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D E C I S I O N
of 23 September 2003

Case Number: T 0015/00 - 3.3.4

Application Number: 89910461.6

Publication Number: 0386222

IPC: C12P 21/00

Language of the proceedings: EN

Title of invention:
Process for preparing human serum albumine by fermenting a genetically engineered microorganism in the presence of a polyalkylene compound

Patentee:
Delta Biotechnology Limited

Opponent:
Yoshitomi Pharmaceutical Industries, Ltd.

Headword:
Serum albumin/DELTA BIOTECHNOLOGY

Relevant legal provisions:
EPC Art. 114, 83, 89, 54, 56

Keyword:
"Late filed documents - admission into proceedings - (yes)"
"Sufficiency of disclosure - (yes)"
"Novelty - (yes)"
"Inventive step - (yes)"

Decisions cited:
T 1052/93, T 0113/96

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0015/00 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 23 September 2003

Appellant: (Opponent)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 12 November 1999 rejecting the opposition filed against European patent No. 0386222 pursuant to Article 102(2) EPC.**

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: A. L. L. Marie
R. A. M. Moufang

Summary of Facts and Submissions

I. European Patent No. 0 386 222 with the title "Process for preparing human serum albumin by fermenting a genetically engineered microorganism in the presence of a polyalkylene compound" and claiming priority from GB 8820951 (7 September 1988) was granted with 8 claims, claim 1 of which read:

"1. A process for preparing human serum albumin by fermenting an albumin-secreting microorganism in a suitable medium such that albumin is secreted into the medium, characterised in that a polyoxyalkylene compound is added to the medium, wherein, if the polyoxyalkylene compound is an antifoam compound, the polyoxyalkylene compound is so added as to give an average level of more than 0.2 g/l."

Dependent claims 2 to 8 defined further embodiments of the process of claim 1.

II. An opposition was filed on the grounds of Article 100(a) EPC for lack of novelty (Article 54 EPC) and inventive step (Article 56 EPC) and of Article 100(b) EPC for insufficiency of disclosure (Article 83 EPC).

III. The opposition was rejected pursuant to Article 102(2) EPC.

IV. The opponent filed an appeal against this decision.

V. The following documents are relevant for this decision:

(1) EP-A-0 322 094

(2) EP-A-0 073 646

(3) EP-A-0 018 609

(4) G. L. Solomons, Process Biochemistry, 1967, pages 47 and 48

(5) B. Naji et al., Appl. Microbiol. Biotechnol., 1987, Vol. 27, pages 174 to 180

(6) W. Guddat and K. Hillger, Folia Haematol. 1982, Vol. 109, pages 840 to 855

(7) S. Pawiroharsono et al., Appl. Microbiol. Biotechnol., 1987, Vol. 27, pages 181 to 185

(8) H. Thurow and K. Geisen, Diabetologia, 1984, Vol. 27, pages 212 to 218

(9) English translation of JP-B-45 30189

(10) English translation of JP-A-41 7439

(11) US 4,622,303

(12) D. Sleep et al., Bio/Technology, 1990, Vol. 8, pages 42 to 46

(13) EP-A-0 201 239

(15) T. Etcheverry et al., Bio/Technology, 1986, Vol. 4, pages 726 to 730

(16) K. Okabayashi et al., J. Biochem., 1991, Vol. 110, pages 103 to 110

(18) EP-A-0 399 455

(20) Experimental Report of T. Ohya dated March 21, 2000

(21) EP-A-0 308 381

(22) EP-A-0 164 556

(23) EP-A-0 327 797

(24) Declaration by Ms D. Wilkinson

(25) Declaration by Dr D. Sleep

VI. Oral proceedings took place on 23 September 2003.

VII. The arguments submitted by the appellant can be summarized as follows:

Article 114 EPC:

– document (20) was submitted in response to the decision of the opposition division to disregard evidence submitted during the oral proceedings in order to show that there was no enabling disclosure for the subject-matter of claim 1 as far as it related to antifoam compounds at a level of just more than 0.2 g/l.

Article 83 EPC:

– it was not possible to carry out the claimed process with the teaching given in the patent in suit, since the plasmid used was not defined. Furthermore, at the priority date of the patent in suit it was not possible to secrete serum albumin from yeast cells. In document (13), referred to in the patent in suit, serum albumin was not secreted from the yeast cells. In document (12) the leader sequence had to be modified and in document (15) the secreted albumin remained attached to the cell membrane. Document (16) confirmed that no conclusion could be drawn from document (15) about the secretion of albumin.

– document (20) showed that there was no increase in serum albumin production and no reduction of serum albumin degradation when raising PPG2000 concentration from below 0.2 g/l to more than 0.2 g/l, in particular to a level of 0.52 g/l.

– there was no proof in the patent in suit that polyoxyalkylene compounds which were not antifoam agents had a stabilizing effect.

Article 87 to 89 EPC:

– the claims of the patent in suit could not enjoy the priority right, since the priority document was restricted to antifoam compounds and to some specifically identified polyalkylene compounds whereas the definition of the term "polyoxyalkylene compounds" in the patent in suit

was different and in particular, was broader than the expression "polyalkylene glycol" of the priority document. Decision T 1052/93 (10 January 1996) was cited.

Article 54(2)(3) EPC:

– if the claims of the patent did not enjoy the priority right, then document (1), the priority, filing and publication dates of which were 30 October 1987, 25 October 1988 and 28 June 1989, respectively (ie earlier than the filing date of the patent in suit (6 September 1989)) and which described the addition of a polyalkylene compound, PPG 2000, to the culture of *S. cerevisiae* for the production of albumin, was novelty-destroying in the sense of Article 54(2) EPC. If the claims of the patent in suit were entitled to the priority date, then document (1) was novelty-destroying under Article 54(3) EPC.

Article 56 EPC:

– if the claims of the patent in suit did not enjoy the priority right, then document (1), which disclosed in Example 5 the addition of PPG 2000, a polyalkylene compound, at a final concentration of 0.2 g/l to the culture of *S. cerevisiae* in a process for the production of serum albumin and its secretion in the culture medium, was the closest prior art. The technical problem to be solved was the improvement of the production of serum albumin by minimizing degradation. The problem of degradation and instability of secreted

proteins was already known from document (3) and the solution found in documents (4) or (10) showing the use of antifoam compounds at a concentration greater than 0.2 g/l. Document (3) already offered a solution, since it described the stabilising effect of polyalkylene compounds on proteins in solution which tended to denature at the air-water interface. Document (8) showed that the protecting effect described in document (3) also appeared in agitated solutions of proteins. Alternatively, the skilled person defined as a team consisting of a microbiologist specialized in fermentation and a protein biochemist, would consider document (11) listing some antifoam agents used in the fermentation of *S. cerevisiae*, some of them being polyoxyalkylene compounds used at a concentration greater than 0.2 g/l and defined in document (3) as stabilisators for proteins.

– if the priority right was acknowledged, then document (2), which described a process for the production of human serum albumin by fermentation of a microorganism secreting said protein, was the closest prior art. The technical problem was the same as that defined from document (1) and the solution again offered by document (3), which furthermore showed that some of the polyalkylene compounds disclosed in document (10) were already known as stabilisators for serum albumin. The combination of documents (2) and (6), the latter showing that PEG 4000 stabilized serum albumin heated at 75°C for 30 minutes, was also detrimental

to the inventive step of the claims of the patent in suit.

– it was further doubtful whether every embodiment falling within the scope of the claims was a solution to the technical problem. For instance, there was no example in the patent in suit using non-antifoam polyalkylene compounds.

– document (20) showed that there was no difference when antifoam polyoxyalkylene compounds were used at concentrations between 0.15 g/l and 0.22 g/l. No unexpected effect was seen using antifoam concentrations beyond the threshold of 0.2 g/l defined in claim 1.

VIII. The arguments submitted by the respondent can be summarized as follows:

Article 114(2) EPC:

– document (20) was late-filed and should not be admitted into the proceedings.

Article 83 EPC:

– the appellant, having the burden of proof in that respect, did not show that the skilled person was not able to carry out the invention using non-antifoam polyoxyalkylene compounds.

– the native serum albumin leader sequence led to secretion of serum albumin into the medium, as shown by document (12), in which the modification

of said sequence was not made for allowing the secretion, but for introducing a restriction site, as confirmed by document (16). In document (15) the interest was not directed toward the secretion, but only to the promoter.

– document (24) showed that increasing the antifoam concentrations from 0.15 g/l to 0.22 g/l reduced the degradation of albumin from 38.8% to 16.7% in *Pichia pastoris* and from 60% to 20% in *Saccharomyces*.

Articles 87 to 89 EPC:

– the claims of the main request enjoyed the priority right, since the priority document on page 2, last paragraph mentioned "*certain chemical reagents...*" and then specified "*In particular, the addition of certain antifoam...*", so that there was no restriction to antifoam agents.

– the objection related to the term "*polyoxyalkylene glycol*" was raised for the first time during the oral proceedings before the Board and took the respondent by surprise and should therefore not be considered.

Article 54 EPC:

– the claims of the patent in suit enjoying the priority right, document (1) was only to be considered under Article 54(3) EPC and was not novelty-destroying, since it disclosed in Example 5 an antifoam concentration of 0.2 g/l,

which was excluded by the wording of the claims. Furthermore, Example 5 was not found in the priority document of document (1).

Article 56 EPC:

– if the priority right was not acknowledged and document (1) considered as the closest prior art, then the problem to be solved was different from that defined by the appellant and was not the increase of the production of serum albumin ***by reduction of degradation***, since post-secretion degradation was not known at that time. The skilled person would not have concentrated on this aspect and would further have had several other possibilities to increase the production of serum albumin:

  – optimisation of the codon selection (document (21)),

  – stronger promoter (document (16)),

  – better leader sequence (documents (16) and (22)),

  – use of protease defective strain as a host (document (23)),

  – multiple copies of the gene encoding serum albumin (document (18)).

– the same applied if the priority right was acknowledged, document (1) was not to be

considered for inventive step, and document (2) was the closest prior art. Furthermore, its combination with document (3) was not straightforward because the latter was not concerned with fermentation, but with the stabilisation of proteins in solution, which were not submitted to the harsh conditions of fermentation (strong aeration and stirring).

– there was no reason for the skilled person to consider documents (10), (11) and (6). Document (10) was not concerned with secreted proteins, but with the production of glutamic acid and Table 3 of this document showed that at the concentrations used in the patent in suit there was a lowering of glutamic acid production. This was confirmed by document (9) showing that an increase of antifoam concentration was detrimental to fermentation and document (4) stating that a suitable antifoam had to work at low concentration, since antifoam basically hindered the oxygen transfer. Document (11) only concerned the production of yeast biomass and not the secretion of expressed proteins. In document (6) PEG 4000 was used as a precipitating agent for serum albumin at 75°C.

– document (24) showed that raising the antifoam concentration from 0.15 g/l to 0.22 g/l resulted in a reduction of degradation of serum albumin.

IX. The appellant requested that the decision under appeal be set aside and that the European patent No. 0 386 222 be revoked.

X. The respondent requested that the appeal be dismissed and that the patent be maintained as granted (main request) or on the basis of the claims of any one of the auxiliary requests I to IV filed on 4 August 1999.

Reasons for the Decision

Procedural matters

1. As a result of a merger (appellant's letter of 28 December 1999), the status of opponent was transferred from The Green Cross Corporation to the legal successor **Yoshitomi Pharmaceutical Industries, Ltd**.

Article 114(2) EPC

2. Document (20) was introduced by the appellant with their statement of the grounds of appeal on 22 March 2000 in order to reinforce an argument under Article 83 EPC already submitted before the opposition division. This is considered by the Board as the normal behaviour of a losing party (cf decision T 113/96 of 19 December 1997).

3. Documents (21) to (25) have been introduced by the respondent with their letter of 15 August 2003 in answer to arguments submitted by the appellant and/or to highlight arguments already present on file.

4. Documents (20) to (25) do not result in an increase of the technical and legal complexity, so that the Board

decides to allow them into these proceedings pursuant to Article 114(2) EPC.

Main request

Article 83 EPC

5. As far as the objection raised against the possibility for the skilled person to carry out the process of claim 1, especially the secretion step, is concerned, document (13)(Figure 3), which is referred to in the patent in suit (page 3, lines 16 and 17) and document (2) (Figure 3; page 3, lines 10 to 15 and page 5, lines 15 to 19) disclose the nucleotide sequence of the full length cDNA of the human serum albumin containing the leader sequence and plasmids for expression of an inserted gene.

6. Post-published documents (12), (15) and (16) are not sufficient evidence for proving lack of enablement. The Board does not share the view of the appellant concerning the disclosure of these documents. Indeed, document (12) shows that the human serum albumin leader sequence directs the secretion of the serum albumin into the culture supernatant of *S. cerevisiae* (Table 1 and page 45, left column, last paragraph). Document (16) discloses that the secretion of serum albumin using its own leader sequence into the culture supernatant of yeast cells yields 40% of correctly processed serum albumin and 60% of shorter forms lacking either the two or the four first amino acids (page 107, left column). Document (15) shows that the expression of a sequence coding for serum albumin containing its own leader sequence under the control of the promoter of the

chelatin gene results in a secretion of said serum albumin, which, however, for unexplained reasons, remains cell-attached (page 728, right column). The above mentioned technical analysis of the disclosure of these documents seems rather to show the opposite of the appellant's objection, namely that the secretion of serum albumin is sufficiently disclosed in the patent in suit.

7. Without convincing evidence to the contrary, it has to be assumed that the skilled person at the priority date of the patent in suit was provided by the patent in suit and the prior art with materials and methods to secrete the serum albumin expressed in yeast cells and was well able to perform this step and the whole process of claim 1.

8. According to the appellant, document (20) showed that the teaching of the patent could not be reproduced, since no increase in serum albumin production and no reduction of its degradation at antifoam concentrations of 0.15, 0.22 and 0.52 g/l were observed. The degradation being at each concentration used (0.15, 0.22 and 0.52 g/l) about 22% (Table 1 of document (20)). The Board is not convinced that the appellant's conclusion under the heading "Article 83 EPC", which requires that an invention has to be described in a patent in such a way that the skilled person can carry it out, can be drawn from the data shown in document (20). If these data were to be considered conclusive as such, they would rather seem to show that two values (0.22 and 0.52 g/l) falling within the claimed range ("more than 0.2 g/l") do work. The fact that a value falling outside the claimed range (0.15g/l) also works

might possibly support an argument under Article 56 EPC (cf infra point 29).

9. The appellant has supplied no evidence supporting his objection that there is no teaching in the patent in suit on the reduction of the degradation of serum albumin in presence of non-antifoam polyalkylene compounds. Therefore, the burden of proof in respect of this objection still lies with the appellant.

10. The Board thus considers that the requirements of Article 83 EPC are met.

Articles 87 to 89 EPC

11. The question of the entitlement of the claims to the priority right does not need to be decided since it only arises because of document (1) (cf *supra* sections VII and VIII) and since the information content of this document, even if it were prior art under Article 54(2) or (3) EPC does not prejudice the novelty and the inventive step of the subject-matter of the patent in suit (*cf infra*).

Article 54 EPC

12. Document (1) discloses the secretion of shorter forms of human serum albumin into the culture supernatant of microorganisms, such as *E. coli*, *B. subtilis* or *S. cerevisiae*. Example 5, on page 8, describes the use of PPG 2000, a polyoxyalkylene antifoam compound, in response to a foam sensor, after the addition of more than 50% of the feed solution. The final level of addition is 0.2 g/l (page 8, lines 10 to 20). Document

(1) does not disclose the use of polyoxyalkylene compounds which are not at the same time antifoam agents.

13. Claim 1 of the main request, which under the term "*serum albumin*" may also embrace shorter forms as indicated on page 3, lines 8 to 13 of the patent in suit, claims the use of polyoxyalkylene compounds in general and requires, in the particular case of a polyoxyalkylene compound with antifoam property, that its concentration be greater than 0.2 g/l. This feature is not disclosed in document (1). Therefore, the Board is convinced that the subject-matter of claim 1 is not contained in the disclosure of document (1) and thus fulfils the requirements of Article 54 EPC.

Article 56 EPC

14. Document (1) discloses the preparation of shorter forms of human serum albumin using recombinant DNA technology. Since this technology is the method of choice for the mass production of a given protein, the purpose of document (1) can be seen in the provision of large amounts of serum albumin. This can be deduced from the concern shown in document (1) about the amount of serum albumin obtained. Example 1 indicates on page 6 (lines 43 to 48) that the yield is "*demonstrably higher*" than with transformants secreting mature serum albumin, but Example 2 states that, nevertheless, "*low yields*" are obtained. Document (1) is considered as the closest prior art and the technical problem to be solved is to provide the skilled person with an improved method leading to an increase of the yield of serum albumin.

15. The solution disclosed in claim 1 of the patent in suit is a process, in which a polyoxyalkylene compound is used, and, if this polyoxyalkylene compound has antifaom property, then it is used at a concentration greater than 0.2 g/l.

16. The question to be answered in view of the assessment of inventive step is whether this solution can be deduced in an obvious manner from document (1) considered alone or in combination with common general knowledge or other cited prior art documents.

17. First of all, document (1) does not provide the skilled person with a suggestion pointing at the solution defined in claim 1 of the patent in suit and even teaches away from it, since it indicates on page 7, lines 53 to 54 that proteolysis occurs, suggesting that this could be the reason for the low yield and, hence, leads the skilled person in the direction of protease inhibitors.

18. The respondent argued that, moreover, the skilled person at the priority date of the patent in suit had several possibilities to increase the yield of the secreted serum albumin. He could have, following his common general knowledge, modified the physico-chemical conditions of the culture or used a multicopy plasmid. He could also have used a different promoter to boost expression, such as those described in document (18) (page, 3, lines 26 to 40; page 4, line 30 to page 13, line 29). Therefore, the solution proposed in claim 1 is only one of several possibilities that the prior art

offered to the skilled person. The Board agrees with this view.

19. On the other hand, Example 1 of the patent in suit, which describes an experiment similar to Example 5 of document (1), in which PPG 2000 is added in response to a foam sensor after the addition of more than 50% of the feed solution to a final level of 0.2 g/l, shows that about 90% of the secreted albumin is degraded and, hence, identifies for the first time post-secretion degradation as the reason behind the low yield of serum albumin in the culture supernatant of the yeast cells (page 3, lines 40 to 41). It is this discovery that has led the respondent to look for a stabilising agent and, finally, to the solution disclosed in claim 1. This crucial teaching is absent from document (1).

20. Since the low yield of serum albumin in document (1) has not been recognized to be due to post-secretion degradation, neither a pointer at a solution to the problem of serum albumin instability, nor a motivation for the skilled person to look for a prior art document concerned with the stabilisation of serum albumin or proteins in general can be found in document (1). If such a document had by chance been found, it could not be recognized as a solution for a problem not identified in document (1) and its combination with document (1) could hence not be considered as obvious (Case Law of the Boards of Appeal of the European patent Office, 4th edition, 2001, page 123, last full paragraph), since it would result from an *ex post facto* analysis.

21. Furthermore, the Board considers that none of the documents cited by the appellant in connection with document (1) would have been taken into consideration by the skilled person.

22. Indeed, document (11) is concerned with a study on the possible negative influence of antifoam agents on the yeast growth. Among the antifoam agents studied and mentioned in the Table of column 3, the substances I to III and C5 to C11 are polyoxyalkylene compounds, but only the substances II, C5 and C7 to C11 have been used at a concentration greater than 0.2 g/l. However, none of these substances are adequate for the purpose of the patent in suit, since they either inhibit yeast growth (substances C8 to C11) or cause a softening of the yeast cells, either immediately or after some days. This softening being indicative of a modification of the permeability of the cell membrane as shown by documents (5) and (7), the skilled person would not have considered such a softened yeast cell as suitable in a secretion process.

23. Document (3) is concerned with the denaturation of proteins in solution, especially insulin (column 2, lines 14 to 31), at the water/air separation surface, and discloses, in order to prevent denaturation, the use of polyoxyalkylene antifoam agents. However, document (3) does not relate to fermentation processes and, although it mentions that movement in the protein solution influences denaturation, this movement cannot be compared with that caused by the harsh agitation and aeration used in growth fermenters. In the Board's view, document (3) thus represents a field of application different from that of the patent in suit. Furthermore,

the polyoxyalkylene antifoam agents are used in a concentration of 2 to 200 ppm (column 5, lines 22 to 25) which lies outside the range specified in claim 1.

24. Document (8), as document (3), relates to the stabilisation of insulin by using antifoam polyoxyalkylene compounds at a concentration of 0.001% (w/v) (page 214, left column) and extends this teaching to other proteins such as albumin. For the same reasons as already given for document (3), document (8) would not be taken into consideration by the skilled person.

25. The skilled person would also not take documents (4) and (10) into consideration. The former, indeed, suggests that the concentration of the antifoam agent should be maintained as low as possible, since its presence lowers the oxygen transfer rate by approximately 50% and is a serious waste of efficiency (page 47, second column, last paragraph) and the latter discloses the use of antifoam polyoxyalkylene compounds in the context of the fermentation of bacteria for the production of glutamic acid, which is a different context from that of the patent in suit. Furthermore, in the experiments reported in Tables 1 and 2 of document (10), the antifoam agents are used at a concentration of 0.002 weight%, ie 0.02 g/l, a concentration which always leads to the best result as shown by Table 3 of document (10), but lies below the limit defined in claim 1.

26. Therefore, the Board is convinced that document (1) *per se* neither identifies the technical problem underlying the patent in suit, nor leads to the solution disclosed in claim 1 of the main request,

which, furthermore, represents only one solution among several available to the skilled person at the priority date of the patent in suit. The Board, furthermore, shares the view of the respondent in considering that, contrary to the appellant's argumentation, the skilled person would not have combined the teaching of document (1) with those of any one of documents (3),(4), (8), (10) and (11).

27. Document (2) was also considered as an alternative closest prior art to document (1) by the appellant. It discloses in Figure 3 the full-length cDNA nucleotide sequence of human serum albumin including the leader sequence and describes the expression of mature human serum albumin in *E. coli* cells (page 15, line 29 to page 16, line 16) which are lysed by lysozyme. Thus, document (2) does not describe the secretion of human serum albumin in the culture supernatant. Said secretion would then be the technical problem, which the skilled person might possibly derive from document (2). However, secretion is not the problem for which claim 1 of the main request is a solution, but rather to improve the yield of secreted serum albumin (cf supra point 14). Therefore, document (2) is inappropriate as a closest prior art.

28. An objection was also raised by the appellant as to whether the technical problem was solved over the whole scope of claim 1, since the patent in suit did not show that non-antifoam polyoxyalkylene compounds used at a concentration greater than zero (page 2, lines 36 to 38 of the patent in suit) were efficient as stabilizers. However, the appellant has submitted no evidence to support this objection.

29. The absence of an unexpected effect over the 0.2 g/l threshold mentioned in claim 1 for antifoam compounds was also objected to by the appellant. This objection was based on the results given in document (20), showing that the reduction of the degradation of serum albumin was the same at antifoam concentrations of 0.15 g/l, a value lying outside the claimed range, and 0.22 g/l. Since the problem to be solved was an improvement of the yield of serum albumin after harsh culture conditions and the solution in claim 1 defined a precise limit of more than 0.2 g/l of an antifoam compound, an inventive step was only to be acknowledged if a protective effect of the amount of antifoam compounds started at this limit which, as evidenced by the data shown in document (20), was not the case.

30. However, the Board is unable to draw this conclusion from document (20) because, while the results as such might support appellant' position that the problem has already been solved according to the conditions of document (20), those important data in document (20), relating to the culture conditions are not identical with those given in Example 1 of the patent in suit. This leaves doubts about the conclusiveness of only 22% serum albumin degradation already below the threshold of 0.2 g/l addition of protective antifoam compounds. The Board also draws attention to the data given in document (1), the closest prior art document, which discloses the addition of 0.2 g/l of an antifoam compound and nonetheless reports low yields, this being the starting point for the formulation of the problem for the claimed solution (cf supra point 14). This also raises doubts whether the precondition for degradation

of serum albumin, ie the harsh culture conditions, was present in document (20). Thus the results reported in this document are counterbalanced by the data of the patent in suit, those of document (1) and finally those of document (24), where, in the Table on the last page, the teaching of the patent in suit on the important degradation at antifoam concentrations below 0.2 g/l and its unexpected reduction at concentrations greater than 0.2 g/l is confirmed. The Board is thus of the opinion that the alleged absence of an unexpected effect for which the appellant bears the burden of the proof, has not been established.

31. As a consequence, claim 1 and claims 2 to 8 as granted, depending directly or indirectly on claim 1, fulfil the requirements of Article 56 EPC.

Order

For these reasons it is concluded that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona U. Kinkeldey