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Datasheet for the decision of 24 June 2014

Case Number: T 1383/10 - 3.3.08

Application Number: 93917602.0

Publication Number: 0717778

IPC: C12N15/57, C12N9/54, C11D3/386

Language of the proceedings: EN

Title of invention:
HIGH ALKALINE SERINE PROTEASES

Patent Proprietor:
GENENCOR INTERNATIONAL, INC.

Opponent:
Henkel AG & Co. KGaA

Headword:
Mutants PB92, S309 serine proteases; low temperature detergent/GENENCOR

Relevant legal provisions:
EPC Art. 123(2), 84, 83, 54, 56
RPBA Art. 13(1)

Keyword:
Admissibility: Main Request, and Auxiliary Requests 1, 3-4, 6-7 (yes); Auxiliary Request 5 (no);
Added subject-matter: Main request, Auxiliary Requests 1-2 (yes); Auxiliary Requests 3-4, 6-7 (no);
Clarity: Auxiliary Requests 3-4, 6-7 (yes);
Sufficiency of disclosure: Auxiliary Requests 3-4, 6-7 (yes);
Novelty: Auxiliary Requests 4 and 7 (yes);
Inventive step: Auxiliary Requests 3-4, 6 (no); Auxiliary Request 7 (yes);

Decisions cited:
G 0002/88, T 0019/90, T 0537/02, T 0660/02

Catchword:

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Case Number: T 1383/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 24 June 2014

Appellant: (Opponent)	Henkel AG & Co. KGaA VTP Patente 40191 Düsseldorf (DE)
Representative:	Ulbrich, C. Henkel AG & Co. KGaA VTP Patente 40191 Düsseldorf (DE)
Respondent: (Patent Proprietor)	GENENCOR INTERNATIONAL, INC. 925 Page Mill Road Palo Alto, California 94304 (US)
Representative:	Kremer, S. M. Mewburn Ellis LLP 33 Gutter Lane London EC2V 8AS (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 16 April 2010 concerning maintenance of the European Patent No. 0717778 in amended form.**

Composition of the Board:

Chairman	M. Wieser
Members:	P. Julià
	D. Rogers

Summary of Facts and Submissions

I. An opposition was filed against European patent 0 717 778 on the grounds of Articles 100(a),(b) and (c) EPC. The patent was based on the European patent application No. 93 917 602.0 and published as International patent application WO 94/02618 (hereinafter "*the application as filed*"). The opposition division decided to maintain the patent on the basis of a Main Request filed at the oral proceedings before it.

II. An appeal was lodged by the opponent (appellant). With the statement of Grounds of Appeal, the appellant filed new documentary evidence (documents D10 and D11).

III. The patentee (respondent) replied to the appellant's Grounds of Appeal and filed a Main Request (the request on which the opposition division decided to maintain the patent), Auxiliary Requests 1 to 3 and new documentary evidence (document D12).

IV. The board summoned the parties to oral proceedings and, in a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the summons, the parties were informed of the board's preliminary, non-binding opinion on the substantive issues of the case.

V. On 23 May 2014, the respondent replied to the board's communication and filed copies of its Main Request (the request allowed by the opposition division) and Auxiliary Request 1, former Auxiliary Requests 2 and 3, renumbered now as Auxiliary Requests 9 and 10, respectively, and new Auxiliary requests 2 to 8.

VI. On 13 June 2014, the appellant requested the board to exercise its discretion pursuant to Article 13(1) RPBA and not to admit the respondent's new requests into the appeal proceedings.

VII. Oral proceedings were held on 24 June 2014 in the presence of both parties. At these proceedings, the respondent withdrew Auxiliary Requests 6 to 8, former Auxiliary Request 9 was amended and renumbered as new Auxiliary Request 6 and former Auxiliary Request 10 was renumbered as new Auxiliary Request 7.

VIII. Claim 1 of the **Main Request** read as follows:

"1. A mutant protease for use in detergents

having greater than 90% homology with either the amino acid sequence of PB92 serine protease having the amino acid sequence:

H_2N-A-Q- [complete amino acid sequence] -T-R-COOH;

or the amino acid sequence of Subtilisin 309 serine protease having the amino acid sequence:

H_2N-A-Q- [complete amino acid sequence] -T-R-COOH;

in which the amino acid residue at a selected site corresponding to position V102 in said PB92 serine protease or said Subtilisin 309 serine protease is changed to A, E, G, H, I, L, M, N, P, Q, S, or T,

having improved wash performance relative to said PB92 serine protease or said Subtilisin 309 serine protease, said improved wash performance being determined in a washing system having the following features:

IEC-zeolite detergent Formulation April 1988 5.6 g/l; sud volume per beaker 200 ml; temperature 30°C; time 30 min; Na-perborate 4aq. 1.4 g/l; TAED 210 mg/l; 2 EMPA 221 10 x 10 cm clean swatch; 15 Stainless steel balls (phi. 6 mm); 2 mM Ca^{2+}; 0.7 mM Mg^{2+}; 0 mM $NaCO_3$; and 2 EMPA 116 or 2 EMPA 117 or 2 CFT As-3 CACAO 5 x 5 cm swatches."

Claims 2-5 were directed to preferred embodiments of claim 1. Claim 6 was directed to a DNA sequence encoding a mutant protease as defined in any of claims 1 to 4. Claim 7 was directed to a recombinant method of preparing a mutant protease as defined in any of claims 1 to 5. Claims 8 and 9 were directed to a detergent additive and a detergent composition, respectively, comprising one or more mutant proteases according to any one of claims 1 and 5 and, if desired, one or more enzymes selected from the group consisting of amylases, cellulases and lipases. Claim 10 was directed to the use of a mutant protease according to any of claims 1 to 5, in a washing process at a temperature preferably in the range of about 15°C to about 45°C.

IX. Claim 1 of **Auxiliary Request 1** was directed to a method of producing a mutant protease for use in detergents, wherein the protease was defined as in claim 1 of the Main Request. Claim 2 of this request read as claim 1 of the Main Request except for the deletion of the amino acid residue isoleucine (I) in the selection list of residues at position V102. Claim 3 of this request was a combination of claim 1 and 2 of the Main Request except for the addition of the amino acid residue tyrosine (Y) in the selection list of residues at position V102 and the deletion of the specific mutation [V102I] in the list of specific mutant proteases. Claims 4-11 of this request read as claims 3-10 of the

Main Request with corrected dependencies. Auxiliary Request 1 further contained claim 12 directed to a preferred embodiment of claim 1.

X. Claim 1 of **Auxiliary Request 2** read as follows:

"1. Use of a mutant protease, which is for use in detergents, in a washing process at a temperature of 20°C, said mutant protease having greater than 90% homology with the amino acid sequence of PB92 serine protease having the amino acid sequence:

H_2N-A-Q- [complete amino acid sequence] -T-R-COOH;

in which the amino acid residue at a selected site corresponding to position V102 in said PB92 serine protease is changed to A, E, G, H, I, L, M, N, P, Q, S, or T,

said mutant protease having improved wash performance relative to said PB92 serine protease said improved wash performance being determined in a washing system having the following features: ... [those features defining the washing system in claim 1 of the Main Request]".

Claim 2-4 were directed to preferred embodiments of claim 1 and essentially corresponded to claims 2-4 of the Main Request.

XI. Claim 1 of **Auxiliary Request 3** was identical to claim 1 of the Main Request except for the features defining the washing system which, in Auxiliary Request 3, required the presence of all three swatches cited at the end of claim 1, i.e. "... *and 2 EMPA 116 and 2 EPMA*

117 and 2 CFT As-3CACAO 5 x 5 swatches.". Claims 2-10 of this request and of the Main Request were identical.

XII. Claims 1-12 of **Auxiliary Request 4** read as claims 1-12 of Auxiliary Request 1 except for the definition of the washing system in claims 1-3 which was amended so as to have the characterizing features of the washing system defined in claim 1 of Auxiliary Request 3.

XIII. Claims 1-4 of **Auxiliary Request 5** read as claims 1-4 of Auxiliary Request 2 except for the definition of the washing system in claim 1 which was amended so as to have the characterizing features of the washing system defined in claim 1 of Auxiliary Request 3.

XIV. Claims 1-4 of **Auxiliary Request 6** read as claims 1-4 of Auxiliary Request 5 except for the fact that, in Auxiliary Request 6, the temperature of the washing process defined in the preamble of claim 1 was "*... at a temperature in the range of about 15°C to about 45°C ...*" instead of 20°C.

XV. Claim 1 of **Auxiliary Request 7** was the sole claim of this request and read as follows:

"1. A mutant protease for use in detergents having the amino acid sequence of PB92 serine protease:

H_2N-A-Q- [complete amino acid sequence] -T-R-COOH;

in which the amino acid residue V102 in said PB92 serine protease is changed to A, I, L, N, P, Q, or T."

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

D2: WO-A1-92/21760 (date of publication 10 December 1992);

D5: "Alignment Blap WT - Subtilisin 309 - PB92.apr", filed by opponent/appellant on 16 July 2008;

D10: EP-A1-0 328 229 (publication date: 16 August 1989);

D11: Letter from wfk-Testgewebe GmbH dated 20 May 2010 signed by Dr. T Hilgers; filed by the appellant on 3 August 2010.

Appellant's Submissions

XVII. Appellant's submissions, insofar as they are relevant to the present decision, may be summarised as follows:

Main Request
Article 100(c) EPC

The functional feature defined in claim 1 required the mutant proteases to have an improved wash performance using a specific washing system. The components of this system were disclosed in Example 1 (table on page 14) of the application as filed. Whereas the washing system in Example 1 contained three swatches (EMPA 116, EMPA 117 and CFT AS-3 Cacao), claim 1 did not require all three swatches but allowed the presence of only one or two, for which no basis was found in the application as filed. Although Tables I to III of the application as filed reported the wash performances of several mutant proteases for only one swatch, the washing system used to perform these wash assays was the washing system defined in Example 1 and thus always contained the three swatches.

Admissibility of Auxiliary Requests 3 and 4

An objection regarding a lack of a basis in the application as filed for a washing system not comprising all three swatches was raised at the beginning of the opposition proceedings and maintained throughout the appeal proceedings. However, none of the respondent's requests took into account this objection. It was only in reply to the board's communication and one month before the oral proceedings that, for the first time in the proceedings, Auxiliary Requests 3 and 4 were filed to overcome this objection. At this stage of the proceedings, these requests were late filed and took the appellant by surprise. The more so since, in the context of Article 54 EPC, the appellant had filed experimental evidence relying on the washing system defined in the former requests. If these late filed requests were admitted into the proceedings, the appellant had to carry out these experiments anew in accordance with the washing system defined in Auxiliary Requests 3 and 4. It was not possible to perform these experiments in a short time. Thus, the admission of Auxiliary Requests 3 and 4 would be unfair to the appellant.

Auxiliary Request 3
Article 100(c) EPC

The washing system defined in claim 1 was disclosed in Example 1 of the application as filed, which was concerned only with PB92 mutant proteases but not with Subtilisin 309 mutant proteases or with mutant proteases having more than 90% homology with PB92 or Subtilisin 309 mutant proteases. The reference in Example 1 to the wash performance of the new protease

mutants, found before the Table describing the components of said washing system, was to be read in this context and had to be understood as referring to PB92 mutant proteases only. There was no basis in the application as filed for generalizing the use of this specific washing system to mutant proteases in general.

There was also no basis in the application as filed for a combination of the features "*greater than 90% degree of homology*", the V102 position and the list of amino acids to be substituted at this position. This combination was a selection from three different lists present in the application, namely i) the position 102 among the list of all possible positions on page 7, line 38 to page 8, line 5, ii) the list of specific amino acid residues used to substitute the valine residue at position 102 (originally disclosed as any amino acid residue except valine), and iii) the selection of 90% homology from the values 70% and 90% on page 6, lines 34 to 37 of the application as filed. A selection made from several lists was not in line with the requirements of Article 123(2) EPC.

Article 84 EPC

The introduction of an amendment requiring the presence of three swatches in the washing system of claim 1 rendered this claim ambiguous. Claim 1 was open to interpretation since it was not clear whether the improved wash performance had to be found for all three swatches or if it was enough when it was determined in only one or two swatches.

Article 100(b) EPC

According to document D11, the "*IEC-zeolite detergent Formulation April 1988*" (IEC-A basis detergent), a component of the washing system defined in claim 1, was not commercially available and had been replaced by a new IEC-A* basis detergent. Although the new detergent had been designed to have a close similarity to the composition and the performance of the old detergent, both detergents had relevant differences in their composition. The effect of these differences on the wash performance of the claimed mutant proteases was not known. Since the actual composition of the old detergent was unknown and it was no longer commercially available, an important parameter of claim 1 was not sufficiently disclosed and characterized in the patent.

Claim 1 did not define the amount of mutant protease required in the washing system for the wash performance test. Thus, another essential feature of the functional test defined in claim 1 was lacking in the claim. Moreover, the wash performance test defined in claim 1 could be carried out on a protease weight basis or on a protease activity basis. Although the latter was not excluded by the claim, the patent did not provide any information how to carry out that embodiment. It was arguable whether such information was provided by the reference to the wash tests of document D10, but even if this was the case, document D10 was concerned only with the PB92 protease, not with Subtilisin 309 protease or the mutant proteases disclosed in the patent.

Articles 87 to 89 EPC

The findings of the opposition division as regards the claimed priority date had not been contested. The

washing system defined in claim 1 was not disclosed in the priority document and therefore, the claimed priority was not valid.

Article 100(a) EPC, Article 54 EPC

Claim 1 was directed to a product, to a mutant protease characterized by structural and functional features. Document D2 disclosed several mutant proteases derived from the BLAP enzyme which, as the BLAP enzyme itself, fulfilled all structural features defined in claim 1. As shown in document D5, the BLAP enzyme had greater than 90% homology to the sequences of the PB92 and Subtilisin 309 proteases and it had an isoleucine at position 102 instead of the valine present in the PB92 and Subtilisin 309 proteases. According to the patent, an isoleucine at position 102 resulted in an improved wash performance over the PB92 and Subtilisin 309 proteases. Thus, document D2 anticipated the claimed subject-matter.

Although no experimental evidence was required, such evidence had been filed to show that the BLAP enzyme actually had an improved wash performance, when tested in a weight- as well as in an activity-based system. Although the washing system used in these experiments - and commonly used in the field - was not identical to the washing system defined in claim 1, the differences were not relevant.

Article 100(a) EPC, Article 56 EPC

The closest prior art document D2 referred to the BLAP enzyme for use in detergents and as having advantageous properties over other commercially available enzymes. In this context, reference was made to a temperature

range of 10 to 60°C, thus including low temperatures. Although wash performance was not explicit mentioned in document D2, both, the increased protease and oxidative stability referred to in this document, were of relevance for achieving such performance. Thus, there was no technical problem to be solved, since document D2 disclosed proteases having all the structural features defined in claim 1 and indicated their advantageous effect in detergents, explicitly at low temperatures.

Nevertheless, if the technical problem was to provide mutant proteases with improved wash performance at low temperatures, the broad scope of claim 1 was not justified since there was no evidence on file to show that all claimed mutant proteases (having a degree of homology as low as 90%) fulfilled the functional requirement defined in claim 1. Claim 1 described only the result desired to be achieved (improved wash performance) but did not disclose a solution to achieve this result with the large number of possible mutant proteases having more than 90% homology to PB92 and Subtilisin 309 proteases. At the best, claim 1 cited a technical problem without providing the means to solve it. Each and every protease of the large group of proteases structurally defined in claim 1 had to be tested in order to know whether it solved the technical problem.

However, if the presence of one of the amino acid residues listed in claim 1 (including isoleucine) at position 102 was enough to fulfil the functional requirement defined in claim 1, the same applied to the BLAP mutant proteases disclosed in document D2. They all had an isoleucine at position 102 and their advantageous properties for use in detergents were

disclosed in the document. No inventive contribution was thus required to obtain the BLAP mutant proteases disclosed in document D2.

Auxiliary Request 4
Article 100(a) EPC; Article 56 EPC

Document D2 referred to the advantageous stability properties of the BLAP enzyme having an isoleucine residue at position 102. These advantageous properties of several BLAP mutant proteases, originally identified by computer-assisted methods, were actually determined by laboratory tests and reported in Tables 3 and 4 of document D2, representing the closest prior art document. Starting from this disclosure, and considering the technical problem, i.e. the provision of alternative mutant proteases with improved wash performance at low temperatures, the BLAP mutant proteases proposed in Table 2 of document D2 were an obvious choice. No inventive contribution was required to produce any of these BLAP mutant proteases or an arbitrarily selected subgroup thereof, such as the one whose members did not have an isoleucine at position 102.

Admissibility of Auxiliary Request 5

This request was late filed and changed the respondent's case with regard to the subject-matter on which the decision under appeal was based and to the subject-matter of the previous requests in appeal procedure. The value of 20°C was not present in any of the requests filed at the first instance or in the previous requests in appeal proceedings, where only a wide range of temperatures (15°C to 45°C) was referred to. The value of 20°C was taken from the description of

the patent and its introduction was of importance for the examination of Article 56 EPC, namely for assessing the alleged advantages of the claimed mutant proteases at this specific temperature. The comparative experimental evidence on file was performed at 30°C, the temperature of the washing assay defined in claim 1, but not at 20°C. Moreover, there was no information on file on the wash performance of the BLAP enzyme at the specific temperature of 20°C.

Admissibility of Auxiliary Requests 6 and 7

Auxiliary Request 6 was based on a request filed in reply to appellant's Grounds of Appeal, however, it had been additionally amended at the oral proceedings before the board, i.e. at the latest stage of the appeal proceedings, and should not be admitted. No objections were raised against the admissibility of Auxiliary Request 7.

Auxiliary Request 6
Article 100(a) EPC; Article 56 EPC

The use of proteases in general for detergents was well known and it did not, as such, provide any technical contribution to the prior art. This use was also suggested for the BLAP mutant proteases disclosed in document D2, as shown by references to prior art directly concerned with detergents and, more particularly, to document D10 as providing a wash test for measuring the wash performance of these enzymes. Indeed, the patent itself acknowledged the use of commercially available proteases at a temperature range of 40-60°C, which included the upper value of the temperature range indicated in claim 1.

Starting therefrom, the technical problem to be solved was the provision of an alternative use of the BLAP proteases. There was no evidence showing any improvement since document D2 already referred to the improved properties of the BLAP enzyme (with an isoleucine at position 12) over other commercially available proteases, namely an improved stability at a wide range of temperatures. The results in Tables 3 and 4 of document D2 showed that these BLAP mutant proteases had also a greater stability at 50°C, which is close to the upper limit of the temperature range indicated in claim 1. An improved stability at 50°C resulted in more stable and active enzyme at this temperature. Therefore, it was obvious that the wash performance of the enzyme at this temperature was also improved. No inventive merits were required to acknowledge this fact and to use the BLAP mutant proteases disclosed in document D2 for detergents at temperatures falling within the temperature range indicated in claim 1, as was shown by the disclosure of document D10.

Auxiliary Request 7

No objections were raised against this request.

Respondent's Submissions

XVIII. Respondent's submissions, insofar as they are relevant to the present decision, may be summarised as follows:

Main Request
Article 100(c) EPC

Throughout the application as filed, such as in Tables I to III, the wash performances of the mutant proteases

were measured on a single swatch. When read in its entirety, the application as filed did not require all three swatches to be present in the washing system defined in claim 1. The presence of all three swatches was not disclosed as an essential feature of this washing system. The relevant question was not what was present in the washing system of Example 1, but what had to be present in this system, i.e. what would have been considered to be an essential component of the defined washing system by a skilled person reading the application. There was an implicit teaching in the application as filed that not all three swatches were necessary for measuring the wash performances of the mutant proteases.

Admissibility of Auxiliary Requests 3 and 4

The objection regarding a lack of a formal basis in the application as filed for a washing system not containing all three swatches was considered not to be relevant by the opposition division. The filing of Auxiliary Requests 3 and 4 was in reply to the board's comments made in its communication. These requests were a *bona fide* attempt to overcome the objection raised under Article 123(2) EPC. The amendment introduced into these requests was straightforward, could be expected by the appellant and did not increase the complexity of the case. These requests did not put the appellant at a disadvantage. The deficiencies of the appellant's experimental evidence were not related to this objection but to other issues that had to be discussed under the relevant Article 54 EPC.

Auxiliary Request 3
Article 100(c) EPC

On reading the application as filed as a whole, it was clear that the washing system disclosed in Example 1 was applicable to the testing of mutant proteases in general. Throughout the description of the application there were several general references to the need for a wash performance test and a washing system for testing the mutant proteases of the invention. Such a wash system was described in Example 1 and expressly taught to be appropriate for all mutant proteases.

Claim 1 as filed was directed to mutant proteases having 70% homology to PB92 or to Subtilisin 309 serine proteases with at least one amino acid residue changed at one of the positions indicated in the claim. Position 102 was explicitly mentioned. Claim 2 as filed was dependent on claim 1 and disclosed the amino acid residues listed in claim 1 of Auxiliary Request 3 for changing V102. The deletion of various options in original claims 1 and 2 as filed and the introduction of a specific washing system for assessing the wash performance did not add subject-matter extending beyond the original disclosure. The limitation of the degree of homology to the preferred value of 90% was also in line with the disclosure of the application as filed. Claim 1 of Auxiliary Request 3 was not derived from a selection from three different lists but was the result of the deletion of subject-matter from the claims as originally filed, which was in line with the entire disclosure of the application as filed.

Article 84 EPC

Claim 1 required the presence of all three swatches in the washing system but did not require an improved wash performance for all of them. The presence of an improvement for one or two swatches was enough to

fulfil the functional feature defined in claim 1. This was shown by some of the PB92 mutant proteases exemplified in the patent. Claim 1 was not ambiguous and not open to interpretation.

Article 100(b) EPC

The detergent referred to in claim 1 was the standard IEC 60456 Type A detergent which had been updated to the new Type A* detergent. Both detergents were equivalent in terms of wash performance. Although the two detergents were acknowledged in document D11 to have a slightly different composition, document D11 did not state that they differed in their wash performances. Document D11 acknowledged the detergent referred to in claim 1 to be referenced as an international standard. Indeed, the standard IEC 60456 Type A, now Type A*, was a detergent commonly used by manufacturers for many test applications. Moreover, the wash performance test of claim 1 was a comparative wash test. Thus, all parameters had to be the same for the proteases to be compared. There was no evidence on file showing that the minor changes between Type A and Type A* detergents affected the comparative test of claim 1.

The wash performance test defined in claim 1 was consistently described throughout the patent as being performed on a weight basis. There was no reason for a skilled person to perform this test on an activity basis, the less so since the disclosure of the patent was in line with the common general knowledge of the skilled person and the prior art on file. The conception of notional embodiments having no bearing to the patent (such as a wash performance test based on protease activity) for assessing the sufficiency of disclosure was not in line with the case law. The

relevant question under Article 83 EPC was not whether the disclosure of the patent was sufficient for a skilled person to perform all possible embodiments of the invention, but whether it was sufficient enough for a skilled person to reproduce the invention as described in the patent. In any case, the patent referred to document D10 which disclosed standard activity assays for proteases. There was no evidence on file showing that the comparative wash performance test defined in claim 1 could not be carried out using such activity assays.

Article 100(a) EPC, Article 54 EPC

The claimed mutant proteases were characterized by structural and functional requirements. The BLAP enzyme referred to in document D2 and the mutant proteases derived therefrom did not fulfil the structural requirement defined in claim 1 since the presence of an isoleucine at position 102 did not result from a mutation as required in claim 1.

Although there was a causal link between the mutation at position 102 proposed by the patent and the desired intended effect (improved wash performance), i.e. the change of valine at position 102 in the sequences of the PB92 and Subtilisin 309 proteases to one of the amino acid residues listed in claim 1 (including isoleucine) resulted in an improved wash performance, it could not be excluded that in a few cases, depending on the background of the specific amino acid sequence of a particular mutant protease, such effect was not achieved. In the appellant's experimental evidence, the washing system used was always different from the system defined in claim 1. Apart from the (Type A or A*) detergent basis used, there were other differences

that were deliberately and without explanation introduced into said washing system. The effect of these differences on wash performance was unknown and not explained. Thus, there was no evidence on file showing - in a conclusive and convincing manner - that the BLAP enzyme or the mutant proteases derived therefrom fulfilled the functional requirement defined in claim 1.

Article 100(a) EPC, Article 56 EPC

Starting from the closest prior art, document D2, the technical problem was the provision of mutant proteases derived from the PB92 and Subtilisin 309 proteases and having an improved wash performance at low or reduced temperatures. Experimental evidence in the patent showed the disclosed mutant proteases to solve this technical problem. On the one hand, there was no evidence on file to show that there was no causal link between the amino acid change at position 102 indicated in claim 1 and the fulfillment of the functional requirement defined in this claim, on the other hand, there was no undue burden for a skilled person to assess the wash performance of a mutant protease structurally falling within the scope of claim 1. Although absolute certainty was not possible and thus, depending on their background sequences, a few mutant proteases possibly did not fulfil the functional requirement defined in claim 1, these mutant proteases were an exception and did not fall within the scope of the claim which only covered mutant proteases having the required functional feature.

Although some of the proteases disclosed in document D2 fulfilled the structural requirement defined in claim 1 and assuming, for the sake of argument, that they

inherently had the functional feature defined in claim 1, there was no information in document D2 as regards their wash performance, certainly not at low temperatures. Moreover, the skilled reader was not provided with any information concerning the relevance of these low temperatures. Hindsight was required to derive this information from document D2, which was concerned only with thermal and surfactant stability of the BLAP mutant proteases at high or increased temperatures, not with their wash performance, as shown by the results of the exemplified BLAP mutant proteases in Tables 3 and 4 of this document. The temperatures indicated there (50°C and 60°C) were high or increased temperatures far away from the relevant low or reduced temperatures referred to in the patent. Although document D2 referred to an advantageous protease and oxidative stability of the BLAP enzyme at a range of temperature that included low temperatures, it was also acknowledged that there was no correlation between stability and wash performance. Indeed these were different, not correlated, parameters. The stability properties of interest in document D2 were not reliable for predicting wash performance. Moreover, document D2 proposed a very large number of possible BLAP mutant proteases (Table 2) but the sole mutant protease actually exemplified was "I102W" (Tables 3-4). Tryptophan (W) was not a substitute residue listed in claim 1.

Auxiliary Request 4
Article 100(a) EPC; Article 56 EPC

The mutant proteases of claim 2 in Auxiliary Request 4 did not have an isoleucine at position 102, thereby the BLAP enzyme and most of the BLAP mutant proteases disclosed in document D2 did not fall within the scope

of this claim. Starting from document D2, the technical problem to be solved was the provision of (PB92 or Subtilisin 309 derived) mutant proteases having an improved wash performance at low or reduced temperatures.

In Table 2 of document D2, a large number of possible BLAP mutant proteases were proposed. However, they were only proposed and their actual properties were unknown. Although the positions and amino acid residues given in Table 2 were identified by computer-assisted methods and predicted to provide an improved thermal and/or surfactant stability, no prediction could be made on the wash performance, let alone at low temperatures, of the mutant proteases since the properties stability and wash performance were not correlated.

Moreover, hindsight was needed to identify - from the large number of BLAP mutant proteases suggested in document D2 - a group of BLAP mutant proteases having an advantageous property (improved wash performance, not even mentioned in document D2), under very specific conditions (at low temperatures, not suggested at all in document D2), and to select from this group of BLAP mutant proteases the subgroup defined in claim 2 of Auxiliary Request 4. There was no hint in document D2 to lead a skilled person to select, firstly, the position 102 and then the amino acid residues listed in claim 2 of Auxiliary Request 4 from all possible "*small amino acids*" cited in Table 2 of document D2 as appropriate for a change at position 102. All the less so, since the stability properties of the single BLAP mutant protease exemplified with a substitution at position 102 ("I102W"), did not show particularly advantageous properties when compared with the other

exemplified BLAP mutant proteases shown in Tables 3 and 4 of document D2.

Admissibility Auxiliary Request 5

This request was filed in direct reply to the board's comments with regard to claim 10 of the Main Request, a claim which had not been mentioned in appellant's Grounds of Appeal. The filing of this request was a justified reaction to the change of the appeal's framework. The (20°C) amendment introduced into this request was straightforward and did not raise any new problem under Articles 123(2), 84, 83 and 54 EPC. As for Article 56 EPC, the amendment did not introduce subject-matter extending beyond subject-matter already present in former requests which had not been objected under this Article. The use-claims of this request overcame objections raised against product-claims of former requests with the result that the disclosure of document D2 was no longer relevant.

Admissibility of Auxiliary Requests 6 and 7

Auxiliary Request 6 was based on Auxiliary Request 2 filed in reply to appellant's Grounds of Appeal and filed again, as Auxiliary Request 9, in reply to the board's communication. Thus, the request had already been on file at the earliest stage of the appeal proceedings. The amendment introduced into Auxiliary Request 6 overcame an objection raised under Article 123(2) EPC, which the board found to be relevant for the Main Request and Auxiliary Requests 1 and 2. The same amendment was present in Auxiliary Requests 3 and 4, which were found by the board to be admissible into the appeal proceedings. Auxiliary Request 7 was identical to Auxiliary Request 3 filed in reply to

appellant's Grounds of Appeal and filed again, as Auxiliary Request 10, in reply to the board's communication.

Auxiliary Request 6
Article 100(a) EPC, Article 56 EPC

The considerations made for product-claims were different from, and did not necessarily apply to, the subject-matter of use-claims (cf. G 2/88, OJ EPO, 1990, page 93). The specific use defined in claim 1 for the disclosed mutant proteases provided an inventive contribution over the closest prior art document D2. There was no indication in document D2 referring to the wash performance of the BLAP mutant proteases. Document D2 was only concerned with the stability of these proteases. Thus, the objective technical problem was not the provision of an alternative use for the BLAP mutant proteases, since no use at all was disclosed in document D2. The use of mutant proteases at the range of temperatures indicated in claim 1, which included low temperatures, was advantageous over the range of temperatures exemplified in Tables 3 and 4 of document D2, namely from 50°C to 60°C. There was no hint in document D2 that could have led a skilled person to the range of temperatures indicated in claim 1 and certainly not with the expectation to obtain any advantageous effect. A greater stability at temperatures of 50-60°C was not a prediction for an improved wash performance at 15-45°C, both properties were not correlated. The use of BLAP mutant proteases at this range of temperatures was not derivable in an obvious manner from document D2, either if taken alone or in combination with any other prior art on file. None of these prior art documents disclosed the washing system and washing assay defined in claim 1.

XIX. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

XX. The respondent (patentee) requested, as its Main Request, that the appeal be dismissed or alternatively that the patent be maintained upon the basis of any of the Auxiliary Requests 1 to 7. Auxiliary Requests 1 to 5 have been submitted under cover of a letter dated 23 May 2014, and Auxiliary Requests 6 and 7 have been submitted at the oral proceedings before the board on 24 June 2014.

Reasons for the Decision

Admissibility of the Main Request and of Auxiliary Request 1

1. The Main Request is identical to the request on which the opposition division decided to maintain the patent and, thus, it already forms part of the present appeal proceedings. Auxiliary Request 1 was filed by the respondent at the beginning of the appeal proceedings in reply to the appellant's statement of Grounds of Appeal. Both requests are admissible.

Main Request
Article 100(c) EPC; Article 123(2) EPC

2. It is contested whether there is a basis in the application as filed for the washing system described in claim 1, in particular a system containing only one or two but not necessarily all three swatches ("*EMPA 116*", "*EMPA 117*", "*CFT AS-3 CACAO*").

2.1 The features characterizing the washing system ("*IEC-zeolite*") used to test the wash performance of the mutant proteases disclosed in Example 1 are summarized in a Table on page 14 of the application as filed. All three swatches are present in this Table. The kinetic parameters and the wash performances of the mutant proteases of Example 1 are disclosed in Tables I to III of the application as filed. In Table III, the wash performances are measured and reported for all three swatches ("*116*", "*117*" and "*choc*"). Likewise, all three swatches are present in the modified ("*low detergency*") washing system described in Example 2 and summarized in a Table on page 15 of the application as filed.

2.2 Contrary to Table III, Tables I and II disclose only a single value for the wash performance of the mutant proteases, i.e. wash performances are reported for only one swatch (cf. footnotes on pages 17 and 21 of the application as filed, wherein it is indicated "*performance measured on EMPA 117*"). However, the ("*zeolite*") washing system is understood to contain all three swatches in accordance with the Table on page 14 of the application as filed.

2.3 The relevant question under Article 123(2) EPC is not whether the use of only one or two swatches is obvious from the disclosure of the application as filed or whether the presence of three swatches is an essential feature of the disclosed washing system. The relevant question is whether there is, either explicitly or implicitly, a basis in the application as filed for a washing system comprising only one or two swatches. In the light of the entire disclosure of the application as filed, the board does not see such a basis.

3. Thus, the Main Request is considered not to fulfil the requirements of Article 123(2) EPC.

Auxiliary Requests 1 and 2 (Admissibility of Auxiliary Request 2)

4. The washing system defined in claim 1 of Auxiliary Requests 1 and 2 is characterized by the same features as the washing system defined in claim 1 of the Main Request (cf. points VIII to X *supra*). Auxiliary Requests 1 and 2 are thus considered not to fulfil the requirements of Article 123(2) EPC.

5. In view thereof, there is no need for the board to consider the admissibility of Auxiliary Request 2 into the appeal proceedings, since it clearly does not fulfil the requirements of Article 123(2) EPC.

Admissibility of Auxiliary Requests 3 and 4

6. These auxiliary requests were filed in reply to the board's communication pursuant to Article 15(1) RPBA. They represent an amendment of the respondent's case, and in accordance with Article 13(1) RPBA may be admitted and considered at the board's discretion.

6.1 Except for an amendment in the features defining the washing system of claim 1 in Auxiliary Request 3 and claims 1-3 in Auxiliary Request 4, these auxiliary requests are identical to the Main Request and to Auxiliary Request 1, respectively (cf. points XI and XII *supra*). This amendment overcomes the objection raised under Article 123(2) EPC against the Main Request and Auxiliary Request 1 (cf. points 2 to 4 *supra*), it is straightforward, clearly derivable from

the application as filed, and it does not add any complexity to the case.

7. The board, exercising the discretion conferred to it by Article 13(1) RPBA, decides to admit Auxiliary Requests 3 and 4 into the appeal proceedings.

Auxiliary Request 3
Article 100(c) EPC; Article 123(2) EPC

8. The amendment introduced to define the washing system in Auxiliary Request 3 overcomes the objection raised under Article 123(2) EPC against the Main Request (cf. points 2 and 3 *supra*). Two other objections have been raised by the appellant under this article in appeal proceedings. These objections were also considered by the opposition division in the context of the Main Request (cf. pages 3-4, point 3 of the decision under appeal).

8.1 As for the first objection, the board does not agree with the appellant that the washing system defined in claim 1 is disclosed in the application as filed only for PB92 mutant proteases (Example 1) but not for Subtilisin 309 mutant proteases or for mutant proteases in general (cf. point XVII *supra*).

On page 6, lines 2-26 of the application as filed, reference is made to a "*test system*" disclosed in document D10 as being "*an efficient selection procedure on the performance*" of mutant proteases in general. In line therewith, similar references are found on page 12, lines 18-28 and page 13, lines 12-19, which explicitly state that the "*screening and selection of the enzymes* [i.e. the mutant proteases according to the invention] *... are essentially the same as described*

in" document D10. These passages are located in the application as filed just before the "*Experimental Section*" in which the wash performance results of Example 1, obtained by using the "*specially developed washing test which is described in detail in*" document D10, are disclosed (cf. page 14, lines 3-5 of the application as filed).

Thus, the reference to "*the wash performance of the new protease mutants*" on page 14, lines 8-10 of the application as filed clearly and unambiguously refers to its application to all mutant proteases disclosed in the application as filed and is not limited to the specific PB92 mutant proteases.

8.2 As for the second objection, the board cannot see that the claimed subject-matter is the result of a selection from three different lists, namely the list of positions open to mutation within the sequence of the PB92 and Subtilisin 309 proteases, the list of amino acids to be used for carrying out these mutations and the list specifying the percentage of homology (90%) to the PB92 and Subtilisin 309 proteases (cf. point XVII *supra*).

Claim 2 as originally filed is directed to a group of mutant proteases characterized by the presence of at least one mutation chosen from a list of specific mutations given in the claim. Position V102 and the residues cited in claim 1 of Auxiliary Request 3 are explicitly disclosed, namely [V102A], [V102E], [V102G], etc. (cf. page 28, lines 5-7, 9 and 13-14 of the application as filed). Claim 2 is a preferred embodiment of claim 1 as filed which is directed to mutant proteases for use in detergents that are structurally defined by "*having at least **70%** homology*

with either the amino acid sequence of PB92 serine protease ... or the amino acid sequence of Subtilisin 309 serine protease" (emphasis added by the board) and wherein the position 102 is also explicitly referred to as "*a selected site*" for mutation.

The same disclosure can be found on page 7, line 13 to page 9, line 11 of the application as filed wherein, just before this disclosure, reference is made to preferred embodiments of the invention, in particular "*... closely related serine proteases, preferably having a homology greater than about 70%, more particularly greater than about **90%**, are very suitable*" (emphasis added by the board) (cf. page 6, lines 34-37 of the application as filed). There is no other reference in the application as filed to any other preferred degree of homology for the disclosed mutant proteases. The limitation of the originally claimed group of mutant proteases (having at least 70% homology to PB92 or Subtilisin 309 proteases) to a preferred subgroup thereof (having greater than 90% homology to PB92 or Subtilisin 309 proteases) does not extend beyond the content of the application as filed and it is clearly and unambiguously derivable from said content.

9. Thus, Auxiliary Request 3 is considered to fulfil the requirements of Article 123(2) EPC.

Article 84 EPC

10. Whereas claim 1 of Auxiliary Request 3 requires the defined washing system to comprise three swatches ("*EMPA 116*", "*EMPA 117*", "*CFT AS-3 CACAO*"), it does not require the claimed mutant proteases to have an improved wash performance for all three swatches. An

improved wash performance determined by a measurement using only one of these three swatches is enough for a mutant protease to fulfil the functional feature defined in claim 1. This is in line with the disclosure of the patent which on page 11 in Table III identifies several PB92 mutant proteases having a worse wash performance for "*EMPA 116*" or "*EMPA 117*" swatches (such as [V102E], [V102N, R164Y] and [V102N, L211E]) but an improved performance for the other swatches. No lack of clarity arises from the wording of claim 1 which, therefore, is not open to interpretation and does not give rise to any ambiguity.

11. Therefore, Auxiliary Request 3 fulfills the requirements of Article 84 EPC.

Article 100(b) EPC; Article 83 EPC

12. Two objections have been raised by the appellant under Article 83 EPC:

12.1 Firstly, the appellant argues that a component of the washing system defined in claim 1, namely the "*IEC-zeolite detergent Formulation April 1988*", is not publicly available. Document D11 has been filed to support appellant's argument.

i) There is no doubt that the functional feature in claim 1, which relies on a measurement of the wash performance carried out with the specific washing system defined in claim 1, is essential for "*screening and selection*" of the claimed mutant proteases. The washing system and its composition is thus an essential feature of the claimed invention.

ii) In the board's view, the situation is similar to the use of a trademark or trade name in a claim. For the purpose of Article 83 EPC, the use of such words in a claim is undesirable. However, they may be allowed when they have become internationally accepted as standard descriptive terms and have acquired a precise meaning (cf. "Guidelines for Examination in the EPO", September 2013, Part F, Chapter III, point 7; see also, Chapter IV, point 4.8). The component of the washing system referred to by the appellant was a component of an accepted standard washing system (Internationale Norm IEC 60456:1998; IEC Referenzwaschmittel Typ A, in document D11).

iii) According to document D11, the IEC-A basis powder (IEC-A, the basis for the "*IEC-zeolite detergent Formulation April 1988*" of claim 1) was substituted by the IEC-A* basis powder, with the intention to be used for the same purpose. The substitution of the old standard product by the corresponding updated standard product is thus straightforward for a skilled person. There are, however, several differences in the composition of these powders. In particular, the substitution of EDTA by phosphonate and that of the defoaming agent by a constituent current at the time. Thus, they are similar standard detergents with some differing ingredients.

iv) The functional feature defined in claim 1 (improved washing performance) is of a relative nature, i.e. a comparative test between mutant proteases (fulfilling the structural features of claim 1) and the PB92 or Subtilisin 309 proteases. Although the appellant argues that the differences in the composition of the IEC-A and IEC-A* detergents are relevant and have an effect on the results of the comparative test of claim 1, there is no

evidence on file to support these allegations. There is nothing on file to demonstrate that the scope of claim 1 differs depending on which of the two washing systems is used, i.e. that different relative results are obtained depending on the use of either the old or the updated washing system. Thus, appellant's allegations do not fulfil the criteria established in the case law for acknowledging an insufficiency of disclosure, namely the presence of serious doubts substantiated by verifiable facts (cf. T 19/90, OJ EPO 1990, page 476).

12.2 Secondly, the appellant argues that an insufficiency of disclosure arises from the absence of any indication concerning the amount of protease added to the washing system defined in claim 1.

As noted in point 12.1.iv) *supra*, the functional feature in claim 1 is of a relative nature and therefore, the amount of both wild-type and mutated protease has to be the same. There is no evidence on file showing that different (relative) results are obtained depending on the amount of proteases used in the washing system of claim 1.

13. In the context of the experimental data submitted for discussion of the requirements of Article 54 EPC (*infra*), the appellant has further elaborated on this second objection. In particular, it argues that there is no requirement in claim 1 for the wash performance test to be carried out on a weight basis and thus, the test may also be performed on an activity basis, i.e. using wild-type and mutant proteases having the same specific activity when measured with a common substrate. The question arises whether the patent provides sufficient information so as to enable a

skilled person to carry out this embodiment without undue burden.

i) The wash performance assay defined in claim 1 is not limited in this respect and both embodiments are *prima facie* technically meaningful. A comparative test performed on an activity basis may take into account and standardize activity differences in protease preparations arising from storage conditions, methods of purification and/or manipulation, etc., disregarding thereby non-significant comparisons between preparations containing a high amount of inactive protease. In line with the case law, there is no reason to interpret claim 1 narrowly (cf. "Case Law of the Boards of Appeal of the EPO", 7th edition 2013, I.C.3.8, page 114; II.A. 6.1, page 266).

ii) In the context of a test system for selecting proteases based on their wash performance, the patent explicitly refers several times to document D10 (cf. point 8.1 *supra*). This document discloses standard methods for measuring the specific activity of the PB92 protease and of other serine proteases, such as the Carlsberg and BPN' subtilisins (cf. page 5, lines 47-57, page 7, line 58 to page 8, line 2, page 11, point 6 of document D10). These methods were well-known to a skilled person and no undue burden would be required to use them for measuring the specific activity of the (PB92 and Subtilisin 309) mutant proteases disclosed in the patent and/or for performing the comparative wash performance assay defined in claim 1 on a specific activity basis.

14. Thus, the requirements of Article 83 EPC are fulfilled.

Articles 87 to 89 EPC - Priority

15. It is not contested by the respondent (patent proprietor) that the wash performance assay according to claim 1 is not disclosed in the priority document. There is thus no reason for the board to deviate from the findings and the decision of the opposition division on this issue. Hence, document D2 is considered to belong to the state of the art within the meaning of Article 54(2) EPC (cf. page 5, point 4 of the decision under appeal).

Article 100(a) EPC; Article 54 EPC

16. Document D2 is the sole document that has been cited by the appellant under Article 54 EPC in appeal proceedings. This document discloses the production of mutants derived from an alkaline protease enzyme from *Bacillus lentus* DSM 5483 (BLAP). As shown by the alignment of amino acid sequences in document D5, the sequence of the BLAP enzyme (269 residues) differs only by six and five amino acids from the sequences of the PB92 and the Subtilisin 309 proteases, respectively. Whereas at position 102 both the PB92 and the Subtilisin 309 protease have a valine (V), the BLAP enzyme has an isoleucine (I) at this position.

16.1 The fact that the isoleucine at position 102 in the mutant proteases of claim 1 results from a change of a valine present at this position in the sequence of the PB92 and the Subtilisin 309 proteases is not relevant for the assessment of novelty. This is because claim 1 is not a method-claim but a product-claim. The method (site directed mutation, genetic engineering, etc.) used for the preparation of this product cannot by itself give the claimed product novelty (cf. "Case Law", *supra*, II.A.7, page 274). It is not contested by

the parties that the BLAP enzyme referred to in document D2 has all the structural features defined in claim 1. Thus, the sole issue which remains to be assessed for the board to decide on the novelty of the claimed mutant proteases is whether the BLAP enzyme or the BLAP mutant proteases disclosed in document D2 fulfil the functional requirement defined in claim 1, namely if they have an improved wash performance relative to the PB92 or the Subtilisin 309 proteases.

16.2 The appellant has filed experimental evidence to show that the BLAP enzyme actually has an improved wash performance. A comparative wash performance assay between Subtilisin 309 (Savinase®) and a relevant BLAP variant with an isoleucine at position 102 was filed on 15 January 2010 at the first instance proceedings. Whereas this assay was carried out on an activity basis, the same assay was repeated on a weight basis and the results were reported in the appellant's statement of Grounds of Appeal. Both assays show an improved wash performance for the BLAP variant with an isoleucine at position 102.

16.3 However, none of these assays was performed using the same conditions as those characterizing the washing system defined in claim 1. The differences are summarized in a table filed by the respondent in reply to the appellant's statement of Grounds of Appeal. Some of these differences may be mere substitutions of standard products by the corresponding updated products (IEC-A and ICE-A*; cf. point 12.1.iii) *supra*). However, the actual effect(s) and relevance of other differences are by no means clear and straightforward so that the board is not in a position to decide (cf. "Case Law", *supra*, I.C.2.4, page 100), if the disclosure in document D2, based upon the experimental reports

submitted by the appellant, anticipates the subject-matter of claim 1.

17. Nevertheless, in view of the decision taken by the board in respect of inventive step (*infra*), it is not necessary to consider this issue in more detail.

Article 100(a) EPC; Article 56 EPC
The closest prior art

18. Document D2 discloses mutant proteases derived from the wild-type alkaline protease enzyme from *Bacillus lentus* DSM 5483 (BLAP) (cf. point 16 *supra*). The BLAP enzyme is stated to be used in detergent formulations and to have an "*increased protease and oxidative stability over commercially available enzymes under conditions of pH 7 to 10 and at temperature of* ***10 to 60°C*** *in aqueous solutions*" (emphasis added by the board) (cf. page 1, line 17 to page 2, line 6). Document D2 refers to the relevance of obtaining further proteases with increased stability for use, in particular, in detergent formulations in line with market trends (cf. page 2, lines 10 to 20). According thereto, it identifies 32 specific positions within the 269 amino acid sequence of the BLAP enzyme (SEQ ID NO: 52) for which replacement of (at least one of) the amino acid residues with the corresponding residues listed in Table 2 is said to result in mutant proteases having superior thermal and surfactant stability relative to the BLAP enzyme (cf. *inter alia*, page 12, lines 9 to 21, page 14, lines 10 to 26, page 15 Table 2 and claims).

19. Although the 32 positions are identified by computer-assisted methods (cf. page 12, line 28 to page 13, line 7, page 23, line 26 to page 33, line 22, claims 157 to

179 of document D2), the properties of several of these mutant proteases are determined by laboratory tests and the results of thermal and surfactant stability are reported in Tables 3 and 4 on pages 16 and 17 of document D2 (cf. page 14, lines 10 to 13 and page 40, Example 3 to page 50, Example 12). Whereas not all mutant proteases show a superior surfactant stability, all of them have a significant superior thermal stability at the measured temperatures, namely at 50°C and 60°C.

Objective technical problem

20. Starting from document D2, the objective technical problem to be solved is seen in the provision of (PB92 and Subtilisin 309) mutant proteases with improved wash performance at low temperatures.

21. The formulation of this technical problem does not contribute to the inventive merits of the patent (Cf. "Case Law", *supra*, I.D.9.10, page 215). In the context of detergent formulations, document D2 itself refers to current "*market trends*" which include, as is well-known in the prior art and acknowledged in the patent, the development of detergent formulations for use at low temperatures preferably for economic reasons (cf. page 2, lines 13 to 15 of document D2 and page 2, paragraph [0007], lines 46 to 47 of the patent). Indeed document D2 describes an advantageous "*increased protease and oxidative stability ...* [of the BLAP enzyme] *... over commercially available enzymes*" which is present over a wide range of temperatures, including low temperatures (cf. page 1, lines 17 to 22 of document D2; point 18 *supra*).

Solution proposed by the claimed subject-matter

22. The subject-matter of claim 1 is a group of mutant proteases, which are structurally defined and further characterized by a functional feature (improved wash performance). An essential feature of this subject-matter is the replacement - in the amino acid sequences of PB92 and Subtilisin 309 serine proteases given in claim 1 - of the valine (V) at position 102 to one of the specific amino acid residues indicated in the claim (cf. point XI *supra*).

23. The results in Tables I, II and III of the patent show an improved wash performance at 30°C for several V102 mutant proteases. In Table IV, the presence of this improved wash performance is shown for some mutants at two different temperatures (30°C and 20°C). Most of the exemplified mutant proteases have only a single mutation relative to the sequences of the PB92 and Subtilisin 309 proteases, namely the replacement at position 102. There are also a few mutant proteases having a second mutation at another position of these sequences, such as [S99G, V102I], [V102I, S130G], etc., and only one mutant protease having three changes, namely [V102N, V197I, N198G].

24. The board notes that:

i) there is a large difference among the wash performances reported in the Tables of the patent (253 for [V102N, N198G] and 106 for [V102H] and [V102S]; cf. page 9, line 16 and page 8, lines 15 and 56);

ii) for the same mutant protease, different wash performances are reported for each of the

three swatches measured (cf. page 11, lines 9 and 10);

iii) uncorrelated wash performances are obtained at two different temperatures (cf. page 12, lines 26 to 36; point 38.2 *infra*; and

iv) there is no mutant protease exemplified with a degree of homology as low as only 90% (i.e. the V102 change and other 25 amino acid residues changed).

Nevertheless, the board finds that there is no evidence on file to cast serious doubts on the claimed subject-matter being a solution to the technical problem formulated above.

25. The present case differs from cases underlying decisions of the Boards of Appeal, wherein it was decided that the absence of a **causal link** between the proposed mutation and the improvement in wash performance rendered it impossible to state that the proposed structural change constituted a solution to the underlying technical problem (cf. *inter alia*, T 537/02 of 19 October 2004, points 17 to 21 of the Reasons, T 660/02 of 9 June 2005, points 19 to 22 of the Reasons; see also page 12, point 19.c) of the board's communication pursuant to Article 15(1) RPBA). Although it is not shown in the patent that an improved wash performance is indeed obtained with each and every possible sequence backgrounds, the board, in the light of all the evidence on file, has no reason to doubt the respondent's assertion that there is nevertheless a causal link between the structural V102 change and the resulting improved wash performance. Therefore, the present invention does not put the skilled person in a

try-and-see situation requiring the checking of each and every mutant protease falling within the structural scope of claim 1 for assessing said improved wash performance.

Obviousness

26. The mutant proteases disclosed in Tables 3 and 4 of document D2 are derived from the BLAP enzyme and have, except for the "I102W" mutant protease, an isoleucine at position 102. Thus, all but one mutant protease exemplified in Tables 3 and 4 of document D2, including the wild-type BLAP enzyme, fulfil the structural requirements defined in claim 1. Moreover, except for a few mutant proteases, wherein the proposed replacements at position Ile102 are the amino acid residues valine, tryptophan or cysteine (cf. page 14, lines 29-31 and page 15, Table 2), also the mutant proteases suggested in Table 2 of document D2 would fulfil the structural requirements defined in claim 1.

27. As stated in point 25 *supra*, in the light of the evidence on file, the board is convinced of the presence of a causal link between a change at V102 to one of the amino acid residues listed in claim 1 (including isoleucine) and the presence of an improved wash performance in the wash performance assay of claim 1.

Although the comparative wash performance assays filed by the respondent were not conclusive for the board to decide on claim 1 lacking novelty over the BLAP enzyme (with an isoleucine at position 102), these assays, having been performed under the specific conditions chosen by the appellant, nevertheless show the BLAP enzyme to have an improved wash performance. In other

words, these assays are not contrary to the presence of this causal link in "V102I" mutant proteases. There is no evidence on file showing that the "102I" mutant in a BLAP background does not result in the predicted improved wash performance. Therefore, the board concludes that, except for the "I102W" mutant, all other mutant proteases exemplified in Tables 3 and 4 of document D2, i.e. those mutants whose properties have been actually "*determined by laboratory tests*" (cf. page 14, lines 10-13 of document D2), also fulfil the functional requirement defined in claim 1.

28. Although claim 1 in its preamble refers to an intended use for the mutant proteases, namely "*for use in detergents*", it is a product-claim, not a use-claim. No inventive merit can be based on this intended use.

Document D2, at the beginning of the description, contains an explicit reference to the BLAP enzyme "*for use in detergent formulations*" (cf. page 1, lines 17-19 of document D2). Indeed, throughout the description of this document, there are several references to "*detergent formulations*" and to prior art documents concerned with improved mutant proteases for "*laundry detergent applications*" (cf. page 2, lines 10-15, page 4, lines 21-26, page 8, lines 8-10 of document D2). In this context, document D2 refers to the disclosure of document D10 as teaching "*the isolation and characterization of PB92 subtilisin mutants with improved properties for laundry detergent applications*" (cf. page 9, lines 5-8 of document D2).

29. It may be argued, as has been done by the respondent (cf. point XVIII *supra*), that there is no explicit reference in document D2 to low temperatures. However, low temperatures are considered to be part of what is

mentioned in document D2 as "*market trends*" (cf. point 21 *supra*). This is also in line with the reference in document D2 that the BLAP enzyme is "*for use in detergent formulations having an increased protease and oxidative stability*" in a range of temperatures which includes low temperatures (cf. point 18 *supra*).

Moreover, document D10 referred to in document D2 and also in the patent in suit as disclosing suitable wash tests, discloses indeed a wash performance test which is "*carried out for 30 minutes at a desired temperature*" (cf. page 12, lines 6-20, in particular, lines 13-14 of document D10). All the exemplified wash performance tests for PB92 mutant proteases were performed at 40°C and **25°C** (cf. *inter alia*, page 12, line 48, page 15, lines 1 and 27, page 21, line 40 and page 22, line 23 of document D10), i.e. the lowest and the highest temperatures of the ranges qualified in the patent in suit as "*enhanced*" and "*reduced*" temperatures, respectively (cf. page 2, paragraph [0007] of the patent). A person skilled in the field of detergents was thus well-aware of the relevance of these temperature ranges (cf. point 21 *supra*).

30. Thus, the skilled person trying to solve the technical problem formulated in point 20 above would have relied on the protease mutants disclosed in document D2 and would have arrived at the claimed subject-matter in an obvious way. Therefore, Auxiliary Request 3 does not fulfil the requirements of Article 56 EPC.

Auxiliary Request 4
Articles 123(2), 84, 83 and 54 EPC

31. Claim 2 of Auxiliary Request 4, directed to mutant proteases, has been amended so as to exclude the

isoleucine present at position 102 (cf. points IX and XII *supra*). The conclusions arrived at above by the board on Articles 123(2), 84 and 83 EPC for Auxiliary Request 3 apply also to Auxiliary Request 4 (cf. points 2-3 and 8-14 *supra*).

32. Moreover, since neither the BLAP enzyme nor any of the BLAP mutant proteases exemplified in Tables 3 and 4 of document D2 falls within the scope of the claims of Auxiliary Request 4, the request is also considered to fulfil the requirements of Article 54 EPC.

Article 100(a) EPC; Article 56 EPC
The closest prior art

33. Table 2 of the closest prior art document D2, discloses all possible BLAP mutant proteases which, according to a computer-assisted method, may have improved stability properties. Among these mutants, "Ile102" is replaced by tryptophan (for which the results are reported in Table 4) or by "*any small a.a. except P*", wherein a "*small amino acid is defined as glycine, alanine, valine, serine, threonine or cysteine*" (cf. page 15, line 15 and page 14, lines 29-31 of document D2). Thus, four of the suggested changes, namely "I102A" (alanine), "I102G" (glycine), "I102S" (serine) and "I102T" (threonine), result in BLAP mutant proteases that fulfil the structural requirements and, in view of the presence of a causal link (cf. point 25 and 27 *supra*), the functional requirement of claim 2 of Auxiliary Request 4.

Objective technical problem and the solution proposed by the claimed subject-matter

34. Starting from the closest prior art document D2, the technical problem is formulated in the same terms as for Auxiliary Request 3, namely the provision of (PB92 and Subtilisin 309) mutant proteases with improved wash performance at low temperatures (cf. point 20 *supra*).

35. The reasons for which claim 1 of Auxiliary Request 3 was acknowledged by the board to solve this technical problem (cf. points 23 to 25 *supra*), apply also to the mutant proteases of claim 2 of Auxiliary Request 4 which, except for deletion of the V102I mutant protease, are the same in both requests.

Obviousness

36. The respondent argues that the subject-matter of claim 2 of Auxiliary Request 4 is not derivable from document D2 in an obvious manner as the selection of the claimed mutant proteases is not evident from this document (cf. point XVIII *supra*). The board, however, cannot follow this argument for the following reasons:

36.1 When looking for alternative BLAP mutant proteases to those actually exemplified in Tables 3 and 4 of document D2, a skilled person would certainly have as a first obvious choice the BLAP mutant proteases proposed on a theoretical basis in Table 2 of this document. All these BLAP mutant proteases, actually exemplified or only suggested, are disclosed in document D2 as sharing advantageous stability properties that render them advantageous for use in detergent formulations. These BLAP mutant proteases are all derivable from document D2 in an obvious manner.

36.2 Document D2 contemplates the production of BLAP mutant proteases comprising "*the replacement of at least one*

amino acid residue" among 32 positions identified within the 269 amino acid sequence of the BLAP enzyme (SEQ ID NO: 52), i.e. about 12% of the full-length sequence of the BLAP enzyme. The amino acid residues used to replace the amino acids present in these identified positions within the BLAP sequence are given in Table 2 of document D2. Although BLAP mutant proteases with a single change seem to be preferred, as shown in Tables 3 and 4 of document D2 (see, in this context, the Tables of the patent; point 23 *supra*), document D2 also relates to a large group of BLAP mutant proteases comprising two or more amino acids replacements, including mutant proteases with all 32 positions changed. There is no doubt that the subgroup of four "I102" mutant proteases referred to in point 33 *supra* represents a selection from a larger group of possible BLAP mutant proteases, actually exemplified or only suggested, in document D2.

However, whereas claim 2 of Auxiliary Request 4 embraces this specific subgroup of BLAP mutant proteases, it is certainly not limited thereto. The claimed mutant proteases are required only to have "*greater than 90% homology with either the amino acid sequence of PB92 serine protease ... or the amino acid sequence of Subtilisin 309 serine protease*" but, except for the V102 change, **neither** the position(s) **nor** the specific amino acid residue(s) used to replace further corresponding PB92 or Subtilisin 309 residues at each of the 269 positions within the BLAP sequence are defined in the patent. Taking into account that 90% homology may allow for the replacement of about 25 residues, it seems highly questionable that claim 2 represents a limited selection of the disclosure present in document D2, as argued by the respondent.

36.3 Moreover, and more important, the deletion of the residue isoleucine in the list of amino acids at position 102 in claim 2 of Auxiliary Request 4 does not actually change the teaching of the patent nor does it, due to the causal link acknowledged by the board in point 25 *supra*, alter the fact that almost all BLAP mutant proteases disclosed in document D2 (with an isoleucine at position 102) fulfil the functional requirement defined in claim 2 of Auxiliary Request 4, namely an improved wash performance at low temperatures (cf. points 26 to 29 *supra*). For the same reasons, these properties are shared by the subgroup of four "I102" mutant proteases referred to in point 33 *supra.* Therefore, a selection, if at all (cf. point 36.2 *supra*), of this subgroup of four "I102" mutant proteases can only be seen as arbitrary and not based on an inventive step justified by the presence of a surprising and/or advantageous effect which is not present in the other BLAP mutant proteases, actually exemplified or only suggested, in document D2.

37. In the light of the above considerations, Auxiliary Request 4 does not fulfil the requirements of Article 56 EPC.

Admissibility of Auxiliary Request 5

38. Auxiliary Request 5 was filed in reply to the board's communication pursuant to Article 15(1) RPBA and is, therefore, an amendment of the respondent's case. In accordance with Article 13(1) RPBA, it may be admitted and considered at the board's discretion.

38.1 Claim 1 of Auxiliary Request 5 is formulated as a use-claim and refers to the use of a mutant protease in detergents "*in a washing process at a temperature of*

20°C" (cf. point XIII *supra*). The specific temperature of 20°C is taken from the description of the patent (cf. page 6, paragraph [0037], lines 15-16 and page 12, paragraph [0050], lines 10-11 and Table IV, which compares the wash performance of the disclosed PB92 mutants at temperatures 30°C and 20°C) and falls within the range of reduced temperatures identified therein ("*at reduced temperatures, e.g. 15-25°C*"; cf. page 2, paragraph [0007], line 48 of the patent) and the range of temperatures of (use) claim 10 of the Main Request ("*at a temperature preferably in the range of about 15°C to about 45°C*").

38.2 Table IV of the patent shows that there is no direct correlation between the wash performance of PB92 mutants at 20°C and 30°C. Whereas for some mutants, such as [V102N, S99G] and [V102N], the wash performance at 20°C is higher than at 30°C, for other mutants this performance does not significantly change or slightly diminishes, such as for [V102N, N198G]. At least for one of the exemplified PB92 mutants, namely [V102N, Y203W], there is a significant decrease in the wash performance at 20°C. Table IV also shows that for a PB92 mutant different wash performances are obtained depending on the swatch measured (EMPA 117 or CFT AS-3 CACAO). Moreover, no results at 20°C are reported for several PB92 mutants that have a relatively small improved wash performance at 30°C, such as for [V102I, S99G] or [V102I].

38.3 The respondent argues that the feature "*in a washing system at a temperature of 20°C*" was introduced into claim 1 in reply to the board's comments made in the communication pursuant to Article 15(1) RPBA. However, these comments were made in relation to a new amended request (present Auxiliary Request 6; cf. *infra*) filed

by the respondent in reply to the appellant's Grounds of Appeal in order to overcome, *inter alia*, an objection raised under Article 56 EPC. Both at first instance proceedings and from the very beginning of the appeal proceedings, a relevant issue under Article 56 EPC was the temperature of the wash performance assay of the claimed mutant proteases. This is mirrored by the fact that the washing system defined in claim 1 is performed at 30°C.

39. In the light thereof, the board considers that Auxiliary Request 5 is late filed and that it could have been filed at an earlier stage of the proceedings. The filing of this request increases the complexity of the case and negatively affects procedural efficiency. Thus, the board, exercising the discretion conferred to it by Article 13(1) RPBA, decides not to admit this request into the appeal proceedings.

Admissibility of Auxiliary Requests 6 and 7

40. Auxiliary Requests 6 and 7 were filed by the respondent, as Auxiliary Requests 1 and 2 respectively, in reply to the appellant's statement of Grounds of Appeal. Auxiliary Request 6 was, however, amended at the oral proceedings before the board in order to overcome the objection under Article 123(2) EPC found by the board to be relevant for the Main Request and Auxiliary Requests 1 and 2 (cf. points 1-4 *supra*).

41. These auxiliary requests were filed at the earliest possible stage of the appeal proceedings and address, in a straightforward manner, the objections maintained and/or raised by the appellant in these proceedings. Thus, the board, in the exercise of its discretion,

decides to admit Auxiliary Requests 6 and 7 into the appeal proceedings (Article 13(1) RPBA).

Auxiliary Request 6
Articles 123(2), 84, 83 and 54 EPC

42. Claims 1-4 of Auxiliary Request 6 are formulated as use-claims of mutant proteases which are, structurally and functionally, defined as the mutant proteases of claim 1 of Auxiliary Request 3 (cf. point XIV *supra*). The used detergents according to claim 1 are further defined by a washing process carried out at a range of temperatures identical to the range present in the use-claim 10 of Auxiliary Request 3, namely "*in the range of about 15°C to about 45°C*". In view of the claimed subject-matter of Auxiliary Request 6, the conclusions arrived at with regard to Articles 123(2), 84, 83 and 54 EPC for Auxiliary Request 3 apply also to Auxiliary Request 6 (cf. points 2-3 and 8-17 *supra*).

Article 100(a) EPC; Article 56 EPC

43. The closest prior art is represented by document D2. Starting from document D2, the technical problem to be solved is the provision of an (alternative/improved) use for the mutant proteases described therein. There is no doubt that the use of these proteases "*in detergents, in a washing process of a temperature in the range of about 15°C to about 45°C*" as defined in claim 1 solves this technical problem.

44. However, in the light of documents D2 and D10, the board considers this solution to be obvious. As stated in point 28 *supra*, document D2 refers to the use of the BLAP enzyme (which fulfils the structural and, as a result of the causal link acknowledged in point 25

supra, as well as having the functional features defined in claim 1) in detergent formulations and to its advantageous stability at a range of temperatures ("*of 10 to 60°C*") that includes the range indicated in claim 1. As stated in point 29 *supra*, there is a direct reference in document D2 to the standard and well-known wash tests disclosed in document D10 which, in the Examples of document D10, are always performed at 25°C and 40°C, both temperatures falling within the range of temperatures indicated in claim 1 (cf. see also the "*reduced*" and "*enhanced*" temperature ranges defined on page 2, paragraph [0007] of the patent). No inventive merit can be seen in the selection of the BLAP mutant proteases of document D2 for use in detergents in a washing process performed in a range of temperatures which are common practice in the art (document D10).

45. Thus, Auxiliary Request 6 does not fulfil the requirements of Article 56 EPC.

Auxiliary Request 7
Articles 123(2), 84 and 83 EPC

46. No objections have been raised under any of these articles of the EPC. In view of the subject-matter of Auxiliary Request 7 (cf. point XV *supra*), the board sees no reason to raise any of its own.

Articles 87 to 89 EPC; Article 100(a) EPC, Article 54 EPC

47. At oral proceedings before the board, the appellant acknowledged Auxiliary Request 7 to be entitled to the priority date claimed by the patent. The sole claim of Auxiliary Request 7 is directed to seven mutant proteases derived from the PB92 serine protease, having an amino acid sequence different from the sequence of

the BLAP enzyme and from all sequences found in the prior art documents on file. No objections were raised under Article 54 EPC and the board has no reason to raise any of its own.

Article 100(a) EPC; Article 56 EPC

48. No objections have been raised under Article 56 EPC. Since the patent is entitled to the claimed priority date (*supra*), document D2 is not prior art under Article 54(2) EPC and cannot be used to assess inventive step. In view thereof and of the prior art on file, the requirements of Article 56 EPC are fulfilled.

49. Therefore, Auxiliary Request 7 fulfils all requirements of the EPC.

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 with the following claim and a description to be adapted:

Claim 1 of Auxiliary Request 7 submitted at the oral proceedings before the Board on 24 June 2014.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated