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Datasheet for the decision of 20 October 2021

Case Number: T 2160/18 - 3.3.08

Application Number: 12151852.6

Publication Number: 2453014

IPC: C12N9/42, C12N15/56, C12P19/02, C12P7/06, C12N1/14

Language of the proceedings: EN

Title of invention:
Treatment of cellulosic material and enzymes useful therein

Patent Proprietor:
Roal Oy

Opponent:
Novozymes A/S

Headword:
Beta-glucosidase/ROAL OY

Relevant legal provisions:
EPC Art. 54, 56, 76(1), 83, 123(2)
RPBA Art. 12(4)

Keyword:
Admittance of the new main request - (yes)
Added matter - (no)
Admittance of new evidence not admitted in opposition proceedings - (no)
Sufficiency of disclosure - (yes)
Admittance of new evidence filed in appeal proceedings - (no)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:
T 0205/91, T 1002/92, T 0386/94, T 0737/00, T 1162/07, T 0971/11, T 0823/12, T 0942/12

Catchword:

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Case Number: T 2160/18 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 20 October 2021

Appellant: (Opponent)	Novozymes A/S Krogshøjvej 36 2880 Bagsværd (DK)
Representative:	Didmon, Mark Potter Clarkson Chapel Quarter Chapel Bar Nottingham NG1 6HQ (GB)
Respondent: (Patent Proprietor)	Roal Oy Tykkimäentie 15b 05200 Rajamäki (FI)
Representative:	Hiebl, Inge Elisabeth Kraus & Weisert Patentanwälte PartGmbB Thomas-Wimmer-Ring 15 80539 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 27 June 2018 concerning maintenance of the European Patent No. 2453014 in amended form.**

Composition of the Board:

Chairman	B. Stolz
Members:	M. R. Vega Laso
	A. Bacchin

Summary of Facts and Submissions

I. European patent No. 2 453 014 with the title "Treatment of cellulosic material and enzymes useful therein" was granted on the European patent application No. 12151852.6 which was filed as a divisional application of the earlier European patent application No. 06830936.8 published as WO 2007/071818 (in the following "the parent application"). In the present decision, references to "the application as filed" are to the original application documents.

II. The patent was opposed on the grounds for opposition under Article 100(a) in conjunction with Articles 54 and 56; 100(b) and 100(c) EPC.

III. In an interlocutory decision posted on 27 June 2018, an opposition division found that, while the subject-matter of claim 11 of the main request then on file extended beyond the content of the application as filed (Article 123(2) EPC), the claims and the invention according to the auxiliary request then on file met the requirements of the EPC. Document (15), which had been filed only three weeks before the oral proceedings, was not admitted into the proceedings.

IV. The opponent (appellant) filed an appeal and submitted a statement setting out the grounds of appeal including new evidence and copies of its written submissions in opposition proceedings including the documents cited therein.

V. By letter dated 20 May 2019, the patent proprietor (respondent) replied to the statement of grounds of appeal and submitted four sets of claims as new main

request and auxiliary requests I to III in appeal proceedings, as well as additional evidence (Annexes IA to IC, IIA, IIB, III and IV).

VI. Claims 1, 2 and 9 of the main request read as follows:

"1. A polypeptide comprising a fragment having cellulolytic activity and being selected from the group consisting of:
a) a polypeptide comprising an amino acid sequence having at least 80% identity to SEQ ID NO: 22; and
b) a fragment of a) having cellulolytic activity.

2. An isolated polynucleotide selected from the group consisting of:
a) a nucleotide sequence of SEQ ID NO: 21, or a sequence encoding a polypeptide of claim 1; and
b) a complementary strand of a).

9. The enzyme of[*sic*] preparation of claim 8, comprising a cellobiohydrolase comprising an amino acid sequence having at least 80% identity to SEQ ID NO: 2, 4, 6 or 8, or to an enzymatically active fragment thereof, and a xylanase comprising an amino acid sequence having at least 80% identity to SEQ ID NO: 18 or 20, or to an enzymatically active fragment thereof."

Independent claims 3, 4 and 5 are directed to, respectively, a vector, a host cell and an *Escherichia coli* strain. Independent claim 6 relates to an enzyme preparation comprising a polypeptide of claim 1, and dependent claims 7 and 8 are directed to embodiments of the enzyme preparation. Claims 10 to 12 relate to the use of the polypeptide of claim 1 or the enzyme preparation of claim 6. Independent claims 13 and 14 relate to, respectively, a method for preparing a

polypeptide as defined in claim 1, and a method of treating cellulosic material. Claim 15 is directed to a further use of the polypeptide of claim 1.

VII. Pursuant to their request, the parties were summoned to oral proceedings before the board.

VIII. On 24 September 2021, the appellant withdrew its request for oral proceedings and informed the board that it would not attend the scheduled oral proceedings.

IX. In a communication sent in preparation for the oral proceedings, the board drew attention to matters which seemed to be of special significance and expressed a provisional opinion on some of the issues raised by the parties.

X. In reply to the board's communication, the respondent submitted four sets of claims as new auxiliary requests IV to VII.

XI. Oral proceedings were held on 20 October 2021 in the absence of the appellant. During the oral proceedings, the respondent filed amended pages 10 and 11 of the description.

XII. The following documents are referred to in this decision:

(2): J. Hong *et al.*, 2007, Appl. Microbiol. Biotechnol., Vol. 73, pages 1331 to 1339;

(3): J. Hong *et al.*, 2006, Appl. Microbiol. Biotechnol., Vol. 73, pages 80 to 88;

(4): N. J. Parry *et al.*, 2001, Biochem. J., Vol. 353, pages 117 to 127;

(7): K. D. Speicher *et al.*, author manuscript available in PMC, 5 August 2010, published in edited form as Curr. Protoc. Protein Sci., May 2001, pages 1 to 41;

(8): Declaration of Paul Vincent Harris, signed and dated 2 March 2017;

(11): C.C. Tong *et al.*, 1980, Biochem. Jnl., Vol. 191, pages 83 to 94;

(12): E. R. de Palma-Fernandez *et al.*, 2002, Folia Microbiol., Vol. 47, No. 6, pages 685 to 690;

(13): Experimental Report, dated 14 March 2018, unsigned;

(14): GENESEQP:AWH58322 Thermoascus aurantiacus beta-glucosidase;

(15): Experimental report – Isolation and Sequencing of *Thermoascus aurantiacus* IMI 216529 genomic DNA; unsigned and undated;

(16): Copy of email dated 25 April 2018;

(17): Declaration of Dr Mark Mogulis; signed and dated 5 November 2018; and

Annexes IA, IB, IC, IIA and IIB, dated 20 May 2019.

XIII. The submissions made by the appellant in writing, insofar as relevant to the present decision, were essentially as follows:

Article 83 EPC – sufficiency of disclosure

The requirements of Article 83 EPC were not met. Claim 1 specified a polypeptide having at least 80% identity to SEQ ID NO:22 which had cellulolytic activity. In view of the errors in the disclosed SEQ ID NO:22 (specifically, 19 amino acids deleted from the middle of the protein, and two frameshifts at the C-terminus of the protein), it was highly doubtful that the polypeptide actually had the purported activity. There was no evidence in the patent that polypeptides having the sequence of SEQ ID NO:22 - let alone sequence variants of up to 80% identity - had any cellulolytic activity (or, in fact, any enzymatic activity whatsoever). The legal burden of demonstrating that the claimed polypeptide had the claimed function was borne by the respondent.

Admittance of document (15) into the proceedings

The opposition division should have admitted document (15) into the proceedings. The document had been filed in direct response to issues raised by the opposition division in the summons; hence, it could not have been filed any sooner. The reasons given in the decision under appeal for disregarding document (15) were flawed. The document had been submitted more than three weeks ahead of the scheduled oral proceedings, admittedly after the Rule 116 EPC date. However, as shown in document (16) a copy had been sent concomitantly to the patent proprietor who could have studied the document closely and replied. Moreover,

contrary to the opposition division's view document (15) was *prima facie* extremely relevant to novelty and inventive step because it confirmed by way of DNA sequencing that the beta-glucosidase described in document (4) fell within the scope of claims 1 and 2 of the patent.

Article 54 EPC – novelty

The opposition division had erred in its decision on novelty. Since claim 1 related to a product *per se*, the disclosure of the same beta-glucosidase in documents (4) and (11) destroyed the novelty of the claimed subject-matter, notwithstanding the fact that neither document explicitly reported the complete sequence of the identified beta-glucosidase. As shown by the evidence on file, a skilled person following the teaching of either document (4) or document (11) would isolate a beta-glucosidase as claimed.

Document (4)

The thermostable beta-glucosidase described in document (4) was the same beta-glucosidase claimed in claim 1. It had the same pH optimum and temperature optimum as the claimed beta-glucosidase. While the N-terminal sequence of the beta-glucosidase described in document (4) contained some amino acid differences compared to SEQ ID NO:22, it was clear from document (7) that this was likely to be due to high background from salts from the purification or the difficulties of accurate sequencing of prolines.

The opposition division's decision on novelty was based on the assumption that beta-glucosidase derived from different strains of the same microorganism were

significantly different. This assumption was not supported by any documentary evidence, and it was disputed that this was "generally known" or even scientifically correct.

A difference in molecular weight between the beta-glucosidase of document (4) and that described in the patent was explainable on the basis of simple error and/or different levels of glycosylation. In any case, molecular weight was not a feature of the claims.

Even though document (4) only contained partial sequence information of the isolated beta-glucosidase, documents (2), (3), (8), (13) and (14) provided experimental evidence that the beta-glucosidase of document (4) must be the same as the beta-glucosidase of SEQ ID NO:22 or a slight variant thereof. As apparent from post-published documents (2) and (3), there were in fact only two beta-glucosidases produced by *Thermoascus aurantiacus*, only one of which was thermostable. Document (8) confirmed from the sequencing of the *T. aurantiacus* genome that – as a fact - the beta-glucosidase described in document (4) must be the same as the beta-glucosidase of SEQ ID NO: 22 or a slight variant thereof. The skilled person repeating document (4) would therefore inevitably arrive at a polypeptide as claimed. Further evidence of the identity between the beta-glucosidase of document (4) and that of claim 1 was provided by documents (13) and (14).

The opposition division had adopted the wrong legal approach for using post-published documents and had failed to give appropriate consideration to the indirect evidence in documents (2), (3), (8), (13)

and (14), which had led it to the wrong conclusions in relation to novelty.

Document (11)

The opposition division had made similar errors when deciding on novelty in light of document (11). It had failed to take proper account of the post-published evidence, and made the unsupported assertion that beta-glucosidases from different strains of *Thermoascus* would "differ significantly" and fall outside of the claim scope.

Article 56 EPC – inventive step

Document (4) as the closest state of the art

Document (4) was directed to the same problem as the alleged invention, namely providing a beta-glucosidase for the conversion of cellulose to soluble sugars that could be used at high temperatures. The solution of providing the thermostable beta-glucosidase from *T. aurantiacus*, as already isolated and characterized in document (4), was therefore completely obvious from that document. Since there was only one thermostable beta-glucosidase in *T. aurantiacus*, a person skilled in the art following the teachings of document (4) would inevitably arrive at a polypeptide falling within the scope of claim 1. As there was no disclosure of specific fragments of the polypeptide in the application, any true fragments would have to be obvious in order for them to be sufficiently disclosed.

Contrary to the opposition division's view, the claimed beta-glucosidase was not actually "vastly different" to the one identified in document (4). Any differences

that might exist would not be so surprising to the skilled person to allow inventive step to be recognised. The skilled person would not place particular significance on a difference in molecular weight. Being aware of the potential for error in the sequence information in document (4), the skilled person would not be surprised to obtain an alternative beta-glucosidase with a slightly different N-terminal sequence. Accordingly, the opposition division had erred by attributing inventive step to "surprising" features of the claimed beta-glucosidase that did not exist. The opposition division regarded the claimed beta-glucosidase as inventive on the basis of its "improved temperature stability". However, claim 1 encompassed a range of beta-glucosidases which could have very different stabilities. There were no comparative data showing an improvement of the claimed beta-glucosidase over the one in document (4).

Document (12) as the closest state of the art

Document (12) reported the presence of multiple beta-glucosidase in *T. aurantiacus* and provided the skilled person with an incentive to look for other beta-glucosidases. The objective technical problem would be finding an alternative beta-glucosidase in *T. aurantiacus*. In view of decisions T 823/12 of 23 August 2016 and T 386/94 of 11 January 1996, neither the isolation of another beta-glucosidase from *T. aurantiacus*, nor its cloning and expression using standard methods could be considered to involve an inventive step over document (12).

XIV. The submissions made by the respondent, insofar as relevant to the present decision, may be summarized as follows:

Admittance of the main request into the proceedings

Since both in the preliminary opinion and the interlocutory decision under appeal the opposition division had regarded the requirements of Articles 83, 54 and 56 EPC as met, there had been no need to present amended claims in opposition proceedings. The main request filed in appeal proceedings was a direct reaction on the appellant's substantiation of the grounds of appeal. Hence, the request was to be admitted.

Article 83 EPC – sufficiency of disclosure

The objection of lack of sufficient disclosure was exclusively based on speculation and by no means complied with the legal requirement of serious doubts substantiated by verifiable facts. The fact that the amino acid sequence of SEQ ID NO:22 contained some errors was not prejudicial, because at the priority date the skilled person could have obtained a beta-glucosidase as claimed by expressing the beta-glucosidase gene included in a plasmid obtainable from the deposited *Escherichia coli* DSM16725.

The appellant had not provided any evidence to support its allegation that neither a polypeptide having the amino acid sequence of SEQ ID NO:22 nor a polypeptide encoded by the nucleotide sequence of SEQ ID NO:21 had beta-glucosidase activity. In contrast, the experimental evidence provided in Annexes IIA and IIB showed that those polypeptides had beta-glucosidase activity and a pH optimum of 4.5.

Admittance of document (15)

The opposition division had exercised correctly its discretion not to admit document (15) into the proceedings. Already when filing the opposition brief, the appellant should have backed up its allegation of lack of novelty over document (4) by means of experimental evidence. The appellant itself admitted that document (15) was not more relevant than document (13) already on file. In line with Article 12(4) RPBA 2007, document (15) was not to be admitted into the appeal proceedings.

Article 54 EPC – novelty

The subject-matter of claim 1 was novel over document (4). The appellant had not proved beyond doubt that the polypeptide isolated in document (4) was the same as that defined in claim 1. The same applied as regards document (11).

Article 56 EPC – inventive step

Starting from document (4), the objective problem to be solved was the provision of a further thermostable beta-glucosidase for use in methods of treating cellulosic biomass, e.g. for the production of biofuel. Four different documents on file (documents (1), (4) (11) and (12)) described thermostable beta-glucosidases of *T. aurantiacus* which were characterized by different molecular weights ranging from 85 to 175 kD. As shown in document (8), sequencing of the *T. aurantiacus* genome carried out after the relevant date had revealed eight predicted members of the Glycosyl Hydrolase family 3 (GH3).

A person skilled in the art could not have isolated a polypeptide having SEQ ID NO:22 on the basis of the information given in document (4). PCR would not have been feasible because the amino acid sequence described in document (4) would have allowed to design only a single primer. In view of the fact that several GH3 beta-glucosidase polypeptides with the same conserved regions were present in *T. aurantiacus*, it had not been obvious to a skilled person to arrive at the polypeptide of claim 1.

XV. The appellant requested in writing that the decision under appeal be set aside and that the patent be revoked.

XVI. The respondent requested that the patent be maintained on the basis of the claims of the main request or any of the auxiliary requests I to III, all filed on 20 May 2019, or on the basis of any of the auxiliary requests IV to VII filed on 1 October 2021.

Reasons for the Decision

Admittance of the main request into the proceedings

1. In the decision under appeal, the auxiliary request then on file was considered to fulfil the requirements of the EPC. The set of claims of the present main request, which was filed together with the respondent's reply to the statement of grounds of appeal, differs from the auxiliary request underlying the decision under appeal in that claim 2 has been deleted, and claim 10 (re-numbered as claim 9) has been amended to (i) omit from the enzyme preparation the endoglucanase defined by reference to SEQ ID NOs:10, 12, 14 and 16,

and an enzymatically active fragment thereof; and (ii) require the presence of a previously optional xylanase.

2. The appellant did not oppose the admittance of the amended claims into the proceedings. As the amendments introduced into the claims were made in response to specific objections under Article 123(2) EPC raised in the statement of grounds of appeal, the board decided to admit and consider the present main request.

Rule 80 and Articles 123(2)(3), 76(1) and 84 EPC

3. The amendments introduced into the claims are occasioned by the ground for opposition of Article 100(c) EPC. Hence, the requirement of Rule 80 EPC is met.

4. In the decision under appeal, the opposition division found that the subject-matter of the claims according to the auxiliary request then on file did not extend beyond the content of either the parent application or the application as filed (see points 3.c) and d) on page 4 of the decision). The appellant contested this finding only with regard to claims 2 and 10.

5. In the present main request, claim 2 has been deleted, and claim 10 amended and re-numbered as claim 9. The appellant did not dispute that the subject-matter of amended claim 9 is disclosed in the parent application and the application as filed. As the board has no doubt that the claimed subject-matter is directly and unambiguously derivable from claims 18, 26 and 28 of the parent application; and page 6, lines 14 to 17; page 18, lines 33 to 36; and page 16, lines 3 to 5 of the application as filed, the amendments introduced

into the claim are considered to conform both Article 123(2) and Article 76(1) EPC.

6. No objections were raised by the appellant with regard to Article 123(3) EPC or Article 84 EPC. The board sees no reason to raise any of its own motion.

Article 83 EPC – sufficiency of disclosure

7. In the decision under appeal, the opposition division found that the objection of lack of sufficient disclosure had not been substantiated by verifiable facts, and considered the invention as defined in claim 1 of the auxiliary request to be sufficiently disclosed in the application as filed.

8. In its statement of grounds of appeal, the appellant disagreed with the opposition division's legal reasoning and contested the findings on Article 83 EPC arguing – for the first time - that there was no evidence that "*... the (incorrectly deduced) polypeptide sequence of SEQ ID NO:22 has cellulolytic activity, as the claims required*". In appellant's view, the respondent "*... bears the legal burden of demonstrating that the claimed polypeptide has the claimed function*" (see sections 10.3 and 10.8 of the statement of grounds of appeal).

9. Annexes IA to IC, IIA and IIB were submitted by the respondent together with its reply to the statement of grounds of appeal in order to address appellant's argument. The board is satisfied that there had been no reason for the respondent to present this evidence in opposition proceedings. This has not been disputed by the appellant. Hence, having been presented in due

time, Annexes IA to IC, IIA and IIB are taken into account by the board for its decision.

10. It is undisputed that the polypeptide sequence of SEQ ID NO:22 of the application as filed contains errors. Annex IA shows the nucleotide sequence and the polypeptide sequence disclosed in the application as filed as, respectively, SEQ ID NO:21 and SEQ ID NO:22; introns and CDSs are indicated. It also shows the errors in these sequences arising from an erroneous intron annotation (see page 5) and three additional nucleotides that in fact do not exist (see nucleotides C3264, T3291 and A3297 on page 6). The corrected sequence is provided for comparison. In Annex IB, the polypeptide sequence of SEQ ID NO:22 is compared to the sequence encoded by SEQ ID NO:21 disclosed in the application as filed and to the correct polypeptide sequence. Annex IC shows the comparison between the polypeptide sequence of SEQ ID NO:22 and the correct polypeptide sequence.

11. The experimental evidence in Annexes IIA and IIB shows that polypeptides produced by expressing either (i) a synthetic gene encoding the polypeptide of SEQ ID NO:22 (Annex IIA) or (ii) the nucleotide sequence of SEQ ID NO:21 (Annex IIB) inserted into an expression cassette for *T. reesei*, have in fact beta-glucosidase activity. As apparent from Figure 2 of each Annex IIA and IIB, the pH optimum of both beta-glucosidase enzymes is about pH 4.5.

12. This experimental evidence was not questioned by the appellant, and the board is satisfied that the burden of proving that a polypeptide having the sequence of SEQ ID NO:22 has cellulolytic activity, has been discharged.

13. As regards appellant's argument concerning the beta-glucosidase activity of variants of the polypeptide encoded by SEQ ID NO:22, the experimental results reported in Annex IIB show that the polypeptide encoded by SEQ ID NO:21, which differs from the polypeptide of SEQ ID NO:22 by 20 amino acids, i.e. is 97% identical (see Annex IB), has cellulolytic activity. The board has no doubts that a person skilled in the art at the relevant date was able to find further polypeptides having cellulolytic activity and at least 80% identity to SEQ ID NO:22, without undue burden or inventive skills.

14. Hence, having considered the arguments and evidence put forward by the parties in appeal proceedings, the board concludes that the patent application discloses the claimed invention in a manner sufficiently clear and complete for it to be carried out by the person skilled in the art. Thus, the requirements of Article 83 EPC are fulfilled.

Admittance of document (15)

15. Document (15) was filed by the present appellant three weeks before the date of the oral proceedings before the opposition division. The document purportedly confirms by way of DNA sequencing that the beta-glucosidase from *T. aurantiacus* described in document (4) falls within the scope of claims 1 and 2 of the patent as granted and, consequently, deprives the subject-matter of these claims of novelty (see submission of the present appellant – then opponent - dated 25 April 2018).

16. In the decision under appeal, the opposition division decided not to admit document (15) into the proceedings, on the grounds that the document had been filed late and not sent to the other party until an even later date, and that, *prima facie*, the experimental evidence therein did not appear to be relevant (see first full paragraph on page 5 of the decision under appeal). The appellant has contested these findings.

17. According to established case law of the Boards of Appeal, evidence first submitted by an opponent after expiry of the nine-month period under Article 99(1) EPC is generally to be regarded as not filed in due time for the purpose of Article 114(2) EPC and the opposition division has in principle discretion not to admit it. In the present case, the objection of lack of novelty in view of document (4) had been raised already in the notice of opposition. Hence, the evidence in document (15) could - and should - have been submitted within the time limit for filing an opposition pursuant to Article 99(1) EPC.

18. Even if the board were to accept appellant's argument that document (15) had been submitted in response to an observation made by the opposition division in the communication attached to the summons to oral proceedings, the document should nevertheless have been submitted, at the latest, at the date fixed by the opposition division for making written submissions in preparation for the oral proceedings under Rule 116(1) EPC, i.e. two months before the date of the oral proceedings (see last sentence on page 8 of the opposition division's communication dated 17 November 2017). Since the document was submitted only three weeks before the date of the oral proceedings, there is

no doubt that document (15) was not filed in due time, and that its admission into the opposition proceedings was at the discretion of the opposition division (see Article 114(2) EPC).

19. The decision of the opposition division to disregard the late-filed document (15) could be overruled only if the board were to conclude that the opposition division exercised its discretion according to wrong principles, or without taking into account the right principles, or in an unreasonable way (see decision G 7/93, OJ EPO 1994, 775, point 2.6 of the Reasons). This is however not the case.

20. According to established jurisprudence of the Boards of Appeal, a decisive criterion to be taken into account by the opposition division when deciding on the admissibility of late-filed documents, is their *prima facie* relevance (see, e.g., decision T 1002/92, OJ EPO 1995, 605). As apparent from the decision under appeal, the opposition division took into account this issue and concluded that document (15) was *prima facie* not sufficiently relevant to change the outcome of the opposition proceedings (see section 5.c on page 5 of the decision under appeal).

21. The opposition division considered also the question whether the patent proprietor had been in a position to adequately react to the submission of document (15). In this context, the opposition division stated in its decision that document (15) had not been forwarded to the patent proprietor "*until an even later date*", i.e. even less than three weeks before the oral proceedings. The appellant contested this finding and submitted document (16) as evidence that document (15) had been sent via email to the other party on the same date as

to the opposition division, i.e. three weeks before the oral proceedings.

22. However, document (16) filed in appeal proceedings does not call into question the exercise of discretion by the opposition division which was based on the evidence then on file. As apparent from the minutes of the oral proceedings before the opposition division, dated 27 June 2018 (see last paragraph on page 1), the patent proprietor declared that no email from the opponent had been received. In the absence of evidence on file that an email including document (15) had been sent to and received by the patent proprietor, the opposition division correctly found that document (15) became available to the patent proprietor only at a later date, i.e. when it was forwarded by the division few days before the oral proceedings.

23. In view of the above, the board is satisfied that the opposition division exercised its discretion correctly and in a reasonable way, and sees no reason to overturn the opposition division's discretionary decision not to admit document (15) into the opposition proceedings in accordance with Article 114(2) EPC.

24. Nor does the board see any reason to exercise its own discretion under Article 12(4) RPBA 2007 to admit into the appeal proceedings either document (15) or appellant's submissions relying on this document, even giving due consideration to the evidence provided in document (16) (see decisions T 971/11 of 4 March 2016, point 1 of the Reasons; and T 942/12 of 17 November 2015, point 7 of the Reasons).

25. Like the opposition division, the board holds the view that document (15) is *prima facie* not sufficiently

relevant to change the outcome of the proceedings. The experimental evidence in document (15) might show that a nucleotide sequence encoding a polypeptide having an amino acid sequence which is at least 80% identical to SEQ ID NO:22 **is present** in the genome of *T. aurantiacus* IMI 216529. However, contrary to appellant's view document (15) does not serve to prove beyond doubt that the method described in document (4) inevitably leads to such a polypeptide.

26. Hence, document (15) was not admitted into the appeal proceedings.

Admittance of document (17)

27. Document (17), which was filed together with the statement of grounds of appeal, is a declaration of Dr Mark Wogulis, an employee of the appellant. In sections 11 to 14 of this document, Dr Wogulis makes some statements on the question whether or not it is generally thought that significant variability in the amino acid sequence of a given protein exists among different strains of a fungal species. Since this issue was brought forward by the examining division in its communication in preparation for the oral proceedings (see second and third sentence in section 3.c on page 4), the board fails to see any reason why this evidence could not have been submitted in opposition proceedings.

28. It is not clear which objection (lack of novelty or lack of inventive step) Dr Wogulis' statements in sections 5 to 10 of his declaration are intended to support. In any case, both objections were raised in the notice of opposition, and in the opposition division's communication in preparation for the oral

proceedings, which was issued six months in advance of the oral proceedings, a provisional view adverse to the present appellant was expressed. Hence, the declaration of Dr Wogulis could and should have been submitted already in opposition proceedings.

29. For these reasons, the board holds the evidence in document (17) not to be inadmissible.

Article 54 EPC – novelty

30. Claim 1 of the present main request is identical to the corresponding claim of the auxiliary request underlying the decision under appeal. The opposition division regarded the subject-matter of claim 1 of the auxiliary request then on file as novel in the light of the content of documents (4) and (11). This applied also to the remaining claims which referred to claim 1 (see section 5c bridging pages 7 and 8 of the decision).

Document (4)

31. It is established jurisprudence of the Boards of Appeal that, for concluding lack of novelty, the claimed subject-matter must be directly and unambiguously derivable from the prior art. For ascertaining the disclosure of a document forming part of the state of the art within the meaning of Article 54(2) EPC, the relevant date is the date of its publication (see T 205/91 of 16 June 1992, T 737/00 of 21 May 2003, and T 1162/07 of 6 October 2010). It has to be beyond doubt - not merely probable – that the disclosure in the state of the art would inevitably lead to subject-matter falling within the scope of the claim.

32. Document (4) describes the purification and biochemical characterization of an extracellular thermostable beta-glucosidase from *Thermoascus aurantiacus* IMI 216529. The beta-glucosidase was purified to homogeneity by DEAE-Sepharose, Ultrogel AcA 44 and mono-P column chromatography (see Abstract and paragraph bridging pages 119 and 120). The enzyme is said to be a homotrimer, with a monomer molecular mass of 120 kDa, the trimer being optimally active at 80°C and at pH 4.5 (see Abstract and page 120, left-hand column). In Figure 8, an N-terminal sequence of 20 amino acid residues of the beta-glucosidase is described. Based on the high degree of N-terminal sequence identity with other beta-glucosidases, the authors of document (4) suggest that the enzyme could be a member of glycoside hydrolase family 3 (see Abstract and page 126, right-hand column, second sentence of the last paragraph).

33. It is undisputed that document (4) does not explicitly report the complete sequence of the isolated beta-glucosidase, and that only 11 amino acid residues out of the N-terminal sequence of 20 amino acid residues described in document (4) are identical to a sequence in SEQ ID NO:22 of the present patent, whereas the amino acids at positions 1 and 13 to 20 differ between the two sequences. Hence, like the opposition division, the board holds that the sequence data provided in document (4) do not allow to establish without doubt the identity between the beta-glucosidase described therein and that defined in claim 1.

34. Relying on document (7), the appellant argued that the differences between the sequence provided in document (4) and that of SEQ ID NO:22 were clearly due to inaccuracies in the sequencing technique used in document (4). However, for the purpose of examining

novelty, document (4) is to be assessed from the perspective of a person skilled in the art at the publication date. The skilled person does not find in document (4) any indication whatsoever of possible errors in the amino acid sequence provided therein, let alone which partial sequence might be erroneous. Thus, there was no reason for the skilled person at the publication date of document (4) to suspect that the amino acid sequence provided therein contained any errors.

35. For its finding on novelty, the opposition division took into account also differences between the beta-glucosidase polypeptide described in document (4) and that of the invention as regards the molecular weight (120 kDa vs. 81 kD) and the optimal temperature (80°C vs. 75°C). The appellant tried to explain the striking difference in molecular weight on the basis of simple error and/or different levels of glycosylation. However, a person skilled in the art cannot derive from document (4) any indication for a potential error when determining the molecular weight of the beta-glucosidase polypeptide described therein. Nor is there any mention in document (4) of a possible glycosylation of the polypeptide.

36. Further, the appellant relied on post-published documents (2) and (3) to support its contention that *T. aurantiacus* produces only two beta-glucosidases, of which only one is thermostable. In appellant's view, the thermostable beta-glucosidase polypeptides described in documents (4) and (2) must be the same as the beta-glucosidase polypeptide of the invention.

37. This argument is not persuasive. Document (12), on which the appellant relied for inventive step,

describes three beta-glucosidases in *T. aurantiacus* (see Figure 1), and characterises two of them (Gl-2 and Gl-3) as being thermostable and having different pH and temperature optima. Moreover, it is apparent from document (8) that, based on the post-published sequence of the genome of *T. aurantiacus*, up to eight putative beta-glucosidases may be produced in this organism.

38. In the board's view, document (2) - and document (8) - may show that a nucleotide sequence encoding a polypeptide having an amino acid sequence which is at least 80% identical to SEQ ID NO:22 **is present** in the genome of *T. aurantiacus*. However, these documents do not prove beyond doubt that carrying out the method described in document (4) inevitably leads to a polypeptide with beta-glucosidase activity and having an amino acid sequence at least 80% identical to SEQ ID NO:22.

39. Similarly, the experimental evidence in documents (13) and (14) may show that a polypeptide having beta-glucosidase activity and sharing several partial amino acid sequences with SEQ ID NO:22 of the patent **is present** in *T. aurantiacus* IMI 216529, which is the same strain used in document (4). However, in view of the fact that *T. aurantiacus* appears to produce several beta-glucosidases (see document (12)), and that the method used in document (13) for isolating the beta-glucosidase polypeptide from which the partial amino acid sequences are obtained, differs substantially from the method used in document (4), documents (13) and (14) cannot be considered to prove beyond doubt that carrying out the method described in document (4) inevitably leads to a polypeptide having beta-glucosidase activity and an amino acid sequence which is at least 80% identical to SEQ ID NO:22.

40. For these reasons, novelty over document (4) is acknowledged.

Document (11)

41. Document (11) describes a thermostable beta-glucosidase with a molecular weight of 87 kDa which is optimally active at pH 4.5-5.0. However, document (11) does not provide any amino acid sequence and there is no proof that carrying out the method described in this document inevitably leads to a beta-glucosidase falling within the scope of claim 1. As stated above, it is apparent from document (12) that *T. aurantiacus* produces at least two thermostable beta-glucosidases. It is stated in this document that the method described in document (11) for the purification of the thermostable beta-glucosidase "*... was not efficient in separating the* [two] *enzymes*", and that ion-exchange chromatography was crucial (see document (12), page 688, lines 1 to 5, and the reference to Tong *et al.* (1980) which is document (11) in the present proceedings). Since the method described in document (11) does not involve ion-exchange chromatography for the purification of the beta-glucosidase, it is uncertain which enzyme(s) result(s) from carrying out the described method. Thus, a polypeptide as defined in claim 1 cannot be considered to be directly and unambiguously derivable from document (11).

42. Consequently, also novelty over document (11) is acknowledged.

Article 56 EPC – inventive step

Document (4) as the closest state of the art

43. It is common ground that, starting from document (4) as the closest state of the art, the technical problem to be solved is the provision of an alternative thermostable beta-glucosidase from *T. aurantiacus*. Hence, for assessing inventive step the question whether or not the claimed polypeptide shows any advantageous properties compared to the polypeptide described in document (4) does not need to be considered, contrary to appellant's view.

44. In view of the experimental evidence in the examples of the patent and Annexes IIA and IIB, there is no doubt that the problem is solved by a polypeptide as defined in claim 1.

45. Having considered the arguments put forward by the appellant, the board is not persuaded that a person skilled in the art relying on the information given in document (4) would have arrived at a polypeptide as claimed in an obvious manner.

46. The appellant argued that providing the same beta-glucosidase already isolated and characterized in document (4) was obvious. However, as discussed in the context of novelty above, the appellant failed to provide convincing evidence that the polypeptide isolated in document (4) was in fact the same as the polypeptide of SEQ ID NO:22, or that a person skilled in the art applying the method described in document (4) would have isolated a polypeptide as defined in claim 1. As document (4) teaches a beta-glucosidase polypeptide with a molecular weight of

120 kD, it was in fact obvious to the skilled person to try to isolate such a polypeptide. However, document (4) does not teach or suggest that *T. aurantiacus* may produce other beta-glucosidases, and without knowledge of the present invention, the skilled person would not have expected to isolate a further beta-glucosidase polypeptide with a **substantially** lower molecular weight, let alone the specific polypeptide defined in claim 1. The appellant failed to substantiate convincingly its allegation that the skilled person would not place particular significance on the molecular weight reported in document (4).

47. Also appellant's argument that the skilled person could have used the sequence information provided in document (4) to clone a nucleic acid encoding the described polypeptide, is unconvincing. The board shares the respondent's view that the amino acid sequence described in document (4) would not be sufficient to allow the skilled person to design PCR primers. As regards hybridization with a degenerated probe designed on the basis of the amino acid sequence described in document (4), in view of the substantial differences between that sequence and the sequence of SEQ ID NO:22 (see paragraph 33 above) it is highly doubtful whether the skilled person would be able to isolate, without undue burden, a nucleotide sequence encoding the claimed polypeptide.

48. For these reasons, the subject-matter of claim 1 cannot be regarded as obvious in view of the teachings of document (4).

Document (12) as the closest state of the art

49. Document (12) describes the partial purification and characterization of two thermostable beta-glucosidases (GI-2 and GI-3) from *T. aurantiacus* having a molecular weight of 175 kD and 157 kD, respectively (see Abstract). There is no evidence on file that the thermostable GI-2 and GI-3 beta-glucosidase polypeptides characterized in document (12) may have any similarity to the polypeptides of the invention. The fact that their molecular weight differs substantially from the molecular weight of the polypeptide isolated by the present inventors appears to indicate that they are in fact different polypeptides. Document (12) does not provide any sequence information for the characterized beta-glucosidases.

50. Starting from document (12), the technical problem to be solved is the provision of an alternative thermostable beta-glucosidase from *T. aurantiacus*. The solution is a polypeptide as defined in claim 1.

51. Since document (12) described at least two beta-glucosidase polypeptides in *T. aurantiacus*, the skilled person could have attempted to isolate a further polypeptide applying the purification method described in document (12), as it is apparent from Figure 1 of this document that a third fraction (GI-1) having beta-glucosidase activity was eluted from the anion-exchanger column. There is however no evidence on file showing that the third fraction described in document (12) contained a polypeptide as defined in claim 1, and the appellant did not argue to this effect.

52. The appellant did not put forward any arguments as to which obvious course of action would have been taken by the skilled person, starting from document (12), to arrive at the claimed beta-glucosidase polypeptides in an straightforward manner. Rather, the appellant substantiated its objection of lack of inventive step basically by referring to decision T 823/12 of 23 August 2016 and decision T 386/94 of 11 January 1996. The facts underlying the cited decisions differ however from the facts in the present case.

53. In decision T 823/12 (*supra*), which relates to polypeptides having cellulolytic enhancing activity produced by the filamentous fungus *Thielavia terrestris*, the document considered to be the closest state of the art ("D1") described the identification and cloning of five genes encoding such polypeptides, by applying an experimental procedure which involved the use of EST sequences to identify sequences encoding the desired polypeptides. In the application then at issue, the same experimental procedure was applied for identifying and cloning a further gene coding for a polypeptide having cellulolytic enhancing activity from the same fungus. The board found that the fact that the closest state of the art "*... had already disclosed that 13 genes from the assembled EST sequences had hits against known glycosyl hydrolase genes* [...] *justified the reasonable expectation that there were more glycosyl hydrolase genes in Thielavia terrestris than the five which were cloned in D1*" (see point 2.5 of the Reasons). Thus, the board concluded that the claimed polypeptides did not involve an inventive step.

54. In the present case, document (12) describes the isolation and characterization of two beta-glucosidase polypeptides from *T. aurantiacus*, but does not suggest,

let alone expressly indicates that *T. aurantiacus* may produce further thermostable beta-glucosidases. Nor does document (12) provide any sequence data on the basis of which the skilled person could have identified genes encoding further beta-glucosidase polypeptides. Instead of the purification method described in document (12), the present invention uses a different approach to isolate the beta-glucosidase polypeptide with the degree of purity required for peptide sequencing. While this may appear trivial, given the large amount of different polypeptides secreted by cellulolytic fungi it is not. In view of these factual differences, the board does not deem the conclusion of lack of inventive step in decision T 823/12 (*supra*) applicable to the present case.

55. To support its allegation that the cloning and expression of the claimed beta-glucosidase using standard methods could not be inventive, the appellant cited the Headnote of decision T 386/94 (*supra*). However, the factual situation underlying the cited decision cannot be compared to that in the present case. Decision T 386/94 (*supra*) relates to a process for producing chymosin polypeptide or its precursors which involves the cloning and expression of a DNA sequence encoding the polypeptides. The document representing the closest state of the art described the chymosin polypeptide and its precursor prochymosin, as well as the isolation of a recombinant clone containing sufficient cDNA to code for 80% of the prochymosin polypeptide (se point 25 of the Reasons). The competent board found that a person skilled in the art would have perceived the cloning and expression of the chymosin DNA "*... as an endeavour likely to succeed and that achieving this cloning did not pose such problems as to prove that this assumption was wrong*". Consequently,

the board concluded that the claimed process did not involve an inventive step (see point 42 of the Reasons).

56. In decision T 386/94 (*supra*), chymosin and its precursors were well-characterised polypeptides, their amino acid sequence was known and a DNA molecule encoding 80% of the precursor prochymosin had been isolated, the actual achievement of the claimed invention being the cloning and expression of the **complete** DNA sequence. In contrast, in the present case it was uncertain at the relevant date whether *T. aurantiacus* produced further beta-glucosidase polypeptides, further polypeptides had not been characterized, their amino acid sequence was unknown and a DNA sequence encoding them had not been identified. As these facts differ substantially from those in decision T 386/94 (*supra*), the board's conclusion in that decision cannot apply to the present case.

57. Summarising the above: the arguments put forward by the opponent to substantiate its objection of lack of inventive step over document (12) fail to persuade the board.

Adaptation of the description

58. At the oral proceedings before the board, the respondent submitted amended pages 10 and 11 of the patent to adapt the description to the amended claim 9.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of claims 1 to 15 of the main request filed on 20 May 2019 and a description consisting of description, sequence listing and figures of the patent as granted, except for pages 10 and 11 of the description to be replaced by amended pages 10 and 11 as filed at the oral proceedings before the board.

The Registrar: On behalf of the Chairman (according to Art. 8(3) RPBA 2020):

L. Malécot-Grob M. R. Vega Laso

Decision electronically authenticated