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**Datasheet for the decision
of 27 February 2014**

Case Number: T 1649/09 - 3.3.08

Application Number: 01973909.3

Publication Number: 1320588

IPC: C12N9/42

Language of the proceedings: EN

Title of invention:

Method for glucose production with a cellulase mixture
comprising a modified cellulase

Patent Proprietor:

Iogen Energy Corporation

Opponent:

Genencor International, Inc.

Headword:

Modified cellulase/IOGEN

Relevant legal provisions:

EPC Art. 123(2), 123(3), 84, 56

EPC R. 80

RPBA Art. 12(4)

Keyword:

Main request - clarity (no)

Auxiliary request 1 - requirements of the EPC met (yes)

Decisions cited:

T 0882/94

Catchword:



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Case Number: T 1649/09 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 27 February 2014

Appellant: Iogen Energy Corporation
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 30 March 2009
revoking European patent No. 1320588 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman M. Wieser
Members: M. R. Vega Laso
J. Geschwind

Summary of Facts and Submissions

I. European patent No. 1 320 588 (application No. 01973909.3) with the title "Method for glucose production with a cellulase mixture comprising a modified cellulase" was filed as international application under the PCT and published as WO 02/24882 (in the following "the application as filed"). The patent was granted with 19 claims.

II. Claims 1 and 10 of the **patent as granted** read:

"1. A method of converting cellulose to glucose comprising treating a pretreated lignocellulosic substrate with an enzyme mixture comprising:

a modified CBHI, selected from the group consisting of CBHI core, CBHI core plus linker, CBHI with inactivated cellulose binding domain, and combinations thereof; and cellulase enzymes, selected from the group consisting of endoglucanases (EG), exo-cellobiohydrolases (CBH), β -glucosidases, and combinations thereof,

said modified CBHI present in said enzyme mixture from 55 to 100 wt%, relative to all CBHI-type enzymes, wherein said pretreated lignocellulosic substrate comprises at least 10% lignin.

10. The method of claim 1, wherein said enzyme mixture comprises modified CBHI and cellulase enzymes selected from the group consisting of CBHI, CBHII, EGI, EGII, β -glucosidase, and combinations thereof."

- III. The patent was opposed on the grounds that the claimed subject-matter lacked an inventive step (Articles 100(a) and 56 EPC) and extended beyond the content of the application as filed (Article 100(c) EPC), and that the claimed invention was not disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 100(b) EPC).
- IV. By a decision of an opposition division of the European Patent Office posted on 30 March 2009, the patent was revoked under Article 101(2), (3) (b) EPC. In the decision, the opposition division found that the subject-matter of the amended claims according to the main request filed at the oral proceedings did not extend beyond the content of either the application as filed or the patent as granted (cf. Article 123(2) (3) EPC), but lacked an inventive step within the meaning of Article 56 EPC. The claims of auxiliary requests 1 and 2 then on file were considered to lack, respectively, clarity (Article 84 EPC) and inventive step (Article 56 EPC).
- V. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division. Together with its statement of grounds of appeal, the appellant re-filed the sets of claims underlying the decision under appeal, and submitted three additional sets of claims as auxiliary requests 3 to 5. Moreover, a sworn declaration from one of the inventors including experimental evidence was filed (see document (34) in section XIV below). As a subsidiary request, the appellant requested oral proceedings.

VI. Claims 1 to 5 and 9 to 11 according to the **main request** read as follows:

"1. A method of converting cellulose to glucose comprising treating a pretreated lignocellulosic substrate with an enzyme mixture comprising:

a modified CBHI, selected from the group consisting of CBHI core, CBHI core plus linker, CBHI with inactivated cellulose binding domain, and combinations thereof, and β -glucosidase;

said modified CBHI present in said enzyme mixture from 55 to 100 wt%, relative to all CBHI-type enzymes, wherein said pretreated lignocellulosic substrate comprises at least 10% lignin.

2. The method of claim 1, wherein the enzyme mixture further comprises one or more of: CBHI, CBHII, EGI and EGII.

3. The method as claimed in any preceding claim, wherein said modified CBHI is a modified *Trichoderma* CBHI.

4. The method as claimed in any preceding claim, wherein said modified CBHI is recovered following said step of treating.

5. The method as claimed in claim 4, wherein said modified CBHI is reused following said step of recovery.

9. The method of claim 2, wherein said modified CBHI is a modified *Trichoderma* CBHI.

10. The method of claim 2 or claim 9, wherein said modified CBHI is recovered following said step of treating.

11. The method of claim 10, wherein said modified CBHI is reused following said step of recovery."

Dependent claims 6 to 8 and 12 to 17 specify additional features of the claimed method. Independent claim 17 is directed to a method of converting cellulose to glucose using specific pretreated lignocellulosic substrates as starting material.

- VII. The opponent (respondent) replied to the statement of grounds of appeal and submitted new experimental evidence (document (35); section XIV below). It requested dismissal of the appeal and, as a subsidiary request, oral proceedings.
- VIII. Further experimental evidence (document (36); section XIV below) was furnished by the respondent together with a letter dated 14 September 2011.
- IX. On 13 January 2012, the appellant filed a reply including experimental data and a new document (document (38); section XIV below).
- X. The parties were summoned 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 made observations with respect to the admissibility of requests and evidence submitted in appeal proceedings, and expressed a provisional opinion on some of the substantive issues to be discussed during the oral proceedings, in particular

- issues in connection with Articles 123(2)(3), 84 and 56, and Rule 80 EPC.
- XI. Both parties replied to the board's communication. While the appellant did not make any submissions in substance, the respondent submitted observations and additional documentary evidence (documents (39) and (40); section XIV below).
- XII. Oral proceedings were held on 27 February 2014. During the oral proceedings, the appellant withdrew the sets of claims according to auxiliary requests 1 and 2 submitted together with the statement of grounds of appeal, and re-filed the claims of the previous auxiliary request 3 as auxiliary request 1.
- XIII. The set of claims according to **auxiliary request 1** differs from the claims of the main request (see section VI above) in that claims 9 to 13 and 15 have been deleted, claims 14, 16 and 17 have been renumbered and the dependencies amended accordingly.
- XIV. The following documents are referred to in the present decision:
- (1): P. Kotiranta et al., August 1999, Applied Biochemistry and Biotechnology, Vol. 81, No. 2, pages 81 to 90;
- (7): J. O. Baker et al., 1998, Applied Biochemistry and Biotechnology, Vol. 70-72, No. 2, pages 81 to 90;
- (17): J. Karlsson et al., December 1999, Applied Biochemistry and Biotechnology, Vol. 82, pages 395 to 403;

- (18):US 5,874,276, published on 23 February 1999;
- (34):Sworn statutory declaration of Ms Theresa C. White dated 24 July 2009, including Annexes 1 and 2;
- (35):Experimental report entitled "Comparison of CBHI holoenzyme and CBHI core activities on pretreated lignocellulosic substrates in the presence of beta-glucosidase";
- (36):Experimental report entitled "Further comparison of CBHI holoenzyme and CBHI core on pretreated lignocellulosic substrates in the presence of beta-glucosidase";
- (37):S. E. Lantz et al., 2010, Biotechnology for Biofuels, Vol. 3, pages 20ff (13 pages);
- (38):T. K. Ghose, 1987, Pure Appl. Chem., Vol. 59, No. 2, pages 257 to 268;
- (39):Ch. M. Hogan and M. Mes-Hartree, 1990, Journal of Industrial Microbiology, Vol. 6, pages 253 to 262;
- (40):US 5,916,780, published on 29 June 1999.

XV. The submissions made by the appellant were essentially as follows:

Admission of evidence filed in appeal proceedings

The experimental evidence submitted as document (34) was filed for the purpose of confirming the experiments in Examples 1 and 5 of the patent, and showed that, contrary to the opponent's allegations in opposition proceedings, glucose production and enzyme recovery

from pre-treated lignocellulosic substrate was not affected by the method of CBH I purification or the purity of the β -glucosidase used. Moreover, the experiments proved that the method of the invention could be applied over the whole scope of the claims. Therefore, document (34) should be admitted into the proceedings.

The experimental protocol of the experiments in documents (35) and (36) filed by the respondent, which allegedly contradicted the results in the patent and the confirmatory experiments in document (34), differed from the protocol in the examples of the patent in many ways. In particular, in document (35) the CBH I holoenzyme and the CBH I core used came from different sources and were not directly comparable to one another. Moreover, the holoenzyme preparation was contaminated with at least one endoglucanase. This explained the better performance of the CBH I holoenzyme preparation compared to the CBH I core preparation. Since due to the differences between the two preparations the results in documents (35) and (36) were erroneous, this evidence should be disregarded.

Main request

Rule 80 and Articles 123(3) and 84 EPC

The amendments introduced into the claims were occasioned by the grounds of opposition, and the claims conformed to Articles 123(3) and 84 EPC.

Auxiliary request 1

Rule 80 and Articles 123(3) and 84 EPC

Due to the amendments introduced into claim 1 of the main request, claims 9 to 13 had become redundant and, therefore, were cancelled.

Article 56 EPC

The subject-matter of the amended claims involved an inventive step. The opposition division's assessment of document (1), which was regarded as the closest state of the art, was flawed. Document (1) was remarkably clear in its findings: CBH I core was a manifestly inferior enzyme compared to CBH I for use in hydrolysis of lignocellulosic feedstocks. Adsorption of cellulases on the cellulosic substrate was an essential step in hydrolysis (see page 82, fifth paragraph, first sentence of document (1)). It would be apparent to a person of skill in the art reading document (1) that CBH I clearly needed a cellulose binding domain for efficient adsorption to and hydrolysis of cellulose. This view was further supported by document (17). Thus, the dogma in the art at the priority date had been that the cellulose binding domain of CBH I was necessary and essential to achieve efficient hydrolysis of the substrate. The teaching of the patent deviated therefrom.

The opposition division had adopted an *ex post facto* analysis of document (1) and attributed the person of skill in the art with a motivation that could only have arisen from hindsight knowledge of the patent. The skilled person could have considered a method for converting cellulose to glucose that used CBH I core

protein instead of CBH I holoenzyme, but having regard to the teaching of document (1) he/she would not have done so because he/she could not have expected any improvement or advantage.

The skilled person would not be in a "one way street" situation. Rather, document (1) taught in entirely the opposite direction. Contrary to the collective teaching of the prior art, modification of the CBH I enzyme by inactivation or removal of the cellulose binding domain did not result in an expected drastic reduction in the efficiency of enzymatic conversion. This provided an unpredictable and unexpected benefit.

XVI. The submissions made by the respondent may be summarized as follows:

Admission of evidence filed in appeal proceedings

The experimental evidence in documents (35) and (36) showed that CBH I holoenzyme performed significantly better than CBH I core on pretreated corn stover and pretreated spruce, when both enzymes were used in combination with β -glucosidase. These documents did not introduce any new findings or arguments for consideration by the board. They confirmed arguments made throughout the proceedings and showed that the data presented in appeal were reliable. They were provided in direct response to document (34) submitted by the appellant together with the statement of grounds of appeal and were clearly highly relevant to the case.

The evidence in question could not have been filed either together with the notice of opposition or during the opposition proceedings. The experimental data addressed the specific combination of CBH I core/

holoenzyme with β -glucosidase. A requirement for β -glucosidase only had become a mandatory feature with the claims filed in response to the summons from the opposition division. There had been no opportunity to produce relevant data at that late stage.

It would not have been instructive to attempt to reproduce the experiments in the patent or in document (34), not least because the proprietary strain used in those experiments was not available to the respondent. Therefore, in documents (35) and (36) a different experimental design was adopted, in which papain digestion of the CBH I holoenzyme was avoided and the β -glucosidase preparation replaced by purified β -glucosidase.

It would be inequitable for the board to consider the appellant's experimental evidence but not the respondent's, especially in view of the fact that there had been nothing preventing the appellant from providing their own data to the opposition division to address the issues of enzyme purity raised already in the notice of opposition.

Document (37) was filed as confirmation that the microtitre assay format used in the experiments described in documents (35) and (36) provided comparable results to a shake assay format as used in the patent.

Documents (39) and (40) were submitted in response to the board's communication as evidence of the common general knowledge in the field.

Main request

Rule 80 and Article 123(2)(3) EPC

Amended claim 2 corresponded largely to claim 10 as granted. The reason for the re-ordering of the claims was unclear and it had certainly not been done to address a ground for opposition.

Claim 1 as granted recited "cellulase enzymes_{plural}, selected from the group consisting of endoglucanases_{EG}, exo-cellobiohydrolases_{CBH}, β -glucosidases_{all also plural}, and combinations thereof". All elements were specified in plural form. In contrast, amended claim 1 merely required the presence of just a β -glucosidase_{singular}. On the face of it, claim 1 was broader than claim 1 as granted, and therefore contravened Article 123(3) EPC.

Article 84 EPC

Claims 3 to 5 were redundant because they were directed to the same subject-matter as claims 9 to 11.

Auxiliary request 1

Rule 80 EPC

The deletion of various dependent claims was not made in response to a ground of opposition.

Article 56 EPC

The method of claim 1 did not involve an inventive step. There was no dispute that document (1) disclosed a method having all features of the claim except for

the presence of β -glucosidase. The effect of adding β -glucosidase was to increase the amount of glucose produced using CBH I core alone. Hence, the technical problem to be solved was to provide a method in which the amount of glucose produced using CBH I core alone was increased.

It was obvious to a person skilled in the art that adding β -glucosidase to the reaction mixture described in document (1) would result in the conversion of the cellobiose produced by the CBH I core to glucose, so increasing the amount of glucose produced in the reaction overall. Furthermore, it was well known at the priority date that CBH I was inhibited by its cellobiose product, and that β -glucosidase could relieve this inhibition by breaking down the cellobiose to glucose. This was apparent from document (17), to which document (1) referred in the passage on page 86, first full paragraph. Thus, in view of document (1), either alone or in combination with document (17), the skilled person would have expected the addition of β -glucosidase to increase the amount of glucose obtained with CBH I core alone. Consequently, the method according to claim 1 did not involve an inventive step.

It was denied that a surprising efficiency of conversion could be achieved using CBH I core. The results in the patent and in document (34) on which the alleged efficiency was based, had been obtained with an enzyme preparation contaminated with other enzymes, particularly endoglucanases, which might be capable of exerting a synergy with CBH I or its core. But even if the process using CBH I core were surprisingly efficient, this represented a mere bonus effect (T 882/94 of 7 August 1997).

The ability to recover the CBH I core enzyme was entirely irrelevant to inventive step unless claim 1 actually recited the step of recovering the enzyme from the reaction mixture. After all, the asserted technical advantage of reduced enzyme costs was only achieved when the enzyme was actually recovered. In any case, the increased "recoverability" of CBH I core compared to holoenzyme was obvious in view of the prior art. It was apparent from document (1) that very little of the CBH I core became adsorbed to the substrate, and that the majority of the enzyme remained in solution and would thus be recoverable. It was common general knowledge that CBH I represented a large proportion of the total cost of generating glucose from lignocellulose, and that recovering and re-using the enzyme could therefore make the process more economically viable. Recoverability was an inherent property of the CBH I core whether or not it was realised by the skilled person.

If "recoverability" should be taken into account as part of the technical problem, then either document (39) or (40), or even the common general knowledge could be taken as the closest prior art. The technical problem could only be seen as the provision of an alternative method in which an increased proportion of the cellulase preparation is "recoverable", regardless of the effect on cellulose hydrolysis. It would have been obvious for the skilled person to replace a proportion of the CBH I holoenzyme with CBH I core, especially if the skilled person were unconcerned about the consequences for efficiency of cellulose hydrolysis. It should be noted that claim 1 made no reference to any particular level of efficiency.

XVII. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with the statement of grounds of appeal, or, in the alternative, on the basis of the first auxiliary request filed during the oral proceedings.

XVIII. The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

Admission of evidence filed in appeal proceedings

1. Pursuant to Article 12(1) of the Rules of Procedure of the Boards of Appeal (RPBA), appeal proceedings shall be based on (a) the notice of appeal and statement of grounds of appeal, (b) any written reply of the other party or parties filed in due time, and (c) any communication sent by the Board and any answer thereto filed pursuant to directions of the board. Even though everything presented by the parties under Article 12(1) RPBA - to the extent it relates to the case under appeal and meets the requirements specified in Article 12(2) RPBA - shall, in principle, be taken into account, the board has the discretionary power to disregard facts, evidence or requests which could have been presented or were not admitted in opposition proceedings (see Article 12(4) RPBA).
2. In the present case, the parties submitted numerous pieces of evidence at different stages of the appeal

proceedings. The appellant filed a statutory declaration including experimental evidence (document (34); see section XIV above) together with its statement of grounds of appeal. The respondent submitted experimental evidence (document (35)) together with its reply and, almost two years later, furnished further experimental evidence (document (36) and a new document (37)). The appellant countered with additional experimental evidence and document (38). Finally, two new documents (documents (39) and (40)) were filed by the respondent together with its reply to the board's communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA).

Documents (34) and (38) filed by the appellant

3. The board, exercising its discretion under Article 12(4) RPBA, decided to admit into the proceedings the statutory declaration of Dr White filed by the appellant as document (34). This document is considered to be a direct response to the opposition division's adverse findings on Article 56 EPC in the decision under appeal; it provides cogent confirmatory evidence that the objective technical problem has been solved and the purported advantage of recoverability of the enzyme is achieved. Essentially, the experiments in document (34) are a repeat of the experiments in Examples 1 and 5 of the patent in suit and show that, when pretreated lignocellulosic substrates are hydrolysed using an enzyme mixture comprising beta-glucosidase and either CBH I holoenzyme or modified CBH I, in particular CBH I core, the conversion of cellulose to glucose by the holoenzyme and CBH I core is at least comparable (see Table 2 and Figure 4 in the patent, and, *inter alia*, Table 1 and Figures 7 to 9 in document (34)). It is shown also that, following

hydrolysis, most CBH I core can be recovered from the solution (see Table 3 in the patent and Table 2 in document (34)).

4. Additionally, document (34) includes experimental data on the purity of the enzymes used for the hydrolysis of lignocellulosic substrates (see experiments on pages 10 to 15), which, according to the appellant, address allegations made by the opponent - the present respondent - in opposition proceedings, as well as the opposition division's adverse findings on inventive step. The respondent opposed to the admission of these experimental data into the proceedings arguing that the objections concerning enzyme purity had been raised already during the opposition proceedings.
5. Contrary to the respondent's view, the board does not believe that this prejudices the admission into the proceedings of document (34) as a whole. Since the issue of purity of the enzymes used in the claimed method is, as will be discussed below (see paragraph 32), not relevant to the assessment of inventive step, and in particular of the question whether or not the technical problem has been solved over the whole scope of the claim, the experimental data in question need not be considered for the present decision.
6. The board decided not to admit into the proceedings the experimental evidence submitted by the appellant at a late stage of the appeal proceedings (see section IX above) because the evidence only addresses the issue of purity of the hydrolytic enzymes or enzyme preparations used in the example of the patent, which, as mentioned above, is not considered to be relevant in the

framework of assessing inventive step. The same applies, *mutatis mutandis*, to document (38).

Documents (35) to (37), (39) and (40) submitted by the respondent

7. The experimental evidence filed by the respondent as document (35), which purportedly supported the objection that hydrolysis of lignocellulosic substrates by the CBH I core fragment was less efficient than by the CBH I holoenzyme, was not admitted into the proceedings. Even though document (35) was submitted early in the appeal proceedings, it must be regarded as late-filed evidence. The objection that this evidence allegedly supports had been raised by the opponent - the present respondent - already in the notice of opposition, but no experimental evidence in its support was furnished during the opposition proceedings.
8. The board cannot accept the respondent's argument that the experimental evidence was a response to the submission of amended claims including β -glucosidase at a late stage of the opposition proceedings. The board remarks that β -glucosidase was already specified in claim 1 of the patent as granted as one of the cellulase enzymes that may be added to modified CBH I.
9. However, the decisive issue that was considered by the board when exercising its discretion under Article 12(4) RPBA is whether or not the evidence in document (35) is suitable for disproving the experimental evidence in the patent and/or document (34). Document (35) was submitted purportedly in response to the appellant's experimental evidence filed together with the statement of grounds of appeal, but because of substantial differences in the

experimental design the results cannot be compared. While in the experiments of document (35) - as in the patent - a CBH I holoenzyme prepared from a crude *Trichoderma reesei* cellulase enzyme mixture by anion exchange chromatography was used, the CBH I core polypeptide was produced by recombinant expression in a *Trichoderma reesei* mutant strain deleted for the CBH I, CBH II, EG1 and EG2 genes and subsequently engineered to overexpress the polypeptide was used. In the examples of the patent and in document (34) the CBH I core polypeptide was obtained from the purified holoenzyme by papain digestion. Whether or not the properties and level of activity of the recombinantly expressed CBH I core polypeptide are identical to those of the enzyme obtained by papain digestion is unclear, and the experimental evidence in document (35) is considered not to be conclusive.

10. The same applies, *mutatis mutandis*, to document (36), in which CBH I holoenzyme and CBH I core activities on pretreated lignocellulosic substrates in the presence of β -glucosidase are compared. The holoenzyme and core polypeptides in the experiments were produced by recombinant expression in *T. reesei* strains deleted for various genes encoding hydrolytic enzymes involved in the conversion of cellulose to glucose. These experiments cannot be regarded as a true repeat of the experiments in either the patent or document (34) and, therefore, are not suitable as a proof that the appellant's experimental data are flawed.
11. The reasons given by the respondent to justify its failure to repeat the experiments in the patent did not convince the board. In particular, there was no plausible explanation as to why CBH I core had not been obtained by papain digestion of the CBH I holoenzyme,

as in the examples of the patent. The board cannot accept the respondent's argument concerning the non-availability of a proprietary strain allegedly used in the experiments of the patent. Apart from the fact that this argument seems to question the sufficiency of the disclosure in the patent, which was not a ground for opposition, the board observes that in Example 1 of the patent purified CBH I was obtained from crude *Trichoderma* cellulase broth, without any mention of a proprietary strain (see paragraph [0088] of the patent). Incidentally, in the experiments described in document (35), *Trichoderma* culture broth was the source of CBH I holoenzyme showing an adequate level of activity (see page 1, first paragraph under the heading "1.1 CBH I and CBH I core from *T. reesei*").

12. Since the board decided not to admit documents (35) and (36) into the proceedings, document (37), which describes the microtitre assay used in the respondent's experiments, has no relevance for this decision and was, likewise, not admitted.

13. Purportedly, documents (39) and (40) were filed to address an observation by the board and as evidence for the common general knowledge at the relevant date. However, in its reply to the board's communication the respondent put forward a new line of argument on inventive step relying on these new documents as the closest state of the art. In the board's view, both the documents and the new line of argument based on them could have been submitted already in opposition proceedings. Moreover, the relevant content of at least document (39) appears to be similar to that of document (18) already on file. For these reasons, the board decided not to admit them into the proceedings (cf. Article 12(4) EPC).

Main request

Rule 80 and Article 123(2) (3) EPC

14. The amended claims filed as main request together with the statement of grounds of appeal are identical to those of the main request underlying the decision under appeal. The opposition division held that, in the present case the requirements of Rule 80 EPC did not apply to the amended claim 2 (see section VI above), because the subject-matter of this claim corresponded to that of claim 10 as granted. Furthermore, it found that the amendments introduced into the claims, in particular the amendment to claim 1 to replace the wording "... and cellulase enzymes, selected from the group consisting of endoglucanases (EG), exo-cellobiohydrolases (CBH), β -glucosidases, and combinations thereof" by "... and β -glucosidase" conformed to Article 123(2) and (3) EPC (see pages 5 and 6 of the decision under appeal). Both findings have been contested by the respondent.

15. As regards Rule 80 EPC, the board observes that amended claim 1 has been restricted to a particular embodiment claimed in claim 10 as granted (see section II above), while the further embodiments of claim 10 have become the subject-matter of amended claim 2. These amendments have been occasioned by an objection under Article 56 EPC raised by the opposition division in the communication accompanying the summons to oral proceedings (see second paragraph of section 5.3 of the summons), and the ground of opposition of Article 100(a) in connection with 56 EPC invoked by the opponent (the present respondent). Thus, the requirement of Article 80 EPC is met.

16. As regards the respondent's objections under Article 123(2) and (3) EPC, the board shares the view of the opposition division that the substitution of the term "*β-glucosidases*" by "*β-glucosidase*" in claim 1 does not introduce subject-matter that goes beyond the content of the application as filed (cf. Article 123(2) EPC), because a method of converting cellulose into glucose using an enzyme mixture comprising modified CBH I and *β-glucosidase* (in singular) is disclosed in claim 5 of the application as filed. Also the opposition division's finding that the scope of amended claim 1 does not extend beyond the scope of claim 10 of the patent as granted, is, in the board's judgement, correct. Thus, the amendments introduced into the claims conform to Article 123(2) and (3) EPC.

Article 84 EPC

17. In the board's view, the requirement of Article 84 EPC that the claims must be clear and concise, not only applies to the individual claims, but also to the set of claims as a whole.
18. In the present case, as a result of the amendments introduced into the claims, the subject-matter of claims 3, 4, and 5 is now identical to that of claims 9, 10, and 11, respectively. This gives rise to a clarity deficiency, because it casts doubts as to the true scope of the claims in question and, therefore, runs counter legal certainty. On these grounds, the board rejects the claims according to the main request for lack of compliance with Article 84 EPC.

Auxiliary request 1

Admission into the proceedings

19. At the time of filing its statement of grounds of appeal, the appellant was apparently aware of the clarity deficiency and filed, as auxiliary request 3, a set of amended claims in which the deficiency has been remedied. During the oral proceedings before the board, this set of claims became the auxiliary request 1. The claims according to this request are identical to those of the main request, except that claims 9 to 13 and claim 15 have been cancelled and the remaining claims renumbered accordingly. The respondent has not opposed to the admission into the proceedings of this set of claims. Thus, the board decides to admit and consider it.

Rule 80 and Articles 123(2) (3) and 84 EPC

20. The cancellation of some claims remedies a deficiency under Article 84 EPC arising from the amendments introduced into claim 1 and does not give rise to any issues under Article 123(2) and (3) EPC. The claims are formally allowable.

Articles 83 and 54 EPC

21. The respondent did not raise any objections with regard to novelty or the sufficiency of the disclosure, and the board sees no reason to raise any of its own motion.

Article 56 EPC

22. In the decision under appeal, the opposition division held that the subject-matter of claim 1 of the main request then on file, which was identical to present claim 1, was obvious in the light of document (1). Moreover, in connection with the auxiliary request 2 then on file, the opposition division found that there was no evidence that the technical problem had been solved over the whole scope of the claim, in particular when 100% modified CBH I and β -glucosidase alone was used (see pages 8 and 15 of the decision under appeal).
23. The board disagrees with the opposition division's assessment of inventive step. In the board's view, the opposition division failed to take into account the whole content of document (1) and, consequently, to recognise what the skilled person reading this document would have learnt from it, and applied the problem-solution approach in an overly formalistic manner.

The closest state of the art

24. Document (1) describes experiments in which the adsorption and hydrolytic efficiency of purified cellulases of *Trichoderma reesei*, in particular cellobiohydrolase I (CBH I) and endoglucanase II are compared to those of their respective core proteins lacking the cellulose-binding domain (CBH I core and EG II core, respectively) using steam-pretreated willow (SPW) as substrate.
25. The results for the hydrolysis of SPW with CBH I and CBH I core are shown in Figure 2A and discussed in page 86 of document (1). In particular, it is stated that:

"... the lack of the CBD [cellulose binding domain] had a drastic effect on the action of CBH I, and only about 1% of the substrate was hydrolyzed by CBH I core even when high-protein concentrations were used" (see page 86, fourth paragraph, penultimate sentence)

With regard to the hydrolysis as a function of adsorption on the substrate, it is stated in the passage on page 87, first paragraph that:

"CBH I showed a linear correlation between the amount of bound enzyme and the hydrolysis of cellulose (Fig. 3). With CBH I core, the hydrolysis of the substrate was very low, and even the highest amount of bound CBH I core did not hydrolyze the substrate efficiently."

From these results, the authors of document (1) conclude that:

"By comparing the results of adsorption and hydrolysis (Figs. 1A and 2A), it seems obvious that CBHI must be bound to cellulose by its CBD for an efficient hydrolysis." (see page 88, first paragraph, penultimate sentence)

and

"CBH I clearly needed a CBD for efficient adsorption to and hydrolysis of cellulose ..." (see page 89, first paragraph, second sentence)

The technical problem to be solved

26. The opposition division held that the sole difference between the subject-matter of claim 1 and the disclosure in document (1) was the addition of β -glucosidase, and that the technical problem to be solved was the provision of a further method for converting cellulose to glucose (see page 7, first to third paragraphs of the decision under appeal).
27. The technical problem formulated by the opposition division comes short because it fails to take into account a further technical effect underlying the invention, i.e. the recoverability of CBH I core enzyme. In the board's judgement, the problem to be solved starting from document (1) has to be formulated in a more ambitious manner.
28. It is stated in paragraph [0014] of the patent that:

"...there is a need in the art to identify enzymes or mixtures of enzymes which enhance the conversion of cellulose to glucose and which are recoverable, recyclable, and reusable."

Based on this statement, the objective technical problem to be solved is defined as the provision of a more efficient, in particular more cost-efficient method of converting cellulose to glucose.

Does the claimed method solve the technical problem over the whole scope of claim 1?

29. This question has given rise to much controversy between the parties. While it was never disputed that replacing the CBH I holoenzyme by the CBH I core

polypeptide in the hydrolysis reaction allows to recover the enzyme from the solution and re-use it, in appeal proceedings the respondent argued that the claimed method does not solve the technical problem over the whole scope of the claim because at least for some embodiments a hydrolytic activity comparable to that of the CBH I holoenzyme cannot be achieved.

30. The board is satisfied that the appellant has discharged the burden of proof by plausibly demonstrating by the examples in the patent and the experimental evidence in document (34) that the technical problem formulated above is, in fact, solved by the method of claim 1. Both the examples in the patent and document (34) show that the hydrolytic activity of an enzyme mixture comprising CBH I core and β -glucosidase is comparable to that of the CBH I holoenzyme plus β -glucosidase, or even higher for some lignocellulosic substrates.
31. There is no evidence to the contrary on file. Although in the decision under appeal the opposition division stated that an embodiment of the claimed method using 100% CBH I core and β -glucosidase alone would not solve the technical problem, it did not indicate which particular evidence justified its finding, and shifted the burden of proof to the patent proprietor (the present appellant) (see last paragraph on page 14 and first paragraph on page 15 of the decision). The experimental evidence submitted by the respondent in appeal proceedings is considered not to be conclusive because of differences in the experimental design compared to that in the examples of the patent and in document (34) (see paragraphs 7 to 11 above).

32. In connection with the question whether or not the technical problem is solved over the whole scope of claim 1, the respondent raised the issue of purity of the cellulase enzymes used in the appellant's experiments. As stated above, in the present case the board regards this issue as not being relevant for the assessment whether the problem has been solved. It should be noted that claim 1 specifies a method comprising treating a lignocellulosic substrate with **an enzyme mixture** comprising a modified CBH I and β -glucosidase. There is no requirement for the enzyme mixture to contain exclusively these two enzymes and, in the practice of the invention, it is probably not even desirable. The issue would become relevant if the technical effect underlying the invention were not causally linked to the modified CBHI and β -glucosidase in the enzyme mixture, but to the presence of other enzymes. However, this has not been plausibly demonstrated.

Is the solution proposed in claim 1 obvious?

33. The board is persuaded that, starting from document (1) as the closest prior art, it was not obvious to a person skilled in the art seeking to improve the efficiency of a method for conversion of cellulose to glucose, to use a enzyme mixture comprising CBH I core and β -glucosidase. Although document (1) describes experiments using CBH I core, in view of the poor hydrolytic activity of the core enzyme compared to the holoenzyme, the skilled person would not derived from this document any motivation to continue working on CBH I core, let alone to combine this enzyme with β -glucosidase to improve the efficiency of the hydrolysis of lignocellulosic substrates. On the contrary, the content of document (1) would rather

discourage the skilled person from using CBH I core because of its much lower performance compared to the CBH I holoenzyme.

34. None of the further documents on which the respondent relied in appeal proceedings (documents (7) and (17)) provides either a motivation or a suggestion to use an enzyme mixture comprising CBH I core and β -glucosidase in order to increase the efficiency of hydrolysis. Document (17) describes a higher hydrolytic activity of the CBH I **holoenzyme** on SPW lignocellulose when β -glucosidase is present in the enzyme mixture, and this is explained by product inhibition of CBHI by cellobiose (see page 255, first paragraph under the heading "Hydrolysis of SPW"). This document is, however, completely silent about CBHI core.
35. The possibility of re-using CBH I core after recovery is, contrary to the respondent's view, not obvious to a person skilled in the art reading document (1). Apart from indicating that only a small portion of CBH I core adsorbed to SPW at 40°C, this document provides no hint whatsoever that this could allow to recover the enzyme. Document (18) mentions that the use of some catalytic domains of cellulase enzymes would provide, *inter alia*, improved recoverability of the enzyme (see column 13, lines 21 to 23). However, even if the skilled person would have combined the two document, it is still not apparent what would motivate the skilled person to chose a domain of CHB I that has scarce hydrolytic activity on lignocellulosic substrate.
36. In the decision under appeal, the opposition division stated that, since claim 1 did not make reference to any efficiency of conversion, any method of converting cellulose to glucose, even one with low efficiency as

described in document (1) for CBH I would fall within the scope of the claim (see page 8, paragraph (d)). A similar argument was put forward by the respondent with respect to the "recoverability" of CBH I. The board cannot accept this argument. The fact that a technical effect causally linked to the features distinguishing the invention over the closest state of the art is not expressly indicated in the claim, does not mean that the technical effect can be disregarded when assessing whether or not the claimed subject-matter solves the technical problem and involves an inventive step. Provided that it is consistently achieved over the whole area claimed, the technical effect is an integral part of the invention.

37. The opposition division held further that, even if efficiency of the conversion were to be considered for the assessment of inventive step, the last sentence on page 87 of document (1) reading:

"... the small amount of the bound CBHI core seemed to be able to release soluble oligomers more efficiently than the corresponding amount of bound CBHI."

would encourage the skilled person to use CBH I core to improve the efficiency of the conversion.

38. However, the passage indicated by the opposition division must be read in connection with the subsequent passage on page 88:

"This might be owing to the presence of a small noncrystalline easily hydrolysable cellulose in SPW that is attacked more readily by CBHI core"

because it does not have a CBD to target the enzyme to a more crystalline part of cellulose."

39. In the board's view, what a person skilled in the art reading document (1) would take from the complete passage is that a possibly higher efficiency of CBH I core applies only to the hydrolysis of a small part of the substrate, namely non-crystalline cellulose, while hydrolysis of SPW as a whole is much more efficient when CBH I holoenzyme having a cellulose-binding domain (CBD) is used (see Figure 2A).
40. In sum: the board is convinced that the method of the amended claims 1 to 11 according to auxiliary request 1 involves an inventive step within the meaning of Article 56 EPC.

Conclusion

41. Since the the first auxiliary request fulfills the requirements of the EPC, the patent can be maintained on the basis of this request.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of claims 1 to 11 of the first auxiliary request filed during the oral proceedings and a description to be adapted thereto.

The Registrar:

The Chairman:



A. Wolinski

M. Wieser

Decision electronically authenticated