DECISION
of 28 August 2001

Case Number: T 0795/97 - 3.3.6
Application Number: 89306974.0
Publication Number: 0351162
IPC: C11D 3/386
Language of the proceedings: EN

Title of invention: Stabilised enzyme dispersion
Opponent: Unilever N.V.

Headword: Enzyme dispersion/ALBRIGHT

Relevant legal provisions: EPC Art. 69, 83, 54(2), 54(3), 56

Keyword: "Interpretation of the claims within the scope of the description - scope of protection is broader than it would appear from the claims alone"
"Sufficiency - yes; late-filed ground of opposition introduced by Opposition Division"
"Novelty yes; insufficient evidence"
"Inventive step - yes; after amendment"

Decisions cited: T 0666/89
DECISION
of the Technical Board of Appeal 3.3.6
of 28 August 2001

Appellant: Unilever N.V.
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Composition of the Board:
Chairman: P. Krasa
Members: G. Dischinger-Höppler
C. Rennie-Smith
Summary of Facts and Submissions

I. This appeal is from an interlocutory decision of the Opposition Division to maintain European patent No. 0 351 162 in amended form. The independent claims 1 and 21 as maintained read:

"1. A method for the preparation of a stabilized aqueous enzyme dispersion comprising a protease, the method comprising:

(1) precipitating a water-soluble polymer from an aqueous solution to form an aqueous dispersion, and

(2) before, during or after (1), contacting the dissolved or dispersed polymer with an aqueous solution or fine aqueous dispersion of the enzyme.

21. A composition comprising a liquid medium having dispersed therein enzyme particles obtained by the method according to claim 1, which particles contain polyvinyl pyrrolidone as a stabilizer therefor."

II. The notice of opposition, based on lack of novelty and lack of inventive step (Articles 100(a), 54 and 56 EPC), cited inter alia the following documents:

(3) GB-A-2 021 142,

(6) GB-A-1 390 503 and


In the course of the opposition proceedings, further
documents were cited by the Opponent (Appellant), including:

(15) US-A-3 860 484,

(16) JP-A-61-254 244 (English translation) and

(20) EP-A-0 301 882.

With a letter of 5 June 1996, the Opponent filed a first experimental report and raised arguments as to insufficient disclosure (Article 83 EPC). In addition, it filed a second experimental report with a letter of 24 February 1997.

III. During the opposition proceedings, the Proprietor (Respondent) filed amended claims including those quoted above and, with a letter of 7 August 1996, an experimental report.

IV. In its decision, the Opposition Division held that the amendments made to the claims complied with the requirements of Article 123(2) and (3) EPC and that the invention was sufficiently disclosed in accordance with Article 83 EPC. It was further held that the claimed subject-matter was novel over the cited prior art since none of the documents disclosed the precipitation of a water-soluble polymer from an aqueous solution to form an aqueous dispersion and contacting the aqueous polymer with aqueous protease as required in Claim 1 or the composition of Claim 21 comprising a liquid medium with particles of enzyme and PVP (polyvinyl pyrrollidone) dispersed therein. Assessment of inventive step was, inter alia, based on documents (3), (6) and (7) as a starting point. It was found that neither of
these documents when combined with any other cited prior art would lead in an obvious manner to the claimed subject-matter.

V. Oral proceedings were held before the Appeal Board on 28 August 2001 in the course of which the Respondent filed further amended claims in three auxiliary requests.

In the first auxiliary request, the words "by contacting it with an effective amount of an electrolyte as precipitant or by evaporation" were inserted in item (1) of Claim 1 between "... aqueous solution" and "to form an aqueous ...".

Further restrictions to Claim 1 were made in the second and third auxiliary requests.

VI. The Appellant, in writing and at the oral proceedings, maintained that the instructions given in the patent were insufficient to achieve the necessary precipitation, this having become evident from the Proprietor's own experiments regarding document (3) filed during the opposition proceedings.

It also maintained that the claimed subject-matter was not novel over documents (3) and (7) since document (3) implicitly disclosed the addition of more than 10% by weight of alkali metal phosphates to the exemplified detergent compositions; and document (7) taught in Example 33 the preparation of a formulation wherein precipitation must occur in the same way as in the patent in suit after the final tripolyphosphate addition. Documents (20) and (16) also anticipated the claimed subject-matter, in particular when considering
that the term "solution" had a broad meaning and covered dissolved polymer as part of dispersions and structured liquids.

Finally, the Appellant submitted that the claimed subject-matter was not inventive, in particular over document (3) as the most suitable starting point when taken in combination with any of documents (6), (15) or (16).

VII. The Respondent supported the opinion set out in the contested decision and submitted in essence the following additional arguments:

- The objection under Article 83 EPC was inadmissible, having been raised out of time.

- Document (3) did not disclose any amounts for the sequestering agents, let alone any amount thereof in the particular compositions described in the examples.

- No evidence was provided that the enzymes in Example 33 of document (7) were stabilised or that the carboxymethyl cellulose was precipitated.

- The disclosure of document (16) differed from the claimed subject-matter not only in that it related to dispersions in liquid hydrocarbon from which the polymer was precipitated but also in that it did not describe any contact with an aqueous solution or dispersion of enzyme.

- There was no certainty that any precipitation of the polymer from an aqueous solution occurred in
document (20) or that the enzyme was added as an aqueous solution or dispersion.

- Concerning inventive step, the Appellant had not presented any conclusive arguments in its statement of grounds of appeal.

VIII. The Appellant requested that the decision under appeal be set aside and that the patent be revoked.

The Respondent requested as main request that the appeal be dismissed and that the patent be maintained, or alternatively that the decision under appeal be set aside and that the patent be maintained in accordance with one of the sets of claims filed as auxiliary requests I, II or III during the oral proceedings.

**Reasons for the Decision**

1. **Main request**

1.1 During the appeal proceedings, the Appellant did not object under Article 123 EPC to the amended version of the claims according the main request nor does the Board see any reason to deviate from the decision of the Opposition Division in this respect. Since the main request fails for other reasons, it is not necessary to consider this issue in detail.

1.2 **Extent of protection (Article 69 EPC)**

The claims relate to a method for the preparation of a stabilized aqueous dispersion comprising protease...
(Claim 1) and to a composition obtained by this method (Claim 21).

1.2.1 The Appellant submitted that - when read in the context of the description - the terms "solution" and "precipitation" used in the method claims must be given a broad meaning. Thus, it followed from page 6, lines 9 to 12 of the patent that the polymer solution could also be part of a system with more than one phase present. Likewise, the term "precipitation" was not limited to solids but included the separation of any new phase since the patent failed to give any definition at all in this respect.

1.2.2 At first sight, Claim 1 appears perfectly clear in that it seems to comprise two steps, namely (1) precipitation of a water-soluble polymer from an aqueous solution, whereby an aqueous dispersion is formed and (2) contacting before, during or after step (1) the dissolved or dispersed polymer with an aqueous solution or fine aqueous dispersion of protease.

1.2.3 On closer inspection, however, in the light of the description of the patent, it becomes evident that clear solutions of polymer and enzyme, whilst being preferred, are not mandatory (page 3, lines 56 to 57).

This is corroborated by the indication that the polymer (= encapsulant) may be precipitated from a micellar solution (page 6, lines 9 to 12).

Moreover, the claimed subject-matter is not restricted to a combination of an aqueous solution or dispersion of the polymer with an aqueous solution or dispersion of the enzyme, but solid polymer may be added to
aqueous enzyme, i.e. dissolved or dispersed, or solid enzyme may be contacted with dissolved polymer (page 4, lines 23 to 24 and lines 33 to 35).

1.2.4 Thus, as was agreed by the Respondent during the oral proceedings, the Board holds that the term "aqueous solution" has to be interpreted as relating to any uniform mixture comprising material dissolved in water without excluding the presence of other ingredients, including structured liquid phases such as those present in some types of liquid detergents, suspended solids or even a dispersed or dispersing non-aqueous phase.

1.2.5 Concerning the definition of "precipitation", the patent offers three distinct methods, namely the salting out method using an electrolyte as the precipitant, precipitation by a water-miscible organic solvent, or evaporation, such as by spray drying (page 3, lines 39 to 48). In particular, in the case of spray drying, the precipitation does not lead to the formation of an aqueous dispersion, but to a finely divided solid which can be dispersed in a liquid later on. Such embodiments are explicitly covered by the patent in suit (page 4, lines 5 to 8).

1.2.6 Further, the Respondent agreed that the patent was not restricted to the precipitation of solids but also covered the formation of other phases, optically identifiable by their different refractory index.

1.3 Sufficiency

1.3.1 The Respondent objected to any consideration of this ground of opposition since it had only been
The Appellant's line of argument concerning sufficiency of disclosure is based on the fact that the Proprietor had shown in its own experiments filed with a letter dated 7 August 1996 (see page 2, third paragraph) that the sodium metabisulfite which was present in the compositions of document (3) (Examples 1 and 2) and covered by the claimed subject-matter (patent, page 3, lines 39 to 42) would not work as a salting out type electrolyte for PVP, even if applied in amounts as preferred in the patent in suit (page 6, lines 24 to 29). The Appellant concluded that the claimed subject-matter should be restricted to those embodiments which had been shown to work.

The Appellant did not contest the general guidance given in the patent in suit (page 6, line 9 to page 7, line 1), according to which the type and amount of electrolyte to be selected depends on the polymer and surfactant used. Nor did it contest the examples of the patent in suit which indicate several ways of verifying such guidance. Thus, the burden of proof was on the Appellant to show that the guidance given in the patent in suit was insufficient or imposed an undue burden on
those skilled in the art to find out what to do if they failed in precipitating a particular water-soluble polymer with sodium metabisulfite. In the absence of any evidence to that effect, the Appellant's submission amounts to no more than an unsubstantiated allegation and has to be dismissed.

Hence, the Board finds no reason to differ in this respect from the decision of the Opposition Division and concludes that the invention as claimed is sufficiently disclosed.

1.4 Novelty

The Appellant contested novelty of the subject-matter of Claim 1 under Article 54(2) EPC as against any of documents (3), (7) and (16) and under Article 54(3) as against document (20). No such objections were put forward with respect to the composition according to independent Claim 21.

1.4.1 Document (3) discloses aqueous liquid detergent compositions containing stabilized proteolytic enzymes obtained by using a stabilizing system comprising a water-dispersible or water soluble antioxidant and an organic hydrophilic water-soluble polyol (page 1, lines 3 to 6 and lines 56 to 57 and page 6, lines 5 to 8). One preferred antioxidant is sodium metabisulfite as used in the compositions according to Examples 1 and 2. Moreover, the composition of detergent system No. 1 of Example 1 and the composition of Example 2 contain PVP, i.e. the preferred type of polymer of the patent in suit (page 3, line 8). Document (3) discloses other suitable ingredients on page 7. Particular attention is paid to the sequestering agents as protection against
hard water (lines 19 to 51) and, with respect to efficiency, condensed alkali metal phosphates are emphasized (lines 20 to 21). In none of the compositions of the examples is any such sequestering agent mentioned.

According to the Appellant it was common practice in the art to add such sequestering or softening agents in amounts of above 10% by weight of the composition. This was corroborated by the amount of pyrophosphate added with the water conditioner to the detergent formulation (document (3), page 9, line 52 to page 10, line 10). He concluded, therefore, that document (3) disclosed formulations as shown in the examples containing, in addition, more than 10% by weight of such alkali metal phosphates. It had been shown during the opposition proceedings, by experiments filed with the Appellant's letter dated 24 February 1996, that incorporation of 10% or 16% by weight of potassium pyrophosphate in the detergent composition No. 1 of document (3), in place of the corresponding water content, would cause precipitation of the polymer.

This line of argument is not convincing since document (3) does not teach any conditions comparable with those of the Appellant's experiments and does not mention any precipitation of the polymer at all. In document (3) pyrophosphate addition is explicitly disclosed only in relation to the soil removal test described on pages 9 and 10 (page 9, line 19 to page 10, line 13) where a particular water conditioner formulation containing 15% by weight of a 60% solution of pyrophosphate is added to 1 litre of water in an amount of 0.25% by weight and the detergent to be tested is added in an amount of 0.1% by weight. As a result, the detergent composition
is heavily diluted in this test and not comparable with either the compositions of Examples 1 and 2 of document (3) or the Appellant's experiments.

Even if one was to combine the detergent composition and the water conditioner directly, i.e. with no additional water (as suggested in document (3) on page 7, lines 45 to 50) at a ratio of the detergent composition to water conditioner of 1 : 2.5 in accordance with the soil removal test, no composition such as in the Appellant's experiments would result. Such a combination would also be very different from the compositions described in the examples of the patent in suit, and would not be one in which precipitation had to be expected from the available information. Nor is there any suggestion in document (3) that, by substituting in the exemplified detergent compositions part of the water content with potassium pyrophosphate as the only ingredient of the water conditioner, one would arrive at the same content of pyrophosphate as in the Appellant's experiments.

Those experiments, therefore, do not advance the arguments bases on document (3). In the absence of any other evidence showing precipitation of the polymer when following the teaching of document (3), the Board concludes that document (3) does not anticipate the subject-matter of Claim 1.

1.4.2 Document (7) concerns non-sedimenting liquid detergent compositions (see abstract) which can be obtained by adding the various ingredients to a 47% solution of silicate whereby the builder is added last (page 49, last paragraph). Only the composition of Example 33 contains detergent enzymes. The builder in this example
is sodium tripolyphosphate. Nothing suggests that the polymer (sodium carboxymethyl cellulose) in this composition, if it was ever in solution, would be precipitated by the final addition of the builder.

The Appellant admitted that the presence of silicate in this example might interact and prevent the cellulose dissolving right from the beginning. He argued, however, that it followed from document (7) that the silicate can generally be contained in amounts as low as 1% by weight (page 26, first paragraph) or even be totally omitted as in Example 25. In the Appellant's opinion, it did not matter that in the composition of Example 25 no enzyme was mentioned since according to page 45, penultimate paragraph, enzymes, e.g. proteolytic enzymes, can be present.

Even if one was to accept the Appellant's combination of the general disclosure with the specific examples of document (7), such as the presence of detergent enzymes in Example 25, there is no disclosure, either explicitly or implicitly, in Example 25 of a precipitation of the cellulose which would stabilise any enzyme present. On the contrary, document (7) suggests adding, as necessary, any enzyme in stabilised form (page 45, penultimate paragraph). Further, any salting out effect is ascribed to the presence of silicate, thus preventing dissolution of the cellulose, rather than to the tripolyphosphate builder in Examples 25 and 33 (page 25, line 23 to page 26, line 6).

The Board cannot accept the Appellant's further argument that the decision T 666/89 (OJ EPO 1993, 495) supports its submission that, by a combination of the
teaching of page 45, penultimate paragraph with Example 25 of document (7), a technical teaching was made available to those skilled in the art which anticipates the subject-matter of Claim 1. While in that case the combination of two passages of a patent specification was found to be a novelty destroying technical teaching (point 4 of the Reasons for the Decision), Decision T 666/89 also stated (point 7 of the Reasons) that such a decision "will depend on the facts of each case". Taking into account that a document must directly and unambiguously disclose the claimed subject-matter to be a true anticipation, the decisive question is whether or not the skilled reader of the alleged anticipation would have combined the respective passages of necessity, as was the case in T 666/89. However, in the present case, the passage on page 45 of document (7) reads "Proteolytic ... enzymes may optionally be present ..." which can by no means be understood as meaning that proteolytic enzymes must of necessity be present in the examples and thus in Example 25.

In the absence of any experimental evidence, the Board concludes therefore that document (7) contains no clear and unambiguous disclosure of the subject matter of Claim 1.

1.4.3 Document (16) discloses a method for micro-encapsulation of enzyme within a water-soluble polymer (Claim 1). Therefor, the enzyme (e.g. protease) is added as a concentrate, culture broth or powder to an aqueous solution of polymer (e.g. polyvinyl alcohol or carboxymethyl cellulose). This aqueous mixture is dispersed in liquid hydrocarbon. Upon addition of acetone, capsule formation and phase separation into a
lower aqueous capsule-containing phase and an upper hydrocarbon phase occur. Dry capsules are separated therefrom by decanting the upper phase and filtration of the aqueous phase (page 3, line 2 to page 4, line 13 and Examples). There is no mention in document (16) that the precipitated polymer capsules are ever dispersed in an aqueous medium as in the patent in suit, either before or after their separation in dry form.

Therefore, the subject-matter of Claim 1 is novel over the disclosure of document (16).

1.4.4 Document (20) is concerned with the stability of viscosity reducing polymers in aqueous detergent compositions (page 3, lines 6 to 12 and abstract). These compositions comprise a more or less water soluble polymer (page 3, lines 53 to 61 and page 4, lines 7 to 8), electrolytes and an enzyme such as protease (Tables 1 and 9, page 5, lines 23 to 29). Enzyme stability is not addressed in document (20).

On page 5, lines 30 to 40, it is mentioned that the order of addition of components can be important. In one preferred method, electrolyte is added last. In particular, caustic material, if necessary, is the final compound to be added.

The Appellant argued that compositions II₂ and II₃ in Table 1 and compositions IX and X in Table 9 anticipated the claimed subject-matter since it was clear from Tables 3 and 4 that polymer precipitation occurred upon addition of alkali at a pH above 8.

However, both Tables 3 and 4 relate to compositions
containing no enzymes at all. Table 3 relates only to compositions III and IV of Table 1 and the composition of Table 4 is further different to all compositions of Table 1 in that it does not even contain a surfactant. In view of these differences, the Respondent contested that the stability results reported in Table 4 could be applied to compositions of Table 1. Since no evidence was submitted that those differences were of no account and could be disregarded, the Board considers Table 4 as irrelevant with respect to the behaviour of the compositions of Table 1 on the addition of NaOH.

Only Table 2 discloses an enzyme containing composition, namely composition II, of Table 1. Table 2 is concerned with the physical stability of this particular composition in relation to the amount of polymer added and shows that up to 4% polymer can be stably incorporated in the composition in which the polymer is only partly dissolved.

However, since enzyme stability is not an issue in document (20) and since no evidence has been provided that compositions result from the process of document (20) in which the enzyme activity is stabilized, the Board does not consider the disclosure of document (20) to be an anticipation of the claimed subject-matter.

1.4.5 The other cited prior art is further distinguished from the subject-matter of Claim 1 and still less suitable for anticipation. This was not contested by the Appellant.

1.4.6 Further, it was not contested that any of the cited prior art document discloses the liquid composition of Claim 21 comprising dispersed protease particles
containing PVP as a stabiliser.

1.4.7 The Board, therefore, concludes that the subject-matter of independent Claims 1 and 21 is novel.

1.5 Inventive Step

1.5.1 In order to assess inventive step, the Appellant used document (3) as the closest prior art. Like the patent in suit (page 2, lines 9 to 10), it is concerned with the problem of enzyme stability in liquid systems such as liquid detergent compositions (page 1, lines 9 to 15). The Board, therefore, agrees that document (3) is a suitable starting point for assessing inventive step.

1.5.2 According to document (3), stabilisation of the enzyme in the liquid detergent is achieved by the inclusion of a stabilising system comprising a water-soluble antioxidant and a water-soluble polyol (see 1.4.1 above).

The technical problem to be solved by the method of Claim 1 can thus be seen as providing an alternative method for enzyme stabilisation. The claimed solution of this problem thus consists in a method where water-soluble polymer is precipitated from an aqueous solution before, during or after the polymer is contacted under aqueous conditions with protease enzyme, and the precipitate is brought into the form of an aqueous dispersion (see 1.2.1 to 1.2.6 above).

It is plausible from the examples given in the patent in suit that this problem is, in fact, solved by the claimed method.
1.5.3 Document (3) does not contain any suggestion that precipitation of the polymer might contribute to any enzyme stabilisation.

Document (16) is also concerned with enzyme stability in detergent compositions. It aims at the provision of microcapsules containing enzyme as core material which capsules remain stable during storage even when combined with a detergent composition (paragraph bridging pages 1 and 2). As explained at 1.4.3 above, water-soluble polymer is precipitated from an aqueous solution in the presence of enzyme and the precipitate is separated and dried (Examples 1 to 3). Present Claim 1 encompasses, however, the possibility that an aqueous solution or dispersion of polymer and enzyme is dispersed in a liquid hydrocarbon (see 1.2.4 above) and that the enzyme is encapsulated in the polymer and precipitated.

One preferred use of the enzyme-containing microcapsules of document (16) is their incorporation into detergents (page 4, lines 19 to 20). Stability of the enzymatic activity was tested in a mixture of the enzyme-containing microcapsules with a granular detergent composition (page 6, lines 5 to 11). Liquid detergents are not mentioned in document (16), so that the disclosure of document (16) differs from the subject-matter of Claim 1 only in that no aqueous dispersion is formed from the precipitate.

No inventive step can, however, be attributed to this difference, since it would be obvious to someone skilled in the art to include the microcapsules uniformly in aqueous detergent compositions, in accordance with the solubility of the polymer, in
undissolved and dispersed form in order to provide another method of stabilising enzymes in an aqueous dispersion.

For these reasons, the Board concludes that the subject-matter of Claim 1 does not comply with the requirements of Articles 52(1) and 56 EPC and that the main request must fail.

2. Auxiliary request I

2.1 By the amendments to Claim 1 in this request, the method has been restricted to the use of electrolyte as precipitant or to precipitation by evaporation. The basis for the amendment can be found in Claims 7, 8 and 11 of the application as originally filed. The requirements of Articles 123(2) and (3) EPC are therefore met. This was not contested by the Appellant.

2.2 The restrictive amendments do not change the situation as far as sufficiency of disclosure and novelty are concerned. In this respect, the same reasoning applies as for the main request (see 1.3 and 1.4 above).

2.3 Nor do the amendments necessitate selection of another starting point than document (3) for assessing inventive step. Also, the technical problem plausibly solved in view of document (3) remains the provision of an alternative method for stabilising enzymes in aqueous dispersions (1.5.1 and 1.5.2 above).

2.3.1 Document (16) no longer qualifies as pertinent prior art since it does not contain the slightest hint that precipitation of the polymer and stabilisation of the enzyme could be obtained by the salting out method
using electrolytes or by evaporation.

2.3.2 The Appellant drew the Board's attention instead to documents (15) and (6) and argued that the method of Claim 1 was obvious in the light of these documents. Neither document, however, concerns systems comprising protease.

2.3.3 Document (15) relates to the stabilisation of oxidoreductase enzyme by evaporating a mixture of aqueous solutions of enzyme and polymer by freeze drying. The dry products are mixed with water to test the activity (see Example 1).

However, the Appellant had shown in its first experimental report of 5 June 1996 filed during the opposition proceedings (page 8, last paragraph) that other enzymes (lipase and cellulase) behave quite differently to protease, in that no stabilisation occurred under otherwise identical conditions. The Board holds, therefore, that a skilled person would not, with any reasonable expectation of success, simply apply the teaching for stabilising oxidoreductase to the stabilising of protease.

2.3.4 Comparable reasoning applies, though with greater force, to document (6) which also concerns encapsulation of active substances in a polymeric material by precipitation from aqueous solution (e.g. Examples 1 and 4) but does not even mention enzymes.

2.3.5 Being silent about any electrolytic or evaporative precipitation of the polymer, document (7) cannot contribute to the solution of the technical problem underlying the patent in suit.
3. Therefore, the Board concludes that none of the cited prior art documents, either individually or in combination, renders the claimed solution of the technical problem obvious, and concludes that the method of Claim 1 of the first auxiliary request is based on an inventive step within the meaning of Articles 52(1) and 56 EPC.

Dependent Claims 2 to 17 which refer to preferred embodiments of Claim 1 derive their patentability from that of Claim 1.

Claims 18 to 20, which correspond to Claims 21 to 23 of the main request and which refer to the stabilised product obtained by the method of Claim 1, also derive their patentability therefrom.

4. Since the Respondent's first auxiliary request is allowable, its second and third auxiliary requests need not be considered.

Order

For these reasons it is decided that:

1. The decision under appeal be set aside.

2. The case is remitted to the first instance with the order to maintain the patent with the claims of auxiliary request I filed during the oral proceedings and the description to be adapted thereto.
The Registrar: G. Rauh

The Chairman: P. Krasa