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D E C I S I O N
of 18 October 2002

Case Number: T 0755/00 - 3.3.8

Application Number: 90901345.0

Publication Number: 0448635

IPC: G01N 33/564

Language of the proceedings: EN

Title of invention:

Methods and compositions for the early detection and treatment of insulin dependent diabetes mellitus

Patentee:

UNIVERSITY OF FLORIDA

Opponent:

The Regents of the University of California

Headword:

Detection of diabetes/UNIVERSITY OF FLORIDA

Relevant legal provisions:

EPC Art. 83, 107, 108, 123(3)
EPC R. 64(b)

Keyword:

"Admissibility of appeal (yes)"
"Admissibility of the main request (claims as granted) (yes)"
"Main request: sufficiency of disclosure (no)"
"First and second auxiliary requests: extension of protection (yes)"
"Admissibility of third and fourth auxiliary requests (no)"

Decisions cited:

T 0331/89, T 0528/93, T 0840/93, T 0794/94, T 0564/98,

T 1052/98, G 0009/91

Catchword:

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Case Number: T 0755/00 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 18 October 2002

Appellant: UNIVERSITY OF FLORIDA
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted 11 May 2000
revoking European patent No. 0 448 635 pursuant
to Article 102(1) EPC.**

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
V. Di Cerbo

Summary of Facts and Submissions

- I. The patent proprietors (the appellants) lodged an appeal against the decision of the opposition division dated 11 May 2000 whereby the European patent 0 448 635, which had been opposed by one party on grounds of Article 100(a) and (b) EPC, was revoked. Basis of the revocation was the only request on file at that time, namely the main request filed at the oral proceedings held on 16 April 1999.
- II. The opposition division found that claim 1 (the only claim) of said main request was not in compliance with Article 56 EPC.

Said claim read as follows:

"1. A method of detecting the onset of insulin-dependent diabetes, comprising the detection, in a serum sample, of antibodies which immunoreact with a protein of approximately 40 kd obtainable from crude membrane preparations of human islet cells by trypsinisation for sixty minutes at 4°C (2 mg/ml 50 mM Tris buffer, pH 7.4), followed by centrifugation and immunoprecipitation, wherein the protein is a fragment of the 64 kd protein obtainable from the islet cells, provided that the detection does not use said 64 kd protein."

- III. In their notice of appeal, the appellants requested that the patent be maintained as granted, or on the basis of any auxiliary request that may be filed.

The patent as granted comprised two claims. Claim 1 read as follows:

"1. A method for detecting the onset of insulin-dependent diabetes, comprising the detection, in a serum sample, of antibodies which immunoreact with a fragment, of approx 40kd, of the 64kd protein obtainable from islet cell preparations."

Dependent claim 2 contained the additional technical feature that the fragment was obtainable by trypsin digestion of the 64 kd protein.

In their statement setting out the grounds of appeal the appellants explained the reasons why they considered that the decision of the opposition division was wrong and presented arguments in favour of the request on the basis of which the patent had been revoked.

- IV. The respondents (the opponents) filed comments to the statement of grounds and requested that the appeal be dismissed.
- V. On 1 August 2002, the board issued as an annex to the summons to oral proceedings a communication with the preliminary view that the claims as granted would be the focus of the discussion at the oral proceedings to be held, the outstanding objections being lack of novelty, lack of inventive step and lack of sufficiency of disclosure.
- VI. In a letter dated 17 September 2002, the respondents submitted that the appeal was not admissible on the ground that the patent proprietors were not a party

affected by the decision of the opposition division as required by Article 107 EPC. In this respect, they explained that the claims as granted, on the basis of which the appellants had requested in their notice of appeal the maintenance of the patent, were not the subject of the decision and that the purport of the notice of appeal was to appeal the rejection of the claims as granted, as their reinstatement was the only identifiable and specific remedy requested therein. The respondents added that, should it be held that the notice of appeal was admissible, the statement of grounds did not meet the requirements of Article 108 EPC and the appeal should accordingly be rejected.

- VII. With a letter dated 18 September 2002, the appellants requested that the patent be maintained on the basis of the claims as granted or on the basis of either the first or the second auxiliary requests filed with the same letter.

The first auxiliary request comprised only one claim which read as follows:

"1. A method for detecting the onset of insulin-dependent diabetes, comprising contacting a serum sample with an autoantigen and detecting autoantibodies which immunoreact with the autoantigen, wherein the autoantigen is a 64kd protein, or a peptide fragment thereof that is specific for the same antibody, obtainable from crude membrane preparations of human islet cells, and capable of being trypsinated for sixty minutes at 4°C (2 mg/ml 50 mM Tris buffer, pH 7.4), followed by centrifugation and immunoprecipitation, to produce a 40kd protein product."

The second auxiliary request also comprised only one claim. Said claim differed from claim 1 of the first auxiliary request in that the wording "wherein the autoantigen **is** a 64kd protein" was replaced by the wording "wherein the autoantigen **consists of** a 64kd protein" (emphasis added).

VIII. With a letter dated 17 October 2002, the respondents informed the board that they would not attend the oral proceedings and requested that the first and second auxiliary requests filed with the letter of 18 September 2002 be rejected as inadmissible on the ground of excessive delay. They also expressed their view that none of the said requests met the requirements of the EPC. In particular they considered that said requests did not comply with the requirements of Article 123(3) EPC. The respondents also requested that no new appellants' request be admitted, upon which they had not the opportunity of presenting any argument.

IX. Oral proceedings took place on 18 October 2002. They were attended by the appellants only. A third and fourth auxiliary requests, each comprising one claim only, were submitted, said requests corresponding to the first and second auxiliary requests, respectively, and differing therefrom in that at the very end of the claim the expression "and wherein the antibodies also immunoreact with the 40kd protein product" was added.

In support of their request that the claims as granted be taken into consideration as their main request, the appellants argued that the observations they made in the statement of grounds apply not only to the claim taken into consideration by the opposition division in

its decision but also to the claims as granted.

As regards the issue of sufficiency of disclosure (Article 83 EPC), the appellants submitted that the content of page 22 of the application as filed provided a sufficient disclosure of the claimed method. It was indicated on that page that there was a protein fragment of 40 kd which could be isolated by standard techniques and could be used as a marker for the onset of insulin-dependent diabetes (IDD). They also referred to the later document D5 (*J. Clin. Invest.*, 96, 1995, 1506-11) arguing that said document showed that a 40 kd marker fragment was identified as a fragment of the IA-2 protein, which confirmed the disclosure in the patent.

As regards the admissibility of the first and second auxiliary requests, the appellants submitted that said requests were filed within the time limit set up in the summons and, therefore, could not have taken the respondents by surprise.

As regards the formal allowability of the first and second auxiliary requests under Article 123(3) EPC, the appellants contended that the objection seemed to rely on a misunderstanding of the claimed subject-matter, the point being for a correct understanding that antibodies recognizing the 40 kd fragment should also recognize the 64 kd protein.

Furthermore, the appellants argued that it was the first time in the proceedings that an objection under Article 123(3) EPC had been raised by the board and that, therefore, they should be authorized to file additional requests aiming at overcoming said

objection.

- X. The appellants requested that the decision under appeal be set aside and that the patent be maintained as granted or on the basis of the first or the second auxiliary request filed with the letter of 18 September 2002. Auxiliary, they requested to be authorized to file new third and fourth auxiliary requests, or failing that, that the case be remitted to the first instance for further prosecution.

Reasons for the Decision

Admissibility of the appeal

1. The decision under appeal is the decision of revoking the European patent. Therefore, the patent proprietors were adversely affected by said decision and were entitled to appeal under Article 107 EPC. They have done so by filing a notice of appeal which contained a statement identifying both the decision which was impugned and the extent to which amendment or cancellation of the decision was requested. This is in full compliance with Rule 64(b) EPC.
2. They have duly filed also a statement setting out the grounds of appeal which exposes the reasons why they considered that the decision of the opposition division was wrong. Therefore, also the requirements of Article 108 EPC are met.
3. The respondents' arguments that the appeal is not admissible as it is based on the request to reinstate the claims as granted which were **not** the subject of the

decision of the opposition division has no bearing on the question of admissibility of the appeal *per se* which is in relation to the compliance with Articles 107 and 108 EPC, as well as Rule 64(b) EPC. The said argument is relevant only in the respect of the different question whether the appellants' main request can be admitted (cf. points 5 to 9 *infra*).

4. Thus, as the requirements of Articles 107 and 108 EPC as well as those of Rule 64 EPC are met, the appeal is admissible.

Admissibility into the appeal proceedings of the main request (claims as granted)

5. According to the case law of the boards of appeal, where the patent proprietors are appealing against the revocation of their patent, they are entitled to revert to a more broadly worded version of the patent, and in particular the one as granted (see T 564/98 of 6 June 2000, point 2 of the reasons), the right to reactivate earlier claims being refused only if it appears to constitute an abuse of procedure (see T 331/89 of 13 February 1992, point 3.2 of the reasons).
6. The respondents argued that the claims as granted had not been the subject of the decision of the opposition division with the result that the patent proprietors are not entitled to revert to said claims. In support of their submission, they cited decision T 528/93 of 23 October 1996.
7. Decision T 528/93 (*supra*) relates to a very particular situation. A request had been considered as being only "virtual" because it had been filed during oral

proceedings and then withdrawn at the same without having been assessed by the opposition division as to its patentability. In view of its virtual character, said request had been regarded as not being part of the decision of the opposition division (see point 1.3 of the decision) and, therefore, had not been admitted into the appeal proceedings. This is not the situation in the present case. The granted claims cannot be regarded as virtual. They have been challenged by the opponents in their notice of opposition, which means that, even if the opposition division did not express any opinion in their respect, because in reply to the notice of opposition the patent proprietors have replaced them by a new request, nevertheless they have been part of the proceedings. Therefore, decision T 528/93 (supra) is not relevant in the present case.

8. The only question here is whether the request to maintain the patent as granted constitutes an abuse of procedure. The main request was submitted at the very beginning of the appeal proceedings. Furthermore, the board is satisfied that the observations contained in the statement setting the grounds of appeal may equally apply both to the claim on the basis on which the patent had been revoked and to the claims as granted, as each of both sets of claims basically relates to the same method comprising the detection of antibodies which immunoreact with a protein fragment of approximately 40 kd. Consequently, the main request cannot be considered as constituting an abuse of procedure.
9. Therefore, the main request is admitted into the appeal proceedings.

Main request: Article 83 EPC

10. Insufficiency of disclosure was a ground of opposition. It was raised and substantiated in the notice of opposition pursuant to Rule 55(c) EPC. Therefore, the board has the power of examining whether the main request meets the requirements of Article 83 EPC (see G 9/91; OJ EPO 1993, 408).

11. In the method of claim 1 the antibodies are specifically defined with reference to a protein fragment. This is a fragment, of approximately 40 kd, of the 64 kd protein obtainable from islet cell preparations. According to claim 2 said fragment is obtainable by trypsin digestion.

12. The question under Article 83 EPC is whether the person skilled in the art would have been in a position to perform the method claimed, i.e. to detect, in a serum sample from a patient not yet identified as a clinically proved diabetic, antibodies immunoreacting with a fragment, of approximately 40 kd, of the 64 kd protein obtainable from islet cell preparations. To this extent, the skilled person would have required to be provided with such a fragment in order to unambiguously detect antibodies specifically immunoreacting therewith, the provision of the 64 kd protein only being insufficient in this respect, as antibodies immunoreacting therewith could recognize epitopes present on that part of the 64 kd protein which does not correspond to the 40 kd fragment.

13. The only passage of the description of the patent specification in which the claimed method would appear to be referred to is located in column 3, lines 25 to

33. Said passage reads:

"The method involves making crude membrane preparations of ³⁵S methionine labeled islet cells, followed by trypsinization for 60 minutes at 4°C (2 mg/ml 50 mM Tris buffer, pH 7.4). The material is then centrifuged, followed by our standard immunoprecipitation technique. Following gel electrophoresis and autoradiography, a 40 [kd] band can be observed with immunoprecipitations from diabetic sera and not in controls."

14. An important point is the fact that the method involves trypsinisation not of a particular protein such as the 64 kd protein but of islet cells as such. The further treatment of the trypsinated islet cells preparation is only evoked without detail. It involves a centrifugation and a gel electrophoresis. What is observed after electrophoresis is a band consisting of an unidentified material having migrated at such a level that said material is considered to have a molecular weight of approximately 40 kd as revealed by immunoprecipitation with diabetic sera.
15. Not only the true nature of said 40 kd material is not indicated but also the description made in said passage provides no evidence that the antibodies which immunoprecipitated therewith are early indicators of the onset of IDD. In this respect, said antibodies are only characterised by their presence not in sera of patients in advance of the clinical stages of IDD but in sera from diabetic patients, i.e., from patients with clinically established diabetes.
16. The appellants have contended that, equipped with the above disclosure and the additional information that

(a), as expressed on column 3, lines 33 to 37, "this 40 [kd] band that is immunoprecipitated directly from trypsin treated islets **most likely represents** the same protein" (emphasis added by the board) as a 40 kd protein which is said to be derived from isolated 64 kd protein treated with trypsin and (b) said method is "an improved method for the detection of autoantibodies to 64 [kd] protein" (see column 3, lines 22 and 23), the person skilled in the art would have easily realized that, indeed, the 40 kd material was a fragment of the 64 kd protein and that antibodies which immunoprecipitated said material represented an accurate and specific early indicator of the onset of IDD, and thereby would have been able to readily perform the invention.

17. This reasoning cannot be accepted. A disclosure which relies upon **a mere speculation** cannot be regarded as sufficiently clear and complete within the meaning of Article 83 EPC. The description fails to disclose that antibodies of patients in advance of the clinical stages of IDD can be detected which react with a 40 kd fragment of the 64 kd protein obtainable from islet cells. As already outlined above (cf. points 13 to 15), the skilled person is left on his or her own resources as regards the isolation of such an immunoreacting fragment. Thus, it has to be considered that the person skilled in the art cannot without undue burden perform a method which as defined in claim 1 aims at detecting antibodies specifically recognising such a fragment and present in the sera at the onset of IDD.

18. The appellants have relied upon the later document D5. Said document, which only shows that 40,000-Mr fragments obtained upon trypsinisation of 64,000-Mr

proteins and immunoprecipitated by sera from patients with IDD are related to a protein designated IA-2, is of no utility to decide on the issue of sufficiency of disclosure. Even if it had provided a more detailed disclosure than the patent, said document could not have been used to compensate the fundamentally insufficient disclosure provided by the patent (see e.g., T 1052/98 of 8 May 2001).

19. For these reasons, the main request is not allowable under Article 83 EPC.

Admissibility into the appeal proceedings of the first and second auxiliary requests

20. The respondents objected to the introduction into the proceedings of the first and second auxiliary requests for reasons of "excessive delay".
21. If patent proprietors whose patent was revoked wish during appeal proceedings to have further requests considered by the board of appeal, admission of these requests is a matter of discretion of the board and is not a matter of right. According to the practice of the boards of appeal, requests filed during the appeal procedure are considered as admissible provided that such requests are *bona fide* attempts to overcome objections raised (see T 840/93, OJ EPO 1996, 335; points 3.1 and 3.2.1 of the reasons).
22. The first and second auxiliary requests have been filed as attempts to overcome the objections raised by the respondents in their observations made in respect of the statement setting the grounds of appeal. Moreover, the respondents have had the opportunity to submit

observations in respect of them and were not taken by surprise. Therefore, exercising its discretion under Article 114 EPC, the board decides to admit said first and second auxiliary requests into the appeal proceedings.

First and second auxiliary requests: Article 123(3) EPC

23. The claims as granted conferred protection for a method based on the detection of a particular class of antibodies, namely those antibodies which immunoreact with a 40 kd fragment of the 64 kd protein.
24. In the method of the only claim of the first and second auxiliary requests, the antibodies to be detected are broadly defined as immunoreacting with either the 64 kd protein or any fragment thereof which upon trypsinisation is capable to produce a 40 kd protein product. This means that said claim aims at conferring protection for a method which is based on the detection of any antibodies susceptible of immunoreacting with any part of the 64 kd protein, regardless of whether said part is comprised or not within the 40 kd fragment referred to in the claims as granted.
25. The argument by the appellants is that because the antibodies to be detected immunoreact with the 40 kd fragment they also react with the 64 kd protein. The converse of this is not necessarily true, since antibodies immunoreacting with the 64 kd proteins could either react with epitopes located in that part of the 64 kd protein which corresponds to the 40 kd fragment or the other part thereof.
26. Thus, the only claim of each of the first and second

auxiliary requests confers an extended protection compared to the claims as granted. Therefore, the requirements of Article 123(3) EPC are not met by both requests.

Admissibility into the appeal proceedings of the third and fourth auxiliary requests

27. Both the third and the fourth auxiliary requests were not before the opposition division. They were filed at a very late stage of the appeal proceedings, namely during oral proceedings, and the respondents had no opportunity to present observations in their respect. The announced intention of the appellants was to find a way of overcoming the objection raised under Article 123(3) EPC.
28. The board considers that the amendment contained in each of the third and fourth auxiliary requests cannot be regarded as a *bona fide* attempt to overcome the objection under Article 123(3) EPC raised against the first and second auxiliary requests, and for that reason, they are not admitted into the appeal proceedings in exercise of the discretion under Article 114(2) EPC.
29. This is because the objections under Article 123(3) EPC to the first and second auxiliary requests stemmed essentially from the introduction into claim 1 of a reference to antibodies immunoreacting with the 64 kd protein or with fragments thereof of undefined length, this being a considerable departure from the language of the claims as granted (cf. points 23 to 26 above). Instead of using the granted claims as basis for the amendments, the appellants have attempted to repair the

only claim of the first and second auxiliary requests by introducing further amendments the implications of which on the extent of protection are *prima facie* unclear (cf. in this respect T 794/94 of 17 September 1998, in particular point 2.2 of the reasons).

Request to remit the case to the opposition division for the continuation of proceedings

30. None of the claim requests submitted by the appellants and introduced into the appeal proceedings have been considered to represent a valid basis for the maintenance of the patent so that the decision under appeal could be set aside. Therefore, there is no reason whatsoever to remit the case to the opposition division for further prosecution. Consequently, the request for remittal is refused.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Wolinski

L. Galligani