BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS | BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE | CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

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File Number: T 877/90 - 3.3.2

Application No.: 81 304 560.6

Publication No.: 0 049 611

Title of invention: T-cell growth factor, and a process of producing the same

Classification: C07K 15/06

D E C I S I O N
of 28 July 1992

Proprietor of the patent: Hooper Trading Co. N.V.

Opponent: Biotest Pharma GmbH

Headword: T-cell growth factor/HOOPER

EPC Articles 54 and 56

Keyword: "State of the art - Paper distributed at a meeting - Availability to the public (yes) - Oral disclosure at the meeting (doubtful)"
"Novelty of the product - (yes), inventive step of the product - (no)", "obvious desideratum"
"Novelty and inventive step of the process - (yes)"

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Case Number : T 877/90 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 28 July 1992

Appellant : (Opponent)
Biotest Pharma GmbH
Flughafenstrasse 4
W - 6000 Frankfurt 71 (DE)

Representative :
Beil, Hans Chr., Dr.
Beil, Wolff and Beil, Rechtsanwälte
Adelonstrasse 58
Postfach 80 01 40
W - 6230 Frankfurt am Main 80 (DE)

Respondent : (Proprietor of the patent)
Hooper Trading Co. N.V.
De Ruyterkade 62
Curaçao (NL)

Representative :
Dixon, Donald Cossar
Gee & Co.
Chancery House
Chancery Lane
London WC2A 1QU (GB)

Decision under appeal :
Decision of Opposition Division of the European Patent Office dated 19 October 1990 rejecting the opposition filed against European patent No. 0 049 611 pursuant to Article 102(2) EPC.

Composition of the Board :

Chairman : P.A.M. Lançon
Members : U.M. Kinkeldey
R.L.J. Schulte
I.A. Holliday
G. Davies

Summary of Facts and Submissions

I. European patent application No. 81 304 560.6, enjoying a priority date of 2 October 1980, was granted as European patent No. 0 049 611 with 17 claims. Claims 1 and 3 read as follows:

"1. A T-cell growth factor derived from the peripheral mononuclear blood cells of a donor and characterised by being serum-free and mitogen-free and that the donor is human, bovine or porcine.

3. A process for producing a serum-free and mitogen-free T-cell growth factor as claimed in Claim 1, the process comprising:

(1) separating peripheral mononuclear blood cells from a human, bovine or porcine donor;

(2) stimulating the cells by incubating the cells in a liquid tissue culture medium supplemented with serum and mitogen;

(3) separating and washing the stimulated cells to remove substantially all of the serum and mitogen; and

(4) conditioning the cells obtained in step (3) by incubating the cells in the presence of a serum-free and mitogen-free liquid tissue culture medium to transfer the T-cell growth factor into the liquid medium."

II. Notice of opposition against the European patent was filed. Revocation of the patent was requested on the ground of Article 100(a) EPC. The opposition was supported by printed prior art documents and also by alleged oral public disclosures. In the appeal proceedings, the following citations remained relevant:

(6) H.-A. Fabricius et al., Immunbiol., Vol. 156, pp. 364-371 (1979);

(12) Arbeitstagung über Leukocytenkulturen, Erlangen, 6th and 7th March 1980, Stahn, R., H.-A. Fabricius and E. Köttgen "TCGF - Biochemical Characterization and Species Specificity";

(13) International Workshop "Interleukin No. 2" Geisenheim, July, 16th to 19th, 1980, H.-A. Fabricius, R. Stahn and E. Köttgen, "The Role of Serum Proteins in PHA-induced Production of Interleukin-2 by Human Peripheral Blood Lymphocytes";

(17) H.-A. Fabricius, R. Stahn and E. Köttgen, "The Role of Serum Proteins in PHA-induced Production of Interleukin-2 by Human Peripheral Blood Lymphocytes", printed abstract of the lecture presented at the meeting defined as document (13).

III. The Opposition Division maintained the patent on the basis of the granted claims, essentially for the following reasons:

(a) When considering the alleged oral public disclosure, the following must be established:

(i) the date at which the alleged prior oral disclosure occurred,
(ii) exactly what was said, and
(iii) under what circumstances the alleged oral disclosure occurred.

As to item (i) one had to conclude that both alleged oral disclosures, documents (12) and (13) (hereinafter called the Erlangen and Geisenheim meetings), took place before the priority date enjoyed by the patent in suit; (ii) that evidence

and declarations provided by witnesses were either contradictory or not supported by material facts bearing a certain date so that it did not seem possible or equitable to deny the validity of the patent; and (iii) that the circumstances under which the meetings took place were to be considered public.

The argument supporting the opposition based on the alleged oral disclosure at the meetings thus failed, since one of the necessary conditions was not fulfilled.

(b) Document (17) had been distributed to the participants at the Geisenheim meeting. In the absence of any proof that the participants at the meeting were bound to keep secret the information received, document (17) must be considered as having been publicly available.

It was also considered to be the closest prior art document.

The object of document (17), was to determine the influence of serum on the production of IL-2 by peripheral blood lymphocytes (PBL) induced by a mitogen (PHA). The main teaching of this study was that the presence of serum was essential for the PHA stimulated production of IL-2 by PBL. The actual technical teaching of document (17) was that no stimulation of IL-2 occurred if the PBL had not been in contact with PHA and then with serum. This taught that cells which had been treated with PHA and were then washed did not produce IL-2. However, adding serum to these cells caused the IL-2 production to start. Document (17) therefore did not teach the

simultaneous incubation of PBL with PHA and serum as claimed in Claim 3. In any case document (17) was not sufficiently detailed to allow the person skilled in the art to reproduce it. He would have had to determine experimental conditions which went beyond his common general knowledge.

The process of Claim 3 was therefore novel.

Document (17) furthermore only mentioned the separation of the supernatant from the cultured cells and not the separation of IL-2 from the supernatant and moreover the culture resulting from the stimulation process had been filtered before it had been assayed. Accordingly it was not proved that the product thus obtained would be usable as such and thus product Claims 1 and 2 were new.

(c) An inventive step was acknowledged in the light of the closest prior art document (17). The difference between the subject-matter of product Claim 1 and document (17) was that document (17) did not disclose pure IL-2 free of PHA and serum. The resulting mixture of the process disclosed in document (17) exhibited some IL-2 activity as evidenced by the reported assays, but this did not prove that the product would be active in the medical treatment for which IL-2 was used. The incubation of PBL cells in the simultaneous presence of a mitogen and serum was a decisive difference which rendered the production process more efficient in terms of activity and thus rendered the process and the products which resulted therefrom unexpectedly better than any process or product known in the prior art.

The teaching of document (6) that PHA and serum could be used concomitantly to produce IL-2 was not to be taken into account because the teaching of document (17) clearly led away from the teaching of document (6) and it would not have been logical for the skilled person to leave the teaching of document (17) which gave no incentive to combine its teaching with other references.

For these reasons an inventive step had to be recognised for the process and the products which were the subject of the claims of the patent in suit.

IV. The Appellants lodged an appeal against this decision.

V. Oral proceedings took place on 28 July 1992.

VI. During oral proceedings, the Respondents submitted four auxiliary requests. Claim 1 of auxiliary request 1 relates to the subject-matter of granted Claim 3 (see above paragraph I).

VII. The Appellants argued during the appeal proceedings essentially as follows:

(a) the evidence provided by the witnesses heard before the Opposition Division were not in essence contradictory so that it was wrong to conclude that there was doubt as to whether the subject-matter of the process claim had been made available to the public at the Erlangen and Geisenheim meetings.

(b) Document (17) disclosed altogether five different methods to prepare IL-2 among which method 1 related to the stimulation of human PBL during four hours

with PHA wherein the culture medium was supplemented with 15% human AB-serum. Then the cells were exhaustively washed and conditioned in a serum-free culture medium for 20 to 24 hours. A filtration followed and finally IL-2 was identified in the supernatant.

From the whole disclosure it followed that both PHA and serum were necessary to achieve IL-2 and that a sufficient yield could be obtained only in cases where PHA and then serum was applied in two steps separated by a washing step (method 5) or where PHA and serum was supplied at the same time (method 1).

Because method 1 was described in the most detailed way, the skilled person had to conclude that this method was the preferred one.

This method 1, however, anticipated the process of Claim 3.

Even if there were any differences between the disclosure of document (17) and the teaching of the contested patent so that novelty of the patent could be established, there was, however, in any case no justification for assuming the presence of an inventive step.

As to novelty and inventive step with respect to product Claim 1 of the main request one had to conclude that the same product as claimed was obtained by the Method 1 disclosed in document (17) because the same methods must result in the same products. Therefore, the IL-2 obtained according to method 1 of document (17) anticipated the product as claimed in Claim 1.

VIII. The Respondents argued essentially as follows:

(a) the "public" character of the Erlangen and Geisenheim meetings was contested because the word "public" in Article 54(2) meant the "public at large". This interpretation was the only possible meaning of Article 54(2) which was unambiguous. It was essential that there be no ambiguity. If availability to a restricted circle of persons was to be sufficient, then doubt immediately arose as to the definition of such a restricted circle. In the present case, the restricted circle could be defined in several ways, but in any case in terms of "skilled persons". If the signatories to the EPC had intended that availability to the public as a whole was not required, but instead that some lesser degree of availability sufficed, Article 54(2) would have been written in such a way that the state of the art should be held to comprise everything made available to the skilled person. Reference was made to two decisions of the Boards of Appeal T 300/86 "Television Receiver", of 28 August 1989 (cited in the Annual Report 1989, supplement to OJ EPO 1990(6), 25) and T 444/88 "Foam Particles" of 9 May 1990 (not published in OJ EPO). There a conclusion was drawn that the "public" within the meaning of Article 54(2) EPC was not identical with colour TV set manufacturers and that a document, to form part of the state of the art, was "available to the public" once it had been made known to third parties.

It was proposed to refer to the Enlarged Board of Appeal the question of what the true meaning of the word "public" was in Article 54(2) EPC.

The public character of the Erlangen and Geisenheim meetings and document (17), which had been distributed during the Geisenheim meeting was contested. No evidence or proof could establish that the man-in-the-street was entitled to attend one of the meetings. Nor was there any evidence that document (17) had reached anyone other than attendees at the Geisenheim meeting prior to the priority date of the patent in suit. It was further contended that the oral disclosures at Erlangen and Geisenheim and the written disclosure of document (17) had all been confidential in any event in the hands of the attendees and recipients until the date of publication of the respective subject-matter in the usual technical journals.

As to the content of the testimony of witnesses heard before the Opposition Division, it was inevitable that the witnesses had difficulties in remembering precisely what had happened and what had been said nine years ago. There were substantial gaps and conflicts in the evidence.

Document (17) was undated, which created an unsatisfactory situation. It further gave rise to difficulties of interpretation on account of its brevity. There was no full technical description of any process at all. In particular the sentence which was believed by the Opponents to disclose the claimed subject-matter was ambiguous and needed interpretation such that the words "substituted with" meant "replaced by". If so, document (17) taught here the use of serum alone, in replacement of the PHA. Further, the gaps in the information provided by document (17) could not be filled by the expert knowledge of the skilled person. Rather the filling

of gaps constituted addition of new information which was not allowed when assessing novelty.

(b) The reasons given in the impugned decision for finding the presence of an inventive step were agreed.

As far as document (17) was concerned, particular attention was drawn to the remarks at page 6, lines 1 to 6, which strongly recommended the use of a first incubation in the presence of PHA alone in the absence of serum followed by a second incubation with serum alone - in other words, the successive use of PHA and serum independently. Line 1 commenced: "Contrastingly, a very good IL-2 activity was seen". Because the skilled person was oriented towards practicalities, he should, if he decided to pursue the teaching of document (17) as it stood, prefer to follow this suggestion. On account of the absence from document (17) of any experimental details, the development was essential.

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

The Respondents requested that the appeal be dismissed and that the patent be maintained as granted or on the basis of auxiliary requests 1 to 4, filed during oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. Novelty (Article 54 EPC)

2.1 Main request

2.1.1 Claim 1 of the main request is a product claim wherein a T-cell growth factor is defined as being derived from the peripheral mononuclear blood cells of a donor and being serum-free and mitogen-free and the donor being human, bovine or porcine.

2.1.2 The documents in discussion as representing the closest prior art are the Erlangen and Geisenheim meetings (citations (12) and (13)) and document (17) which is an abstract of the lecture presented by the inventors of the patent in suit at the Geisenheim meeting.

2.1.3 As to the question whether or not the Erlangen and Geisenheim meetings constitute prior art within the meaning of Article 54(2) EPC, the Board confirms the position taken by the Opposition Division in its impugned decision. For the same reasons as those adequately developed under point 2.2 in the impugned decision (see paragraph III(a) above), the Board considers both meetings as constituting prior art.

2.1.4 It is an undisputed fact that the date of both meetings fall before the priority date of the patent in suit.

2.1.5 Further, the Board is unable to follow the submissions of the Respondents to the effect that the meetings were not "public" within the meaning of Article 54(2) EPC.

An oral disclosure is regarded as made available to the public if, at the relevant date, it was possible for members of the public to gain knowledge of the content of the disclosure and there was no bar of confidentiality restricting the use or dissemination of such knowledge. It is plausible that the meetings at Erlangen and Geisenheim were not open to everybody, because only certain persons were invited to participate. Those, however, were not subject to a secrecy agreement. So the oral disclosure of the meetings was freely available to the public. Everything that was said at the Erlangen and Geisenheim meetings was therefore made available to the public.

2.1.6 There is no need to refer this question to the Enlarged Board of Appeal under Article 112 EPC. In this connection, however, the Board would like to remark that the conjunction made by the Respondents between the words "made available to the public" in Article 54(2) EPC and "to be carried out by a person skilled in the art" in Article 83 EPC cannot be understood as meaning that the word "public" in Article 54(2) EPC refers not to the person skilled in the art but to the man in the street. It is the converse which makes sense, i.e. that an oral disclosure before a skilled person makes it "public" in the sense that the skilled person is able to understand the oral disclosure and is potentially able to distribute it further to other skilled members of the public.

Had the oral disclosure taken place before a circle of persons, all of whom were unable to understand its technical teaching, it could be argued that the disclosure had not been made available to the public because the teaching would not have been understood by the audience. Therefore, in this respect the word "public" in Article 54(2) EPC has the same meaning as the words "skilled person" in Article 83 EPC, but whereas in the case of Article 54(2) EPC the making available to the

public of a disclosure is seen from the stand-point of passive reception, Article 83 EPC requires sufficient disclosure for a skilled person to be able to actively reproduce the invention.

In any event, the term "made available to the public" in Article 54(2) EPC cannot be interpreted in such a way that the addressees of an oral disclosure were only to be considered as being "public" if they were to be considered as unskilled persons. This, however, would be the consequence of the Respondent's arguments.

2.1.7 Finally, after consideration of the minutes of the thorough hearing of witnesses before the Opposition Division and all further evidence on file, the Board shares the Opposition Division's opinion in its impugned decision under point 2.22 that there remain doubts about the true content of what was said at the meetings about the method to stimulate and produce IL-2. In the Board's opinion, it is not likely that now, 12 and 13 years after the two meetings took place, the facts could be elucidated more clearly than they were before the Opposition Division. All the written facts on file about the meetings, i.e. handwritten notes taken during the meetings by the witnesses, have been correctly assessed by the Opposition Division. In view of this situation the Opposition Division correctly decided that any oral disclosure at the Erlangen or Geisenheim meetings could not be considered as state of the art within the meaning of Article 54(2) EPC.

2.1.8 Disregarding the oral disclosures at the meetings as relevant state of the art, the disclosure of document (17) remains to be considered. The Appellants contended that this document had been distributed at the Geisenheim meeting and represented an abstract of what had already been presented orally at a lecture at the Geisenheim

meeting by one of the inventors. The Respondents did not seriously contest that this paper had been distributed to the participants at the Geisenheim meeting. Document (17), therefore, is a written disclosure of the role of serum proteins in PHA-induced products of IL-2 by human peripheral blood lymphocytes before the priority date of the patent in suit.

2.1.9 Independently of the different interpretation put on the true teaching of document (17) by the parties, there is agreement among them, and this was also the position of the Opposition Division, that document (17) represents the closest prior art. The Board shares this view.

As already stated correctly in the decision of the Opposition Division, the technical teaching of document (17) is ambiguous. The purpose of the experiments carried out and described in document (17) was, as the title of this paper already indicates, to investigate the role of serum proteins in PHA-induced production of IL-2. There is to this extent a clear and unambiguous disclosure in this document as two methods are compared. The one comprises a stimulation of the peripheral blood cells by PHA in the absence of serum, a situation in which no production of IL-2 could be detected (page 5, paragraph 3, lines 5 to 7). Literally, it is said that "if the cells first were incubated with serum then washed and incubated with PHA in absence of a serum, hardly any IL-2-activity could be seen either. Contrastingly, a very good IL-2-activity was seen in the conditioned supernatants if the cells first were incubated with PHA-containing culture medium in the absence of serum, then washed and incubated in culture medium supplemented with serum only, before the cells were washed and allowed to condition the supernatants" (page 5, third paragraph, lines 7 to 10, page 6, first paragraph, lines 1 to 6).

2.1.10 From these results, the authors of document (17) drew the conclusion that for the lectin-mediated induction of IL-2-production a double signal was needed, namely that first PHA reacted with the membrane of the IL-2-producer cell and uncovered or activated a receptor, which secondly interacted with serum protein. The production of IL-2 did not begin until after this double signal. It was then the purpose of the presentation given in document (17) to characterise the endogenous co-mitogenic factor. The more ambiguous information given in document (17) has to be interpreted in the light of the above-cited disclosure read with knowledge of the purpose of the experiments carried out and described therein. In doing so, the sentence which has led to controversy between the parties and reads "during PHA stimulation the culture medium is substituted with 15% human AB serum, whereas production of IL-2 and bio-assays are performed in absence hereof", can only have the meaning that PHA as a mitogen and human AB serum are applied in sequence and not at the same time so that the words "substituted with" have to be interpreted as meaning "replaced by".

2.1.11 Document (17) further mentions assay systems for IL-2 activity, namely growth support of human T-cell lines and proliferation and blast transformation of PBL in absence of serum. From the above literal citation (see point 2.1.9) it becomes apparent that by the experiments carried out an IL-2 activity could be established by one of the assay systems. There is no mention in document (17) about purity or concentration of IL-2.

2.1.12 Independent product Claim 1 has as its essential characteristic that the T-cell growth factor is serum-free and mitogen-free. The analysis of the teaching of document (17) above shows that by the experiments carried out in document (17) an IL-2 activity could be demonstrated. There is no clear and unambiguous disclosure that any

product was obtained containing IL-2 but no PHA, i.e. mitogen and no serum at all. The purpose of any washing step described in document (17) was to make sure when applying in sequence either PHA or serum that any effect observed could be distinguished as being the result of the action of PHA or of serum. The disclosure of document (17) cannot be understood therefore, as to provide a real mitogen- and serum-free T-cell growth factor, as claimed in Claim 1. A product of this kind is, therefore, novel.

2.1.13 Besides independent Claim 1 there is an independent Claim 3 the novelty of which has to be examined. It refers to a process for producing a serum-free and mitogen-free T-cell growth factor (see above paragraph I).

2.1.14 Following the analysis of the technical teaching of document (17), as given above, it may be concluded that there are two process steps in Claim 3, which are not clearly and unambiguously disclosed in document (17) namely step (2) to stimulate the cells by incubating the cells in a liquid tissue culture medium supplemented with serum and mitogen and process step (4) to condition the cells obtained in a preceding step by incubating the cells in the presence of a serum-free and mitogen-free liquid tissue culture medium. Process Claim 3 has, therefore, also to be considered novel.

2.1.15 The Appellants mentioned document (6) in an aside, where on page 365 under the headline "Materials and Metals, No. 2 Conditioning of Media", it is mentioned that PBL were incubated in a medium, containing 15% pooled inactivated human AB serum and 4 µg/ml of PHA, which was considered to be the same process step as that defined under step (2) in Claim 3. For the sake of completeness the Board notes that the mentioned paragraph further contains the process steps that after thorough washing the cells were incubated in a culture medium supplemented only

with AB serum. This process step differs, thus, from process step (4), where it is an essential feature that further conditioning of the cells is to be carried out in the presence of a serum-free culture medium. Therefore, process Claim 3 is novel also with regard to document (6).

2.1.16 The claims of the main request thus fulfil the requirements of Article 54 EPC.

3. Inventive step (Article 56 EPC)

3.1 Main Request

3.1.1 Product Claim 1 of the main request being novel, it is necessary to examine whether it involves the required inventive step.

3.1.2 In the light of the technical teaching of document (17) (see points 2.1.9 to 2.1.11 above), the technical problem can be seen in the improvement of the purity and concentration of a T-cell growth-factor product.

The problem is solved by providing a product as claimed in Claim 1 and a process as claimed in Claim 3. The specification states in column 2, lines 52 to 55, that through serum-free production the growth factor could be highly concentrated and the activity thereof could be increased between 300 and 500 times. Examples 1 to 3, in particular, provide sufficient evidence that the problem was actually solved.

3.1.3 The question to be answered is whether a mitogen-and serum-free T-cell growth-factor constitutes an inventive contribution to the art.

In the specification of the patent in suit there is a discussion of certain prior art documents which disclose a T-cell growth-factor product which is contaminated either by PHA or by serum. Serum is necessary for cell growth and as a result, serum was always used in cell culture. It is, apparently, highly desirable to provide a T-cell growth factor product which does not contain any toxic substances. It is known that PHA has toxic effects and further on that the presence of serum may mask the true effect of IL-2 because of numerous proteins being present in serum and repeated injections of such a serum-containing preparation regularly cause allergic and anaphylactic reactions in patients. On the other hand, any process to remove undesired contaminating substances resulted in a decrease of the activity of a T-cell growth factor. This discussion of the prior art shows that the Respondents, at the time of the priority of the patent in suit, were well aware of the disadvantages of the presence of mitogen and serum in a T-cell growth factor product. This is further supported by other prior art documents filed before the Opposition Division by the Appellants, for example by document (6) (page 365) mentioned above. Thus, as far as product Claim 1 is concerned, the Board considers the mitogen- and serum-free T-cell growth factor product as such to be an obvious desideratum.

3.1.4 In the view of the Board, starting from document (17), the next obvious step in the light of the problem to be solved would have been to develop the process described unambiguously in document (17) in such a way that the desired end product, as obtained by the scientific experiments described in document (17), would have been freed from any contaminating and toxic substances.

3.1.5 The Board accepts that there are cases in which an acknowledged inventive step of a process may also

influence the inventive contribution for a product claim. In the present case, however, document (17) provides the information that, in the supernatant of a culture medium containing PBL, incubated with PHA, then washed and incubated in a culture medium supplemented with serum only, a very good IL-2-activity could be observed. Being equipped with the information that neither mitogen nor serum are desired in a pharmaceutically acceptable end product it would have been the next obvious and evident step for the skilled person within the meaning of an obvious desideratum to further develop the substance whose activity was determined in documents (17) to make the product completely mitogen- and serum-free.

3.1.6 Since an inventive step for the product as claimed in Claim 1 cannot be accepted, the main request, containing a non-allowable claim, thus is not allowable.

3.2 Auxiliary request 1

3.2.1 Claim 1 of this request relates to a method for producing a serum-free and mitogen-free T-cell growth factor comprising several steps (see above paragraph I). The closest prior art document with respect to this process claim is also document (17) as correctly analysed by the Opposition Division. The differences between the method clearly and unambiguously disclosed in document (17) and the method as claimed are stated above under point 2.1.14. The question remains whether these variations of the method to obtain IL-2 disclosed in document (17) contribute to the art in an inventive way or whether these measures would have been an obvious technical development which would not be patentable.

3.2.2 The purpose of the experiments described in document (17) was to investigate the role of serum proteins in PHA-

induced production of IL-2 by human peripheral blood lymphocytes. From those investigations, as summarised above under point 2.1.9, it follows that it was not within the frame of the teaching of document (17) to supplement mitogen and serum simultaneously for stimulating the PBL to produce IL-2 because in this case an unambiguous scientific answer to the question of the role of serum and mitogen cannot be given. If, therefore, an IL-2 production showing good activity is one of the desired aims, the skilled person would turn to that sequence of addition of mitogen or serum which was shown to be good. Any hint to supplement mitogen and serum simultaneously cannot be derived from document (17).

3.2.3 Moreover, neither step (3) of the claimed process to separate and wash the stimulated cells to remove substantially all of the serum and mitogen nor step (4) to condition the cells obtained by further incubating the cells in the presence of serum-free and mitogen-free culture medium was obvious in the light of the teaching of document (17), because nowhere is there any hint that any one could achieve, faced with the problem to be solved, a reasonable yield of the desired T-cell growth factor when incubating the cells in a serum-and mitogen-free culture medium. Thus, taking the technical teaching of document (17) alone, the skilled person could not arrive at the claimed process without an inventive contribution.

3.2.4 It remains to investigate whether there are possibly other documents which could have led the skilled person on the basis of the teaching of document (17) and in the light of the problem to be solved, to arrive at the claimed process. Besides less relevant prior art it is the disclosure of already mentioned document (6) which could possibly be relevant. It deals with a method of establishing human T-cell lines in tissue culture media

containing T-cell growth factor but not PHA. It is thus the technical teaching of document (6) to investigate whether it is PHA or the T-cell growth factor which is causing the T-cells to grow for a certain period of time. The result of the experiments carried out according to this document was that not PHA but T-cell growth factor was considered to be the T-cell mitogen. Even if, as already stated above (see point 2.1.15), a medium is described which contains serum and PHA, the process disclosed is such that PBL were firstly incubated with the mentioned media, thereafter thoroughly washed and then incubated for 48 hours in the medium supplemented only with serum. After centrifugation the supernatant were then decanted off and stored. In particular, on page 370 under the heading "Discussion", it is disclosed that PHA is needed for the production of T-cell growth factor in PBL-cultures but is only needed during an initial stimulation period. After several washing steps, a virtually PHA-free T-cell growth factor conditioned culture medium was obtained without need for further manipulation. It is concluded that PHA is able to induce a **short-lasting** production of the growth factor upon which the respondent cells mount their mitogenic response. After the decline of the growth factor production and exhaustion of the supply, the respondent cells die (page 370, fourth paragraph). Accordingly, this teaching does not give any indication to the skilled person that an incubation of the PBL in the simultaneous presence of mitogen and serum, followed by a washing step to remove any mitogen and serum and a further incubation step in a medium not containing mitogen and serum, could result in an effective, long lasting production of IL-2, ending up with a mitogen- and serum-free product.

3.2.5 The fact that the process as claimed appears to be simple does not necessarily mean that it is obvious. In the

Board's opinion, the prior art disclosures as analysed above would lead a person of ordinary skill to a process according to which PHA and serum, each playing apparently sensitive roles in the process of inducing IL-2, could not be applied at the same time and furthermore should not be removed from the growth media completely without the process being terminated or at least disturbed. In the light of this, the simplicity of the claimed method comprises an elegant feature which is considered by the Board to go beyond ordinary skill.

3.2.6 Claim 1 of the first auxiliary request, therefore, is inventive and this request consequently is allowable; a discussion of the remaining auxiliary requests is not necessary.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Opposition Division with the order to maintain the patent on the basis of Claims 1 to 12 of the auxiliary request 1 and a description to be adapted.

The Registrar: The Chairman:

P. Martorana P.A.M. Lançon