhoI and NotI restriction fragment of SEQ ID NO:4. None of the sets of claims submitted in examination proceedings, including those on which the decision under appeal was based, included claims directed to this subject-matter.

3. In its communication under Article 15(1) RPBA in preparation of the oral proceedings, the board drew attention to Article 12(4) RPBA and indicated that it was not aware of any circumstances that may have prevented the appellant from filing this new set of claims in examination proceedings. The board also observed that the objections that the appellant tried to overcome with the new claims had been raised early in the examination proceedings, and that the examining division had given the appellant the opportunity to reply to the objections and amend the claims.

4. The appellant replied to the board's communication and submitted three sets of claims as main request and auxiliary requests I and II. The set of claims according to the main request differs from the claims previously on file in that several claims have been amended to address a clarity objection raised by the
board; however, all further claims - including product claims 1 and 2 - are identical to those of the request filed together with the statement setting out the grounds of appeal.

5. Neither in its reply to the board's communication nor during the oral proceedings has the appellant put forward persuasive reasons that may justify the filing in appeal proceedings of a set of claims which, for the first time, includes product claims directed to a thermostolerant phytase and a nucleic acid molecule encoding a thermostolerant phytase. The board cannot accept the appellant's allegation that during the oral proceedings the examining division did not give any reasons for its finding on inventive step. It is apparent from the minutes of the oral proceedings before the examining division dated 9 February 2011 that the relevant differences between the content of document (1) and the claimed subject-matter were discussed, and that the examining division regarded the latter to be an obvious alternative. While the applicant argued that the examining division had not given valid arguments for its finding, it is not apparent from the minutes that the examining division's view had not been made clear to him. What is apparent from the minutes is that, although the examining division expressly asked whether further requests would be filed, the applicant decided against (see sections 8 to 12 of the minutes).

6. Auxiliary request I has been filed at a late stage of the appeal proceedings, namely after the oral proceedings were arranged. Claim 1 is drafted as a method claim which appears to be directed to a combination of the methods according to the corresponding claims of the main request and auxiliary
request underlying the decision under appeal, as it
defines the nucleic acid expressed in the host cell as
either encoding the amino acid sequence of SEQ ID NO:1
(as in the auxiliary request before the examining
division) or as a fragment of the nucleotide sequence
of SEQ ID NO:4 (as in the main request). The appellant
has not put forward any arguments as to why this
request could not have been submitted in examination
proceedings, or how the combination of the two
embodiments as alternatives in a single claim may
overcome the objection of lack of inventive claim which
lead to the refusal of the application.

7. Under these circumstances, the board exercises the
discretion conferred by Article 12(4) RPBA to not admit
amendments to the case that could have been introduced
during the proceedings before the examining division,
especially if the amendments are introduced at a late
stage of the appeal proceedings (Article 13 RPBA). The
main request and auxiliary request I are not admitted
into the proceedings.

Auxiliary request II

8. Claims 1 to 34 according to the present auxiliary
request II are identical to those of the auxiliary
request filed during the oral proceedings before the
opposition division and underlying the decision under
appeal (see sections III and IV above). Apart from the
statement that the amendments introduced into the
claims submitted during the oral proceedings "appear to
be allowable" in view of Article 123(2) EPC, the
examining division's findings in the decision under
appeal concern solely the issue of inventive step
(Article 56 EPC). Thus, the present decision on
auxiliary request II is confined to the same issue.
Article 56 EPC

9. In the decision under appeal, the examining division considered document (1) to be the closest state of the art for the assessment whether the method of claim 1 involves an inventive step. This finding has not been contested by the appellant.

10. Document (1) describes a recombinant phytase derived from E. coli, as well as active fragments, analogs and derivatives thereof, including a modified variant having increased thermostability. When the modified variant is recombinantly expressed in, e.g., S. pombe or P. pastoris, a glycosylated form with additional thermal tolerance is produced (see page 14, lines 13 to 17). The use of recombinant expression constructs comprising the (wildtype or modified) gene linked to a promoter to produce the enzyme in a host cell is described in pages 62 to 65.

11. The nucleotide sequence of the wildtype (i.e. not modified) phytase gene from E. coli is set forth in SEQ ID NO: 1 or SEQ ID NO: 7 of document (1), while the encoded amino acid sequence is shown in SEQ ID NO:2 or SEQ ID NO:8 (see page 68, lines 5 to 8). Specific examples of variant phytase nucleotide sequences are provided on page 68, lines 9 to 25. In particular, in lines 22 to 25 a variant phytase polynucleotide that "... encodes a polypeptide having substantially [the sequence] as set forth in SEQ ID NO:8, but having an W68E, Q84W, A95P, K97C, S168E, R180Y, N226C, Y277D or any combination thereof and retain phytase activity" is described.
12. As the phytase in document (1), the amino acid sequence of the thermotolerant phytase of SEQ ID NO:1 of the present application is derived from the sequence of the E. coli phytase. Moreover, the amino acid substitutions in SEQ ID NO:1 are the same as those suggested in the passage of document (1) quoted above, except that in the latter the R->Y substitution is said to be at position 180 (instead of 181 as in the application).

13. For a skilled person trying to put in practice the teaching of document (1) by introducing the modifications suggested in the passage on page 68, lines 22 to 25 of document (1) into the amino acid sequence of the E. coli "wildtype" phytase, it is immediately apparent from either SEQ ID NO:2 or SEQ ID NO:8 that the amino acid at position 180 is a histidine, whereas the arginine is found at position 181.

14. Thus, starting from document (1) the problem that the skilled person is actually confronted with is finding out whether the method for preparing a thermotolerant phytase as described in document (1) is to be carried out with a nucleic acid encoding a modified E. coli phytase with tyrosine instead of histidine at position 180, or rather with tyrosine instead of arginine at position 181.

15. The solution to this problem is, as proposed in the present application, the substitution of the arginine at position 181 for tyrosine.

16. In the decision under appeal, the examining division held that this solution was obvious to a person skilled in the art. The board is of the same view. Confronted with the inconsistency between the position and nature
of the amino acid to be substituted, and motivated by
document (1) itself to prepare a thermotolerant
phytase, the skilled person could and would test the
two possible variants which arise from the ambiguous
disclosure of document (1) (tyrosine at position 180 or
at position 181) to find the variant that retains
phytase activity - as required in the passage quoted in
section 11 above - and has improved thermostability - as
it is the object of the invention disclosed in
document (1) (see page 14, lines 12 to 15). It has not
been disputed that, for this purpose, the skilled
person would have to apply only methods which belonged
to the common general knowledge at the priority date,
and would not require any inventive skills.

17. There is no reason to doubt - nor has it been
disputed - that, as a result, the skilled person would
arrive at a sequence comprising SEQ ID NO:1 of the
present application. With this information and
following the technical teaching of document (1), the
skilled person would, without applying any inventive
skills, arrive at a method for preparing a
thermotolerant phytase as proposed in claim 1.

18. In appeal proceedings, the appellant relied on
Examples 1 and 4 and SEQ ID NO:10 of document (1) in
support of its argument that the skilled person would
have assumed that the thermostable variant described
therein had an amino sequence which - compared to the
SEQ ID NO:1 of the present application - was two amino
acids shorter.

19. This argument cannot be accepted. Nowhere in
document (1) it is mentioned that the amino acid
sequence of the thermotolerant variant described on
page 68, lines 22 to 25 is two amino acids shorter than
the amino acid sequence of the wildtype phytase. It is
stated in Example 1 that "... the modified enzyme, SEQ
ID NO:10, containing 8 amino acid changes, is tolerant
to temperatures greater than the wild type enzyme. (see
Figure 3)" (see page 137, lines 2 and 3 from the
bottom; emphasis added by the board). Those 8 changes
are clearly shown in Figure 8, in which the substituted
amino acids are bold-underlined in the amino acid
sequence of the wildtype (SEQ ID NO:8; upper sequence)
and the modified enzyme (SEQ ID NO:10, bottom
sequence). There is no indication whatsoever, either in
Examples 1 and 4 or in Figure 8 of document (1), that,
in addition to the 8 amino acid substitutions, two
amino acids present in the wildtype sequence have been
deleted in the sequence of the thermostable variant.

20. Thus, it is doubtful whether a person skilled in the
art reading document (1) would be aware of the two
missing amino acids in Figure 8 and SEQ ID NO:10. But,
if so, he/she would consider the shorter sequence to be
either a substantially identical amino acid sequence as
contemplated in the passage on page 23, last paragraph
of document (1) or, as it might be the case, the result
of a typographical error. If still in doubt, the
skilled person could and would test the two variants
differing in two amino acids for phytase activity and
thermostability. Carrying out such straightforward and
routine tests with only two variants is within the
normal capabilities of a person skilled in the art and,
contrary to the appellant's view, cannot be equated
with embarking in a research program.

21. In appellant's view, it was unexpected that, in spite
of having two additional amino acids, a modified
phytase having SEQ ID NO:1 accordig to the present
application would fold and have the same activity as
the variant phytase with SEQ ID NO:10 in document (1). In support of its argument, the appellant cited decisions T 1139/08 of 12 July 2010 and T 915/94 of 6 July 1999.

22. The passage of T 1139/08 (supra) on which the appellant relied (see section 28.1 of the Reasons) relates to the issue of sufficiency of disclosure (Article 83 EPC) and the question whether or not, in that particular case, it was credible that deletion and substitution variants of a protein as defined in the claims had a specific function. In T 915/94 (supra; see section 11 of the Reasons) the board found that the fact that finding "respective positions" in the amino acid sequence of a protein was within the reach of the skilled person did not render obvious the problem of identifying correct sites for mutation.

23. These decisions do not support the appellant's line of argument. It should be noted that the circumstances in the cited cases were different from those of the present case. As stated above, following the teaching in the passage on page 68, lines 22 to 25 of document (1) the skilled person would be able to prepare a thermostolerant phytase variant which differs from the wildtype phytase in 8 amino acid substitutions. Having regard to the statements in Example 1 (see sections 19 above) and in view of the results in Example 4 of document (1), there was no reason for the skilled person to doubt that the modified variant retains phytase activity.

24. In its statement of grounds of appeal, the appellant cited also decision T 923/92 (OJ EPO 1996, 564). In this decision, the then competent board held that the primary amino acid sequence of a protein constituted a
true technical feature which had to be taken into account for assessing whether or not the same invention was disclosed in an earlier application, the priority of which was claimed. It should be noted that, in the framework of Article 87 EPC, the question to be answered is whether or not the skilled person can derive the claimed subject-matter directly and unambiguously, using common general knowledge, from the previous application as a whole. In contrast, for assessing, as in the present case, whether or not claimed subject-matter involves an inventive step, not only the content of the document considered to be the closest state of the art has to be taken into account, but also what measures would be obvious to a person skilled in the art to take in order to solve a particular problem. Thus, the rationale of decision T 923/92 (supra) cannot be applied to the present case.

25. Summarizing the above, the board concludes that the subject-matter of claim 1 does not involve an inventive step within the meaning of Article 56 EPC.

Conclusion

26. In view of these findings, the appellant's request to set aside the decision under appeal must fail.
Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:  

The Chairman:

A. Wolinski  

M. Wieser  

Decision electronically authenticated