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Datasheet for the decision of 21 January 2022

Case Number: T 2648/16 - 3.3.08

Application Number: 11743899.4

Publication Number: 2591119

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Language of the proceedings: EN

Title of invention:
Fermentation process with GH61 polypeptides

Patent Proprietor:
Novozymes North America, Inc.

Opponent:
Danisco US Inc.

Headword:
Fermentation using GH61 polypeptides / NOVOZYMES

Relevant legal provisions:
EPC Art. 83, 54, 56

Keyword:
Main Request - requirements of the EPC met (yes)

Decisions cited:

Catchword:

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Beschwerdekammern

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Case Number: T 2648/16 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 21 January 2022

Appellant: (Patent Proprietor)	Novozymes North America, Inc. 77 Perry Chapel Church Road P.O. Box 576 Franklinton, NC 27525 (US)
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Appellant: (Opponent)	Danisco US Inc. 925 Page Mill Road Palo Alto CA 94304-1013 (US)
Representative:	Andrews,R.A. Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 28 October 2016 concerning maintenance of the European Patent No. 2591119 in amended form.**

Composition of the Board:

Chairman	B. Stolz
Members:	D. Pilat
	A. Bacchin

Summary of Facts and Submissions

I. European patent No. 2 591 119 is based on European patent application No. 11 743 899.4, (published as International patent application WO 2012/006642; hereinafter "the patent application") and was opposed on the grounds of Articles 100(a), (b) and (c) EPC. An opposition division considered Article 100(c) EPC to prejudice the maintenance of the patent as granted. Auxiliary request 1 contravened Article 123(2) EPC, whereas Auxiliary request 2 and the description adapted thereto complied with the requirements of the EPC.

II. Both the patent proprietor (appellant I) and the opponent (appellant II) lodged an appeal and submitted their statement of grounds of appeal.

III. Appellant I submitted, in reply to appellant II's statement of grounds of appeal, a further Auxiliary request 3.

IV. Both parties were summoned to oral proceedings. In a communication sent in preparation of the oral proceedings, the board provided observations on procedural issues and expressed a provisional opinion on some issues concerning Articles 100 (c), 123(2), 83, 54 and 56 EPC.

V. Appellant II informed the board with a letter dated 11 October 2021 that it would not attend the scheduled oral proceedings.

VI. In reply to the board's communication, appellant I submitted a new claim request replacing former Auxiliary request 2 and made it its new main request.

If the Board considered that this request complied with the requirements of the EPC, then the appellant/ proprietor would withdraw its request for oral proceedings.

VII. Oral proceedings were cancelled.

VIII. Claims 1 and 8 according to the main request read as follows:

"1. A process of producing a fermentation product from lignocellulose-containing material, comprising the steps of:
(a) pre-treating lignocellulose-containing material;
(b) hydrolyzing the material of step (a);
(c) fermenting with a fermenting organism wherein one or more GH61 polypeptides are added after hydrolysis is complete, wherein the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation, and the hydrolysis is taken to completion before initiation of fermentation.
...
8. Use of GH61 polypeptides in a fermentation process to increase the rate of fermentation during fermentation, wherein one or more GH61 polypeptides are added after hydrolysis is complete, wherein the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation, and the hydrolysis is taken to completion before initiation of fermentation."

Dependent claims 2 to 7 and 9 define particular embodiments of the method of claim 1 and of the use of claim 8.

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

D2: WO 2009/135898 A2 (publication date 12 November 2009);

D5: WO 2005/074656 A2 (publication date 18 August 2005);

D10: T. Isaksen *et al.* "A C4-oxidizing lytic polysaccharide monooxygenase cleaving both cellulose and cello-oligosaccharides", The Journal of Biological Chemistry, vol. 289(5), pages 2632-2642, (2014);

D11: S.J. Horn, *et al.* "Novel enzymes for the degradation of cellulose", Biotechnology for Biofuels, vol. 5(1):45, pages 1-12, (2012);

D16: WO 2010/080407 A2 (publication date 15 July 2010);

D17: WO 2008/151079 A2 (publication date 11 December 2008);

D18: Additional experimental data, submitted by the proprietor on 18 May 2016.

X. The submissions made by the **appellant I**, insofar as relevant to the present decision, may be summarized as follows:

Main request

Former auxiliary request 2 filed with the statement of grounds of appeal (see the letter of 14 February 2017,

page 1, point 1.3), was intended to be identical to auxiliary request 2 as filed before the Opposition Division.

However, an obvious typographical error was introduced in claim 1 of the retyped version of auxiliary request 2 filed in the appeal proceedings such that it included at the end of step (b) i.e., "and then separately".

This erroneous wording was redundant given the amendment in former auxiliary request 2, which specified that "the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation".

The deletion of "and then separately" in the main request amounted to a correction of an obvious error.

Article 83 EPC

The skilled person would apply a practical test in biomass conversion for determining whether hydrolysis is complete or not. Even appellant II in its submission of 13 July 2016 at page 15, second and third paragraphs stated:

> "As can be seen from the activity vs. time plots in documents such as documents D16 and D17, the time course of a hydrolysis reaction follows a hyperbolic path with rapid cellulolysis in the early stages giving way to an extended "tail" of reduced activity as the concentration of substrate and enzyme activity falls. (...)."

Appellant II failed to provide any evidence showing that the skilled person could not arrive at the claimed subject-matter without unreasonable effort. It provided

no verifiable facts supporting serious doubts that the subject-matter claimed was enabled under Article 83 EPC.

Article 54 EPC

In document D2, the polypeptide with cellulolytic enhancing activity was added to the cellulase to carry out the hydrolysis. Although document D2 at page 14, lines 10 to 13 mentioned that "hydrolysis and/or fermentation" might be carried out in the "presence of a cellulolytic enzyme in combination with a polypeptide having enhancing activity", the skilled person would not seriously contemplate carrying out only fermentation but not hydrolysis (the "or" option) in the presence of a cellulolytic enzyme in combination with a GH61A polypeptide. Document D2 failed to describe the addition of one or more GH61 polypeptides after hydrolysis.

The continuous process disclosed in document D16, where the addition of substrates and cellulase, and the removal of fermentation products were carried out continuously or at regular intervals and furthermore where saccharification and fermentation proceeded at the same time, were not covered by the claims.

Article 56 EPC

The inventive step approach set out in the decision under appeal was essentially agreed with, except that the objective technical problem was set out more specifically in paragraph [0004] of the patent as the provision of processes with shortened fermentation time, increased rate of fermentation, increased yield

of the fermentation product and reduced production costs.

In the prior art, GH61 polypeptides were only known to have an effect as cellulose enhancers, i.e. to boost the hydrolysis of cellulosic material with cellulases. The beneficial activity of GH61 polypeptides in the fermentation of hydrolysates of lignocellulosic materials was not recognised in the prior art.

The beneficial effect attributed to the GH61 protein during fermentation could not simply be explained by its effect in increasing the rate of cellulose hydrolysis, which was not 100% complete.

In example 1 of the patent, after the hydrolysis was complete, the solid and liquid phases were separated from each other by centrifugation. The GH61 polypeptide was added to the liquid phase, essentially free of residual cellulose, in the fermentation step. Due to the separation of the substrate, the effect of the polypeptide could not come from the hydrolysis of residual cellulose.

Figures 2 and 3 of the patent showed that the concentration of glucose and xylose fell more rapidly during fermentation when GH61 polypeptide was present. This effect could not be explained by an increased residual cellulose hydrolysis.

The increase in ethanol yield in Table 1 of the patent could not be attributed to an increase in cellulase activity, since the cellulose was removed by centrifugation and the increase in percent ethanol yield was too important to be attributed to the hydrolysis of the residual cellulose.

XI. The submissions made by the **appellant II**, insofar as relevant to the present decision, may be summarized as follows:

Article 83 EPC

The skilled person was unable to determine when hydrolysis was complete. There was no definition in the patent how this feature had to be interpreted and how it had to be determined so as to reliably reproduce the invention claimed. The skilled person had first to determine when hydrolysis was "complete" before being able to add the GH61 proteins and reproduce the invention. However, there were multiple ways to define "complete hydrolysis". For example, by setting a minimum activity threshold and defining any reaction falling below this threshold as "complete", or by defining the time point when the hydrolysis reaction rate fell to zero on a hydrolysis activity versus time plot. Since there was no definition of "complete hydrolysis", the skilled person could choose among several alternative definitions which prevented him from determining the area claimed and from knowing whether he was operating in this area or not and thus to reliably reproduce the claimed invention.
The effect of a hydrolysis reaction having a rate similar in magnitude to the effect of interest (increase in ethanol yield) should not be ignored.

Article 54 EPC

Document D2 anticipated the process of claim 1 in that is specified that "[I]n a preferred embodiment the hydrolysis and/or fermentation is carried out in the presence of a cellulolytic enzyme in combination with a

polypeptide having enhancing activity. In a preferred embodiment the polypeptide having enhancing activity is a family GH61A polypeptide." (emphasis added by appellant II)(see page 2, lines 3 to 9 and page 14, lines 10 to 13).

The term "A and/or B" is "A (only) or B (only) or both (A+B)". Thus, the passage on page 14 of document D2 explicitly disclosed "a process where the fermentation (only) was carried out in the presence of a cellulolytic enzyme in combination with a polypeptide having enhancing activity". Thus, where the fermentation (only) was carried out in the presence of the polypeptide having enhancing activity, and it was absent during hydrolysis, the polypeptide having enhancing activity must have been added after the "completion" of hydrolysis.

Document D16 anticipated the subject-matter of both claims 1 and 8. It described a continuous fermentation reaction (cSSF) to which enzymes (including GH61) were added when the previous round of hydrolysis came to an end (see page 2, lines 2 to 9 and claim 11; page 28, lines 2 to 3, claim 13; page 15, lines 33 to 16, line 21).
The enzyme composition comprised a polypeptide having cellulolytic enhancing activity (see page 45, line 36 to page 46, line 1) and reference was made to inter alia patent application WO2005/074656 disclosing GH61A (document D5 in the present proceedings). The pre-treatment of cellulosic material (i.e PCS) was disclosed on page 9, line 34 to page 10, line 3 and claim 15. In the cSSF reaction the substrate was gradually consumed during the reaction until the point at which the addition of further substrate was required. At this time point in the cSSF reaction the

hydrolysis reaction reached an end point where further substrate along with further cellulase composition, as needed, had to be added. Thus, the addition of additional cellulase mixture (comprising GH61) to the cSSF vessel after this time point fell within the scope of "...one or more GH61 polypeptides are added after hydrolysis is complete".

Article 56 EPC

For assessing the inventive step of the subject-matter of claim 1, it was essential to determine whether the technical difference between claim 1 and the method disclosed in document D2 led to the technical advantage shown in the patent. The term "after hydrolysis is complete" might have two definitions:

1) the reaction rate has fallen to zero **or**
2) the reaction rate is coming to an end but is still ongoing at a low non-zero rate.

1) When complete hydrolysis meant that the rate of the hydrolysis reaction has fallen to zero

The patent did not disclose a process of producing fermentation products in which hydrolysis was complete, i.e. that the hydrolysis rate equals zero. The term "after hydrolysis is complete", used in claims 1 and 8, had not been defined in the patent. There was no proof that the claimed subject-matter by adding GH61 polypeptide to the fermentation step enhanced the production of fermentation product after hydrolysis of pre-treated lignocellulose containing material was complete (i.e. when the rate of the hydrolysis reaction has fallen to zero). The alleged effect was prima facie

not credible and unsupported. The burden of proof for establishing that the claimed subject-matter led to an advantageous technical effect or not rested with the party claiming it or disproving it (see decisions T 97/00 and T 1409/04).

Documents D16 and D17 indicated that after 8 days the hydrolysis reaction remained ongoing, albeit at a low rate. Thus, the addition of a cellulolytic enhancing GH61 protein to such a reaction was expected to result in an uplift in ethanol yield of approx. 1 to 3%, in line with the hydrolysis stimulating effect assigned to GH61 reported in Table 1 of the patent. It was also noted that the rate of hydrolysis reactions after 8 days was at the level of about 1 % day, similar in magnitude to the ethanol yield increase observed in Table 1.

If "complete hydrolysis" meant that the rate of the hydrolysis reaction had fallen to zero, then there was no technical evidence in the patent that the advantageous effects were obtained under these circumstances. The objective technical problem thus had to be reformulated in less ambitious terms as the provision of "alternative fermentation method".

The skilled person, faced with the technical problem of providing an alternative method to the one disclosed in document D2, would have reasonably expected that the claimed method was such an alternative process. Thus, the claims lacked an inventive step.

2) When complete hydrolysis meant that the reaction rate is coming to an end but is still ongoing at a low non-zero rate

The use of GH61 proteins in hydrolysis and fermentation reactions and their advantages were well known in the prior art (see documents D2, page 2, lines 3 to 7 and page 14, lines 10 to 13; D5, especially paragraph bridging pages 45 and 46).

It was obvious to the skilled person that adding a protein known to enhance cellulolytic activity, GH61, to an ongoing cellulolytic reaction would enhance that reaction (see document D2, p.11, lines 20 to 23). This enhanced reaction increased the fermentable breakdown product which in turn increased the levels of fermentation product even if said level was low (such as ethanol). The hydrolytic activity in the medium was expected to be ongoing after 8 days of hydrolysis (see Example 1 of the patent, paragraph [0149] and document D18; document D16, Figure 1b). On the basis of the present definition of "complete hydrolysis", the claims did not meet the requirements of Article 56 EPC.

The experiments carried out in the patent could not exclude that - at least in some embodiments covered by the claims - the observed ethanol increase was due to an increased low level of hydrolysis of residual lignocellulosic material.

First, a centrifugation step did not completely separate the substrate from the liquid phase. Some poly- and oligosaccharides remained in the reaction medium and the hydrolysis of these at an increased rate following the addition of GH61 was consistent with the observed increase in ethanol yield. In document D18, the hydrolysed slurry was not centrifuged before the GH61 polypeptide was added. As such the hydrolysed medium contained more substrate than the medium used in the examples of the patent. The boost of ethanol yield,

observed in document D18, arose therefore from the hydrolysis of the still available substrate in the hydrolysed medium compared to the centrifuged substrate when GH61 was added.

Secondly, post-published documents D10 and D11 described multiple effects of the GH61 polypeptide, one of which was an enhancement of hydrolysis activity resulting from the opening of the substrate structure, leading to faster production of cellulose products. The GH61 polypeptides were also identified as oxidases (document D10, Fig. 1 on page 2633; document D11, Fig. 3 on page 5). However, the oxidising 3,5-dinitrosalicylic acid (DNS) assay, detecting sugar reducing ends, to measure the glucose concentration in the patent might not detect oxidised glycosyl products resulting from the GH61 polypeptide oxidase activity. Hence, whilst the GH61 polypeptide oxidising activity led to an increase in the concentration of cellulose lysis products, the proportion of products detectable by the DNS assay might be lower. Moreover, an increase in cellulose lysis products through the GH61 polypeptide's oxidizing action might promote yeast cell growth, leading to an increased consumption of fermentable products and thereby contributing to a more rapid decrease in glucose and xylose. The reduced concentration of glucose and xylose levels in the presence of GH61 polypeptide could not demonstrate that cellulolysis was not increased when GH61 was added (see Figs 2 and 3 of patent).

Thirdly, in document D18, the solid substrate was not removed by centrifugation. The conditions used for the activity assessment closely mirrored those used by the patent. The enhanced ethanol yield in document D18 was attributed to the hydrolysis of a greater proportion of

substrate present in document D18 than in the examples of the patent.

Thus, the technical advantage of increased ethanol yield was not demonstrated for hydrolysis reactions where the reaction rate has fallen to zero, and was not unexpected for ongoing hydrolysis reactions (even at a low rate).

XII. Appellant I requested that the appeal of the opponent be dismissed.

XIII. Appellant II requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

Main request (claims 1-9)

1. According to appellant I, auxiliary request 2, filed with the statement of grounds of appeal, was intended to be identical to the auxiliary request 2 filed before the Opposition Division. However, a typographical error was introduced in claim 1 of the retyped version of auxiliary request 2, as filed in appeal proceedings. Given the amendment introduced with auxiliary request 2, the erroneous inclusion of the wording "and then separately" was clearly redundant. Correction of such an obvious error was thus requested.

Rule 139 EPC provides that:

"Linguistic errors, errors of transcription and mistakes in any document filed with the European Patent Office may be corrected on request. However, if the request for such correction concerns a description,

claims or drawings, the correction must be obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction".

Furthermore, in accordance with the Enlarged Board of Appeal decision G 3/89 (OJ EPO 1993, page 117, point 2 of the decision), the requirement laid down in Rule 88, second sentence, EPC 1973 that a correction must be obvious further implies that "the incorrect information is objectively recognisable too". It must be established that (i) an error is in fact present, and that (ii) the correction of the error is obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction.

1.1 In the decision under appeal, the opposition division concluded that the patent could be maintained on the basis of auxiliary request 2 and a description adapted thereto. Claim 1 of then auxiliary request 2 was only amended in that it specified that "the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation". Claim 1 step (b) was not amended.

1.2 In the statement of grounds of appeal of 14 February 2017, page 1, point 1.3, appellant I explicitly mentioned that auxiliary requests 1 and 2 (AR1 and AR2) "are identical to the correspondingly numbered requests that were filed before the Opposition Division". Claim 1 of the auxiliary request 2 enclosed for consideration however comprised a further amendment. This discrepancy unambiguously highlighted that there was an error.

1.2.1 Since the wording "and then separately" in step b) of claim 1 of auxiliary request 2, submitted with the statement of the grounds of appeal, is missing in the auxiliary request 2 upheld by the opposition division and is redundant in view of other amendments present in both auxiliary requests 2, this wording was clearly introduced in error.

1.2.2 Given appellant I's statement of grounds of appeal on point 1.3, the wording of auxiliary request 2 claim 1 attached to the decision under appeal, and the redundancy of the wording in step b) of claim 1 compared to the original amendment introduced in claim 1, which specified that "the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation", the board considers that the deletion of the term "and then separately" in step b) of claim 1 amounts to the correction of an obvious error. It is immediately evident that nothing else is intended than what is offered as the correction.

1.2.3 Thus, the board accepts that the correction may be granted so that the request filed with appellant I's letter of 15 October 2021 replaces former auxiliary request 2 and is made its main request.

Article 83 EPC

2. Appellant II considered that the term "after hydrolysis is complete" was not defined in the patent. The failure to provide a definition for this term prevented the skilled person from reproducing the claimed method and from determining whether it fell under the scope of protection when it carried out the claimed method.

2.1 In the board's view, there is a distinction between the meaning of "clear" in Article 83 EPC, which concerns the *disclosure* (the "technical teaching") of the patent on the one hand, and in Article 84 EPC, which relates to the *claims* which "shall define the matter for which protection is sought" on the other hand. Accordingly, it is not sufficient to establish that an ambiguity in the wording of the claims exists in order to establish insufficiency of disclosure. It is rather necessary to show that the patent as a whole does not enable the skilled person, relying on the description and common general knowledge, to carry out the invention (see "Case Law of the Boards of Appeal of the EPO", 9th edition 2019, II.C.8.2).

2.2 Examples 1 and 2 in the patent describe a process with discrete steps of hydrolysis and fermentation. The hydrolysis was carried out on unwashed PCS at 20% total solids for 8 days in the presence of a cellulase. The hydrolysed substrate was separated into a solid and a liquid phase and the liquid supernatant was subsequently fermented. The skilled person has no difficulty in performing hydrolysis to completion. Nor is there any difficulty for the skilled person in adding the GH61 polypeptide and fermenting the hydrolysate. Hydrolysis "is complete" when the hydrolysis reaction rate equals zero or is negligible and can no longer be measured. This can be ascertained using routine experimentation.

2.3 There are no facts and evidence showing that a skilled person cannot ferment a hydrolysed pre-treated lignocellulose-containing material, whose hydrolysis is complete. Although different degrees and variations of hydrolysed cellulosic material may be possible when the rate of hydrolysis is measured as zero, and considered

to be "complete", this result is highly dependent on the technique used. This uncertainty in the envisaged scope of protection amounts to a matter of clarity of definition of the claimed subject matter rather than of lack of sufficiency of disclosure.

2.4 The skilled person knows that the rate of a chemical reaction decreases as the level of conversion to product increases so as to arrive at a chemical equilibrium: a state in which both the reactants and products are present in concentrations which have no further tendency to change with time, so that there is no observable change in the properties of the system. Hydrolysis has come to an end. There is no reason why processes where hydrolysis is "coming to an end", i.e not yet ended and complete, should fall under the term "after hydrolysis is complete". This interpretation is excluded by the skilled person as claim 1 specifies that the "...hydrolysis is taken to completion before initiation of fermentation". The skilled person knows that a biomass conversion to zero starting material and 100% product takes extremely long, if achievable at all - as the rate of reaction is limited by the diffusion of the hypothetical "last molecule" of starting material. Thus, the only sensible interpretation for the term "after hydrolysis is complete", is to apply the practical test - in which the chemical reaction rate is zero, as opposed to a theoretical approach requiring the total conversion of reactants into substrates, which is impossible to achieve in practice.

2.5 Although the hydrolysis reaction is mentioned as complete, no threshold hydrolysis reaction rates are disclosed in the patent. As elaborated above the hydrolysis reaction rate can only be zero or zero yet taking into account uncertainty and/or experimental

errors. As no threshold hydrolysis reaction rate is disclosed in the patent, let alone one having a magnitude similar to the increase of ethanol yield, no effect could have been disclosed for this hydrolysis reaction rate either. Apart from its percentage value, the appellant II failed to establish a direct relationship between the percentage yield and the percentage hydrolysis rate per day.

2.5.1 For all the reasons presented above, the board considers that since the patent does not disclose any minimum activity threshold value below which the reaction should be considered "complete", appellant II's second interpretation must be disregarded. On the other hand, in accordance with the contested decision, the only sensible definition which can be attributed to a complete hydrolysis is that of the end of the chemical reaction because no substrate or no reactant/ active catalyst is left for carrying out the chemical reaction. A chemical reaction mixture at its equilibrium requires only routine experimentation and may be readily determined. Thus, although doubts were raised that the claimed invention could not be carried out without undue burden, they were not substantiated by verifiable facts. The requirements of Article 83 EPC are met.

Article 54 EPC

Document D2

3. Appellant II asserted that the process of claim 1 was anticipated by the disclosure of document D2.

3.1 Document D2 describes a process for producing a fermentation product from lignocellulose-containing

material, comprising the steps of, (a)(i) pre-treating a lignocellulose-containing material, (a)(ii) hydrolyzing the pre-treated lignocellulose-containing material, (b) fermenting the hydrolyzate obtained in step (a) using a fermenting organism (see page 2, lines 3 to 9). The cellulolytic enzymes used in the processes are defined on page 10, line 27 et seq. and may comprise cellulolytic preparations including cellulolytic enhancing activity polypeptides (GH61A). In a preferred embodiment the hydrolysis and/or fermentation is carried out in the presence of a cellulolytic enzyme in combination with a polypeptide having enhancing activity. In a preferred embodiment the polypeptide having enhancing activity is a family GH61A polypeptide.

3.1.1 The term "presence" in document D2 on page 14, lines 10 to 13 or on page 10, lines 27 to 29 of document D2 cannot only mean an addition of GH61 to a fermentation step.

3.1.2 The cellulolytic enhancing activity, defined in the paragraph bridging pages 13 and 14 of document D2, aims at enhancing the hydrolysis of a lignocellulosic derived material. The "presence" of a cellulolytic enzyme in combination with a cellulolytic enhancing activity polypeptide, e.g. a GH61A polypeptide, during hydrolysis or hydrolysis and fermentation is undisputed, while the "addition" of a combination of cellulolytic enzyme with a cellulolytic activity enhancing polypeptide during fermentation only is controversial and notional.

3.1.3 Even if document D2 discloses, due to the conjunction "and/or", a process comprising a fermentation step in which cellulolytic enzymes in combination with a

cellulolytic activity enhancing polypeptide are present, there is no direct and unambiguous disclosure in document D2 specifying that the preceding hydrolysis step is taken to completion before initiation of fermentation.

3.1.4 The "presence" of a cellulolytic activity enhancing polypeptide during fermentation with a cellulolytic enzyme refers to processes in which hydrolysis is carried out, but not yet complete, while fermentation begins and proceeds. Even if the presence of cellulolytic enzyme in combination with a cellulolytic activity enhancing polypeptide during fermentation may be due to the "addition" of a cellulolytic activity enhancing polypeptide during fermentation, said addition does not directly and unambiguously imply that the preceding hydrolysis step is complete as required in claim 1.

3.2 Appellant II asserted that the skilled person was familiar with the concept of supplementing a completed hydrolysis with additional proteins so as to improve the degradation of cellulosic material and, therefore maximise ethanol yield.

3.3 In the board's view, even if it is known and technically sensible to supplement proteins during fermentation so as to improve the degradation of cellulosic material and to maximise its fermentation yield, this also means that the preceding step of hydrolysis had not been taken to completion. Thus, the process disclosed in document D2 does not fall under the scope of claim 1.

3.3.1 The term "after hydrolysis is complete" as explained above in items 2.4 and 2.5.1 cannot "...refer to

situations where hydrolysis is coming to an end and fermentation is in turn becoming the main process". It defines a state and not a time span during which an activity declines while another one expands. The reaction rate "is complete" when the hydrolysis reaction rate using routine experimentation equals zero or is negligible so that it can no longer be determined.

3.3.2 In view of document D17, Table 2, complete hydrolysis will be achieved when the conversion rate is either zero or negligible and graphically on the plateau, given the gradual tailing off of the hydrolysis (see appellant II's statement of grounds of appeal on page 13). The same reasoning applies to the hydrolysis of document D16 shown in Fig 1B.
How long it takes to achieve complete hydrolysis and thus the plateau on the graph of hydrolysis rate versus time is reached is irrelevant. Thus, whether or not a hydrolysis reaction is complete on day 8 after its initiation is not an issue to be addressed as no time limit is specified in claim 1.

Document D16

3.4 Appellant II asserted that document D16 anticipated the subject-matter of both claims 1 and 8. This document described a continuous fermentation reaction (cSSF) to which enzymes (including GH61) were added when the previous round of hydrolysis had come to an end.

3.5 In the board's view, the process of claim 1 excludes continuous processes as described in document D16, because the hydrolysis and fermentation steps are carried out as separate hydrolysis and fermentation, and the hydrolysis is taken to completion before

initiation of fermentation. For this reason alone, the method of claim 1 cannot be anticipated by the method disclosed in document D16.

3.6 Even disregarding this aspect, the board can neither directly nor unambiguously identify in document D16 a process specifically combining the pre-treatment of lignocellulose-containing material - which is only a fraction of what constitutes a cellulose-containing material - with the addition of the GH61 polypeptide having cellulolytic enhancing activity comprised in enzyme compositions involved in the processing of a cellulose containing material to glucose, because the mere mention of several patent numbers describing enzyme compositions having cellulolytic enhancement activity is not a direct and unambiguous disclosure of a composition comprising GH61 (see WO2005/074656: document D5).

3.6.1 The board considers that the subject matter of claims 1 and 8 is not anticipated by the contents of documents D2 and D16.

Article 56 EPC

3.7 It seems common ground between the parties that document D2 represents the closest prior art for the subject-matter of claim 1.

3.8 Document D2 describes a process of fermenting a mash of hydrolysed lignocellulose-containing material at a higher pH than usual and controlling contamination by spoilage bacteria at the same time (see page 1, line 34 to page 2, line 15). This is achieved by using a very high dry solids concentration during fermentation. The process steps defined in claim 1 : pre-treatment,

hydrolysis and fermentation are also disclosed (see page 2 lines 3 to 9). Examples 1 to 3 describe the use of a cellulase preparation A comprising a GH61A polypeptide during hydrolysis in combination with cellulolytic enzymes.

3.9 The difference between the process described in document D2 and the subject-matter of claims 1 and 8 is that the hydrolysis of the lignocellulosic substrate is taken to completion before initiation of fermentation and that one or more GH61 polypeptides are added to the separated fermentation substrate after hydrolysis is complete.

3.10 The technical effect underlying these differences is that the addition of GH61 polypeptide during fermentation, initiated after hydrolysis is complete, increases ethanol yield, irrespective of its level.

3.11 The problem underlying the claimed invention can therefore be defined as the provision of an enhanced process of producing a fermentation product.

3.12 The solution to this problem is defined in claim 1.

3.13 The board considers that in assessing inventive step it must be convincingly shown that the problem underlying the claimed invention is effectively solved by the process according to claim 1.

3.14 Appellant II pointed out that the patent did not disclose a process of producing fermentation products in which hydrolysis was proven to be complete.

3.14.1 The board considers that the hydrolysis reaction "is complete" when the hydrolysis reaction rate using

routine experimentation equals zero or is negligible so that it can no longer be determined (see also items 2.4, 2.5.1 and 3.3.1 above).

3.15 Appellant II contended that there was no experimental proof neither in the patent nor elsewhere that the claimed method led to an enhanced production of fermentation product.

3.16 The board notes that examples 1 and 2 of the patent and the supplementary data submitted as document D18 describe the use of a "cellulase preparation 2" for 8 days (see paragraphs [0096], [0141] of the patent). Examples 1 and 2 of the patent describe centrifugation of the hydrolysed slurry to separate the solid from the liquid fraction. The separate fermentation of the supernatant with yeast and the GH61 polypeptide shows an increased ethanol yield, while the glucose and xylose concentrations drop more rapidly in the presence of GH61 polypeptide than in its absence (see Fig. 1, 2 and 3 of the patent). In Example 2 the percentage increase in ethanol is too important to be attributable to the hydrolysis of residual cellulose (see Table 1). Likewise, in document D18, the increase in ethanol of up to over 15% at 24 hours and over 4% at 48 hours, after having hydrolysed lignocellulose-containing material for 8 days and having fermented the hydrolysed substrate with GH61 polypeptides for 2 days, compared to the same material to which no GH61 polypeptide was added, cannot be attributed to the conversion of residual substrate to sugars as the percent conversion to sugar is, accepting opponent's calculations from the graph on page 13 of its statement of grounds of appeal, on day 7 less than 1.5% / day (see document D17, Table 2).

3.17 Thus, the board considers that none of the results reported can be attributed to an increased hydrolysis of residual cellulose. The increased ethanol yield obtained by first hydrolysing the substrate and then, once hydrolysis is complete, separately fermenting the hydrolysed pre-treated lignocellulosic material in the presence of GH61 is considered plausible.

3.17.1 Each of the parties to the proceedings carries the burden of proof for the fact they allege. Since it is plausible, based on the available experimental results, that the effect was not due to a concurrent hydrolysis of residual cellulose by cellulase in combination with GH61 during fermentation and appellant II provided no corroborating evidence to the contrary, appellant II has not discharged its burden of proof (see decisions T 97/00 point 3.1.6 of the reasons and T 1409/04 point 3.1 of the reasons).

3.17.2 The board finds no convincing facts nor evidence demonstrating that the ethanol increase observed in the experiments carried out in the patent and claim 1 is due to an increased hydrolysis of residual lignocellulosic material in the separated liquid phase following centrifugation.

3.18 Although the board accepts that a centrifugation step might not lead to a complete separation of substrate from the liquid phase, there is however no evidence that poly- and oligosaccharides remaining in the separated reaction medium are present in sufficient quantity to allow the re-initiation of hydrolysis after the addition of GH61, which is completed in the previous step, so as to increase the concentration of fermentable sugars in the medium thereby obtaining a higher ethanol yield.

3.18.1 Although the board agrees that Figures 2 and 3 of the patent do not demonstrate that there is no increase in cellulolysis when GH61 is added, the board finds no evidence to the contrary either, namely that the addition of GH61 polypeptide to the fermentation medium re-initiates cellulolysis.

3.18.2 Even if the post-published documents D10 and D11 provide information on the catalytic mechanism of GH61 polypeptides, and that they generate oxidized products which are not detected by the DNS detection assay described in the patent, the board finds no evidence that the addition of GH61 polypeptide to the fermentation medium re-initiates cellulolysis. First there is no evidence that the reduction in detectable so-called reducing sugars, containing an hemiacetal functional group, is due to the action of GH61 polypeptide on its substrate rather than on its consumption by the fermenting organism (yeast) during fermentation. Secondly, there is no evidence that the reduction in reducing sugars is due to increased yeast growth caused by the increased presence of fermentable sugars due to the hydrolysis/oxidizing activity of GH61 polypeptide, rather than their consumption by the yeast during fermentation. The board finds no support for any of the appellant II's allegations.

3.18.3 Although the solid substrate was not removed by centrifugation in the process of document D18, the board cannot see why the greater magnitude of the increase in ethanol observed in D18 compared to the patent is evidence that said increase comes from the hydrolysis of the substrate by the GH61 polypeptide, in particular when the process claimed specifies that the

previous hydrolysis step of the pre-treated lignocellulose-containing material must be complete.

3.19 In view of the above findings, the technical problem identified in item 3.11 above must be considered to be plausibly solved.

Obviousness

3.20 As summarised above, document D2 refers to a process of fermenting a mash of hydrolysed lignocellulose-containing material at a higher than usual pH and to controlling contamination by spoilage bacteria at the same time at high dry solid concentration.

3.21 The skilled person starting with the content of document D2 and faced with the technical problem of providing an enhanced process of producing a fermentation product, in the absence of any indication of the role of the GH61 polypeptide may have during fermentation, would not have arrived at the subject-matter of claims 1 and 8 in an obvious way. The board concurs with the findings of the opposition division in point 11.5 of the decision under appeal.

3.22 The board concludes that the process of claim 1 and the use of claim 8 involve an inventive step.

Order

For these reasons it is decided that:

The appeal of appellant II is dismissed.

The Registrar: The Chairman:

L. Malécot-Grob B. Stolz

Decision electronically authenticated