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Bezeichnung der Erfindung:
Title of invention:
Titre de l'invention : A process for producing single cell protein material and culture

Klassifikation / Classification / Classement : C12N 1/16

ENTSCHEIDUNG / DECISION

vom / of / du 5 July 1989

Anmelder / Applicant / Demandeur :

Patentinhaber / Proprietor of the patent /
Titulaire du brevet : Phillips Petroleum Company

Einsprechender / Opponent / Opposant : Linde Aktiengesellschaft

Stichwort / Headword / Référence : Single cell protein/PHILLIPS PETROLEUM

EPÜ / EPC / CBE Art. 56 EPC

Schlagwort / Keyword / Mot clé : "Inventive step (affirmed) - obvious to try with a reasonable expectation of success."

Leitsatz / Headnote / Sommaire

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Case Number : T 419/87

D E C I S I O N
of the Technical Board of Appeal
of 5 July 1989

Appellant : (Opponent)
LINDE AKTIENGESELLSCHAFT
Zentrale Patentabteilung
D-8023 Höllriegelskreuth

Representative :

Respondent : (Proprietor of the patent)
PHILLIPS PETROLEUM COMPANY
5th and Keeler
Bartlesville Oklahoma 74004
USA

Representative :
Dr. W. Dost
Patent- und Rechtsanwälte
Bardehle, Pagenburg, Dost, Altenburg
Frohwitter, Geissler und Partner
8000 München 86

Decision under appeal :
Interlocutory Decision of the Opposition Division of the European Patent Office dated 1 October 1987 concerning maintenance of European patent No. 0 017 853 in amended form.

Composition of the Board :

Chairman : P. Lançon
Members : U. Kinkeldey
E. Persson

Summary of Facts and Submissions

I. European patent No. 0 017 853 was granted on 24 October 1984 on the basis of 25 claims contained in European patent application No. 80 101 752.6, filed on 2 April 1980 and claiming the priority of two prior US applications, Nos. 29 418 and 110 457, filed on 12 April 1979 and 15 January 1980 respectively. Claim 1 of the patent as granted reads as follows:

"1. A continuous process of producing a single cell protein material which comprises culturing under aerobic fermentation conditions in aqueous mineral salts ferment at least one yeast species employing effective yeast culturing fermentation conditions, including amounts of carbon energy substrate, assimilable nitrogen source, make-up water, oxygen and aqueous mineral salts medium comprising a primary mineral salts medium and a trace mineral salts medium and recovering the resulting micro-organisms as a single cell protein material, wherein said carbon energy substrate is selected from carbohydrates, alcohols, ketones, aldehydes, acids, and esters of 1 to 20 carbon atoms per molecule, and normal paraffins of 10 to 20 carbon atoms per molecule, characterized by feeding said mineral salts to said aqueous ferment at such a rate to maintain in said aqueous ferment the following elements in at least the designated weights per liter of aqueous ferment P-1.9g, K-1g, Mg-0.15g, Ca-0.06g, S-0.1g, Fe-6mg, Zn-2mg, Cu-0.6mg, and Mn-0.6mg, thereby maintaining a cell density in said aqueous ferment of at least 60 and up to 160 grams, on a dried basis, per liter of aqueous ferment."

II. On 24 July 1985 the Appellants (Opponents) filed a notice of opposition against the European patent requesting

revocation of the patent on the ground that its subject-matter lacked inventiveness.

Eight prior art documents were cited in support of the opposition out of which the following remain relevant in this Appeal:

(1) M. Kuraishi, J. Terao, H. Ohkouchi, N. Matsuda and J. Nagai "SCP-Process development with methanol as substrate" Dechema-Monographien Nr. 1704-1723, "Microbiology applied to Biotechnology", Band 83, pages 111-123,

(4) GB-PS-1 375 189,

III. The Respondents (Proprietors of the patent) contested the alleged lack of inventiveness, relying inter alia on affidavits of Mr John A. Cruze and Mr George T. Sperl dated 22 and 23 April 1983 respectively and stating that in their view as skilled persons the effect of the claimed process of producing single cell protein material was completely unexpected and surprising.

IV. The Opposition Division maintained the patent in amended form by decision of 1 October 1987 stating that there was no clear evidence as to the exact publication date of citations (1) and (3). However, even if these documents had been published prior to the first priority date none of the citations (1) to (8) would destroy the novelty of the invention nor render it obvious.

The decision discussed each document separately in relation to the subject-matter of Claims 1 to 25 and drew the conclusion that it was evident to one skilled in the art that even a combination of two or more of the citations (1) to (8) did not render the subject-matter of

Claims 1 to 25 obvious, whatever the underlying technical problem might be.

V. On 27 November 1987 the Appellants filed a notice of appeal against this decision, paying the appeal fee in due time and filing a statement of grounds on 3 February 1988. The main arguments submitted were as follows:

Claim 1 lacked inventiveness because citation (1) disclosed a process for the production of single cell protein comprising four out of six features of the contested Claim 1. The remaining two features contained in the characterising clause of Claim 1 were also derivable in essence from that document. Particular attention was drawn to the last paragraph on page 121 of that document where there was reference to a cell density of 130 to 140 g/l being achieved, anticipating that feature of Claim 1 "at least 60 and up to 160 grams". The Appellants emphasised that this cell density could only be achieved by supplementing the growth medium with a mineral salt solution containing, in appropriate quality and quantity, the mineral salts constituting the other feature of the characterising clause of Claim 1. This view was confirmed by data presented in Table 5 of citation (1) which analysed the mineral salts as such and their amount in cell masses as produced by the process as claimed. It was possible to derive from these data the composition and amount of mineral salts contained in the aqueous fermentation broth in which the cells were grown. When calculating the amount of mineral salts in the cell mass according to Table 5 of citation (1) and comparing the results with the same figures in Claim 1, it became clear that the mineral salt concentrations in the fermentation broth used in citation (1) must have been similar to those claimed. The fact that copper and sulphur were not mentioned in citation (1) was irrelevant because it was

evident to a skilled person that yeast cells necessarily needed these elements in certain specific amounts for growth. If the claimed cell densities of at least 60 to 160 g/l were to be achieved, corresponding amounts of these elements had to be added to the fermentation medium.

Moreover, citation (4) and particularly Table II of that document, already disclosed all the mineral salts mentioned in Claim 1. It was also clear from that document that appropriately higher copper concentrations would be necessary to achieve higher cell densities.

The features of sub-claims 2 to 21 were obvious from the prior art as cited.

VI. In reply the Respondents argued that citation (1) did not provide clear evidence as to whether the process described for achieving cell densities of 130 to 140 g/l was the same as the process claimed. Furthermore, it was doubtful whether this process actually had been carried out successfully, since it was described in a chapter headed "Process under Development". The cell concentrations of 67 and 91 g/l reported in Table 11 on page 123 of document (1) might therefore reflect cell densities achieved by conventional fermentation processes having disadvantages compared to the continuous fermentation process as claimed and differing from it.

Although citation (4) disclosed the same mineral salts as were claimed in the present application, this document only provided evidence of maximum cell densities of 20 to 30 g/l being achieved - thereby underlining the surprising effect of the process as claimed.

VII. During oral proceedings which took place on 5 July 1989, it was generally agreed that high cell densities could be achieved in various ways. One such way was to effect more intensive aeration or to increase the pressure. In the Respondents' opinion it had, however, not been obvious to try using mineral salts in the combination and concentration claimed in the reasonable expectation of success.

VIII. Questioned by the Board, the Appellants confirmed that they did not dispute the admissibility of Claims 22 to 25 concerning a process for the production of single cell protein using three specific deposited yeast strains (Claim 22) and concerning three such deposited strains (Claims 23 to 25).

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

The Respondents requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.

2. Claim 1 of the contested patent was amended during the opposition proceedings before the body of first instance by replacing the feature "... and recovering the resulting micro-organisms as a single cell protein material ..." contained in Claim 1 of the patent as granted by the wording "... continuously withdrawing aqueous ferment for recovering the resulting micro-organisms as a single cell protein material ...". The Opposition Division held this

replacement to be allowable under Article 123(3) EPC because the new feature was clearly more specific than formerly. The new wording refers to a "continuous fermentation process" which is indisputably the subject-matter of the present patent. The Board accepts that this amendment does not contravene Article 123(2) or (3) EPC.

3. The Appellants have never contested the novelty of Claim 1 (Art. 54 EPC) and the Board sees no reason to raise this issue of its own motion (Art. 114(1) EPC).

4. The only issue to be dealt with, therefore, is whether the present invention involves the inventive step required by Article 56 EPC.

4.1 The Board's opinion, which differs from that of the Appellants, is that citation (4) rather than citation (1) represents the closest state of the art because - as is made clear by the detailed discussion below - more features as claimed are more unambiguously described therein.

Citation (4) relates to a continuous process for producing a single cell protein by culturing a yeast species under conditions of aerobic fermentation in aqueous mineral salts ferment, thus ensuring an appropriate culturing environment. Use is made of carbon energy substrate, assimilable nitrogen source and mineral salts. The resulting micro-organisms are recovered as a single cell protein material. These mineral salts, according to Table II, are added in the following amounts (nutrient element input, wt./100 g cells produced): P-1g, K-1g, Mg-0.2g, Ca-0.001g, Na-0.01g, Fe-1mg, Mn-1mg, Zn-0.5mg, Cu-0.1mg. The amount of sulphur is not specified, although several compounds mentioned in connection with other nutrient elements contain sulphur. It is apparently

possible, by a process under the conditions mentioned, to achieve a cell density ranging from 15 to maximum of 30 g/l (page 5, left-hand column, lines 30 to 33).

4.2 Bearing in mind the closest prior art as represented by citation (4), the problem to be solved can be defined as considerably increasing the cell density with the purpose of reducing costs of single cell protein production.

In order to solve this problem, the main claim of the patent in suit suggests to modify the process for the production of single cell protein of citation (4), by feeding the nutrient elements to the fermentation broth at such a rate to maintain their concentrations at defined minimum levels. As stated in Claim 1, the process permits the maintenance in the aqueous ferment of at least 60 and up to 160 g, on a dried basis, per litre of aqueous ferment. This is also confirmed by the examples (100.7 g/l in Example I; 133.3 g/l in Example II; 73.3 g/l in Example III; 110.3 g/l in Example IV; 128.4 g/l in Example V; 76.2 g/l in Example VI). Therefore, the problem identified above has actually been solved by the process described in Claim 1.

4.3 The process described in citation (4) is identical to that of the patent in suit except for the fact that the minimum amounts of the nutrient elements used in their special combination have to be maintained in the fermentation broth while the cells are growing. The minimum amounts mentioned in citation (4), Table II, and the minimum amounts of the nutrient elements claimed in the patent in suit are not directly comparable. The specific feature of Claim 1 is that the designated minimum amounts of the nutrient elements are fed into the aqueous ferment at such a rate as to **maintain** these minimum amounts. Only by so doing can the desirable high cell density in the aqueous

ferment be maintained. There is no indication in citation (4) that specific minimum amounts of the nutrient elements mentioned have to be maintained. Instead, an estimate is given of the quantity of inorganic nutrients required in the fermentation broth for a given amount of cells to be produced. A further factor impeding comparison of the data in Table II of citation (4) with the features given in Claim 1 is that the nutrient elements mentioned are added to the fermentation broth as specific compounds which are thought to be easily assimilable by the cells. Thus, there is no express mention in citation (4) of sulphur, which is definitely essential for cell growth. Sulphur is in fact contained in certain compound elements in the fermentation broth in combination with other elements such as copper or magnesium. It is specifically stated in citation (4) that "the added inorganic nutrients are effective in promoting yeast growth only to the extent of their solubility in the fermentation broth". There is also mention of the possibility of adding the nutrient elements separately to the broth in order to accelerate yeast growth. Thus it is stated that iron, for example, may be introduced as the water-soluble salt of an organic polycarboxylic acid or, preferably, as iron citrate, because this salt may be formed in the aqueous solution by the appropriate addition of an inorganic iron salt, such as ferric chloride, and citric acid (page 4, left-hand column, lines 17 to 35).

4.4 It is apparent, therefore, that the data given in Table II of citation (4) and the further information concerning the the addition of mineral salts to the fermentation broth in order to promote yeast growth do not teach a skilled person to select the specific and very effective minimum amounts mentioned in Claim 1 of the patent in suit and to maintain their levels in the fermentation broth during cell growth. Nor is there anything else in citation (4) that hints at this solution.

4.5 During the proceedings before the Board, there was also discussion of citation (1) as a secondary document illustrating the prior art on the assumption that it formed part of the state of the art under Article 54(2) EPC.

4.6 Citation (1) described several different processes for the production of single cell proteins, including continuous culturing of the yeast cells. In this respect, therefore, it relates to the same type of process for producing single cell protein material as does the patent in suit. It also describes research work designed to improve cell yield, cell productivity and cell density. Citation (1) suggests that there are a variety of parameters contributing to the desired effect, such as the micro-organism used, the pH-value of the fermentation broth, the growth temperature, the pressure in the fermenter, the oxygen-enrichment of the air used for aeration and the type and concentration of the nutrient in the fermentation broth. It is clear from Table 11 in columns 3 and 6, which show results obtained by a "conventional" method, that cell concentrations of 67 g/l and 91 g/l were achieved. The data given show clearly that the degree of concentration of the feed methanol influences cell concentration. Thus, a methanol concentration of 193 g/l resulted in a cell concentration of 67 g/l and a methanol concentration of 278 g/l produced a higher cell concentration of 91 g/l. However, it is not clear from the document as a whole what is actually meant by a "conventional" method.

Moreover, the calculations done by the Appellants and based on comparative examples in Table 11 of citation (1) are not convincing because there is no definition of the "conventional" method. When considering the term "conventional" it is not obvious to a skilled person to

refer to the other method described in citation (1). As a matter of fact, this other method provides a cell density of 35 g/l only (page 120, 12th line from the bottom).

4.7 Table 5 in citation (1) gives an analysis of elements contained in a single cell protein produced by the process described in the citation. The Appellants insisted that it was possible on the basis of this analysis to work out the amounts of nutrient elements that were contained in the fermentation broth, claiming that when this was done, it became evident that the fermentation broth had contained at least the amounts of nutrient elements stated in Claim 1 of the patent in suit. The Board cannot agree. As already pointed out in the discussion of citation (4), one cannot with certainty conclude from nutrient element values relating to the cell mass the minimum levels of nutrient elements which have to be maintained in the fermentation broth, in order to maintain a cell density of at least 60 to 160 g/l of aqueous ferment. It is impossible to predict how much of which element in which type of compound will be incorporated into the cells during the growth period. Thus, as stated in the description of the patent in suit (page 2, column 2, lines 56-58; page 3, column 4, lines 63-65 and, particularly, page 5, column 7, lines 25-31) one is left with mineral salts that are not incorporated into the cells in the fermentation broth and at a rough estimate the rate of uptake is such that the cells in the fermentation broth contain about two-thirds of the mineral salts content of the ferment. However, such a rough estimate is not sufficient to work out from certain mineral contents in the cells produced the amounts of mineral salts that have to be added to the broth for certain minimum levels of all the mineral salts mentioned to be maintained.

4.8 As the parties generally agree, there are apparently a number of parameters influencing cell growth. While a person skilled in the art could well have tried to manipulate the mineral salts parameter knowing the technical teaching of citations (4) and (1), in view of the various possibilities of developing other parameters known to influence, one way or another, cell growth, there is no justification for the opinion that he would have concentrated only on maintaining the combination of specific minimum amounts of the mineral salts in the fermentation medium claimed for the patent in suit in order to solve the problem raised in the present patent.

Citation (3) is very similar to citation (1) and does not contain any information extending that of citation (1).

4.9 Certainly, none of the documents cited contain a teaching to the effect that when the claimed combination of minimum amounts of the necessary mineral salts is maintained in the fermentation broth, a considerably higher cell density can be achieved and maintained throughout the whole fermentation process. This is, in the Board's view, to be considered a surprising effect.

4.10 Moreover, the effect is convincingly demonstrated by the examples given in the patent in suit, not only with regard to certain specific yeast strains which are also claimed and have been deposited with a recognised depositary institution, but also with regard to a yeast strain which is not covered by the patent in suit but is apparently freely available (Example VI). This shows that the high cell density may be obtained not only with the new and inventive yeast strains covered by the patent in suit, but also with common yeast strains.

4.11 In conclusion, the Board takes the view that the subject-matter of the patent in suit does involve an inventive step as required by Articles 52(1) and 56 EPC. It follows, that the appeal has to be dismissed.

Order

For these reasons, it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

F. Klein P. Lançon