BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

A	X	B		C	

File Number: T 815/90 - 3.3.2

Application No.: 85 904 746.6

Publication No.: 0 196 316

Title of invention: Hepatitis A virus purified and triply cloned

Classification: C12N 7/08

Interlocutory D E C I S I O N

of 26 February 1993

Applicant: The United States of America as represented by the United States Department of Commerce

Headword: Hepatitis A virus/UNITED STATES OF AMERICA

EPC Article 83, 112(1)(a) and Rule 28

Keyword: "Sufficiency of disclosure" - "Culture deposit information" - "Referral to the Enlarged Board of Appeal"

Headnote

The following question is referred to the Enlarged Board of Appeal:

May the information concerning the file number of a culture deposit according to Rule 28(1)(c) EPC be submitted after expiry of the time limit set out in Rule 28(2)(a) EPC?"

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : T 815/90 - 3.3.2

Interlocutory D E C I S I O N of the Technical Board of Appeal 3.3.2 of 26 February 1993

Appellant : The United States of America
as represented by the Secretary,
United States Department of Commerce,
National Technical Information Service,
Office of Government Inventions and Patents,
5285 Port Royal Road
Springfield, Virginia 22161 (US)

Representative : Daley, Michael John
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London, WC2A 1JQ (GB)

Decision under appeal : **Decision of the Examining Division of the European Patent Office dated 12 July 1990 refusing European patent application No. 85 904 746.6 pursuant to Article 97(1) EPC.**

Composition of the Board :

Chairman : P.A.M. Lançon
Members : U.M. Kinkeldey
R.L.J. Schulte

Summary of Facts and Submissions

I. European patent application No. 85 904 746.6 filed on 18 September 1985, claiming priority of 19 September 1984 and published under No. WO-A-86/01826, was refused by the Examining Division. The refusal was based on nine claims filed on 10 February 1989. Claims 1 and 7 read as follows:

"1. A uniform hepatitis A live attenuated virus composition adapted to produce a protective antibody response in higher primates, characterised in that the composition is triple cloned material of strain ATCC VR2097, VR2098, or VR2099.

7. A method for the production of a uniform hepatitis A live attenuated virus composition which comprises the step of serially diluting uncloned hepatitis A virus ATCC VR2097, VR2098 or VR2099, and inoculating each dilution into a respective mammalian cell culture, culturing the same, harvesting cloned virus particles and repeating said step at least twice more, thereby to produce a master seed lot therefrom for the formation of a vaccine composition."

II. The grounds given for refusal were that the application did not meet the requirements of Article 123(2) EPC, because the mention of three clones having respectively the deposit numbers VR2097, VR2098 and VR2099 constituted subject-matter extending beyond the original disclosure.

For the sake of completeness and in view of a possible appeal by the Applicant, the Examining Division observed further that, even if the information about the deposit numbers of the three clones had been formally acceptable

under Article 123(2) EPC, the problem of its late filing with respect to the requirements of Rule 28(2)(a) EPC would have arisen. The Examining Division was well aware of Decision J 8/87 (OJ EPO 1989, 9) which dealt with a similar problem but did not feel bound by it in the case in hand. It was more inclined to agree with a decision of another Examining Division (published in OJ EPO 1990, 156) whereby an application was refused because of late filing of the deposit number of a micro-organism.

III. The Appellants appealed against this decision and paid the corresponding fee. They further filed a written statement setting out the grounds for appeal.

IV. With a letter dated 21 August 1991 the Appellants filed a set of new Claims 1 to 7, Claims 1 and 6 of which read as follows:

"1. A uniform hepatitis A live attenuated virus composition adapted to produce a protective antibody response in higher primates, characterised in that the composition is triple cloned material of strain HM-175 (VR 2093), in that the material is of a passage level of at least 10 to 30, and in that the triple cloning is effected by terminal dilution.

6. A method for the production of a uniform hepatitis A live attenuated virus composition which comprises the step of serially diluting uncloned hepatitis A virus HM-175 (ATCC VR 2093), and inoculating each dilution into a respective mammalian cell culture, culturing the same, harvesting cloned virus particles and repeating said step at least twice more, thereby to produce a master seed lot therefrom for the formation of a vaccine composition."

In addition, an affidavit on behalf of the National Institute of Health (NIH) in the United States of America was filed.

The Appellants essentially argued that by cancelling the deposit numbers of the three clones contained in the set of claims which had been submitted to the Examining Division, the grounds for rejection of the application - i.e. non-compliance of the claims with Article 123(2) EPC - were no longer valid.

Although the deposit number now contained in Claims 1 and 6 was not filed within the 16-month period provided for in Rule 28(2)(a) EPC, this fact was not decisive in meeting the requirement of sufficient disclosure within the meaning of Article 83 EPC because the respective strain of hepatitis A virus was available to the public as required by Rule 28 EPC, this being evident from the terms of NIH policy submitted as part of the said affidavit.

V. The Board communicated its provisional opinion to the Appellants that the requirement of sufficient disclosure of the application was not fulfilled, either by the written disclosure of the application or by the terms of NIH policy. Therefore, the question of the late filing of the deposit number, now contained in Claims 1 and 6, became decisive. The Board expressed the position that it would not follow decision J 8/87 of the Legal Board of Appeal (see paragraph II above) and that under these circumstances it would be necessary to refer the question to the Enlarged Board of Appeal in accordance with Article 112 EPC.

VI. The Appellants request that the decision of the Examining Division be set aside and that either the application be forwarded to grant on the basis of the claims submitted on

23 August 1991 or that the case be returned to the Examining Division for further prosecution.

Reasons for the Decision

1. The appeal is admissible.

2. The claims on which this appeal is based no longer refer to the deposit numbers VR2097, VR2098 and VR2099, which were considered by the Examining Division to contravene Article 123(2) EPC, and therefore, the Examining Division's grounds for rejecting the claims are no longer relevant.

For the sake of completeness, the Examining Division explicitly stated in paragraph V of its decision that, had the question of the late-filed deposit number been decisive, it would have agreed with a decision of another Examining Division (see paragraph II above) and disagreed with decision J 8/87 (see paragraph II above).

It is precisely this problem which is relevant in the case of the claims which now form the basis of the appeal and which refer to a deposit number.

3. Article 83 EPC states that the invention must be disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. In cases where this requirement cannot be fulfilled by means of a written disclosure, because the invention concerns a microbiological process or the product thereof and involves the use of a micro-organism which is not available to the public, Rule 28(1) states that "the invention shall only be regarded as being disclosed as prescribed in Article 83 if:

(a) a culture of the micro-organism has been deposited with a recognised depositary institution not later than the date of filing of the application;

(b) the application as filed gives such relevant information as is available to the applicant on the characteristics of the micro-organism;

(c) the depositary institution and the file number of the culture deposit are stated in the application".

3.1 Sufficiency of disclosure by written description

3.1.1 According to the written description the invention as now claimed in Claims 1 to 6 is specified such that a cell culture adapted HM-175 human hepatitis A virus at passages 10 and 20 in primary African green monkey kidney cell culture was found to be attenuated for chimpanzees but produced sero-conversions as evidenced by induction of hepatitis A antibody without biochemical evidence of liver disease (page 2, lines 13-18, and Table 1). Master seed lots of the HM-175 strain of hepatitis A virus have been triply cloned by terminal dilution at passage levels 10, 20 and 30 (Figure 2). Two clones from passage level 20 have been evaluated for evidence of attenuation in chimpanzees. Of the two clones tested minimal or no hepatitis was produced in inoculated chimpanzees. With clone No. 1 antibody was produced in three of six animals and with clone No. 2 antibody was produced in three of four inoculated animals. The utilisation of triply cloned virus material of the HM-175 strain of hepatitis A virus illustrates that it is an effective vaccine for chimpanzees as a live HAV (page 3, lines 2-12).

The HM-175 strain of human hepatitis A virus is described in Infection and Immunity, 32 (1), April 1981, pages 388-393 (document (1)). This document is mentioned in the present application and incorporated into the description (page 3, line 35 to page 4, line 1).

3.1.2 Three examples given in the description and representing working examples for carrying out the invention relate to the cloning of the virus (Example 1), the use of master seed material (Example 2) and the inoculation of animals (Example 3).

The description does not contain any characteristics or indications where to find and/or how to create this strain of human hepatitis A virus but refers in this connection to document (1).

3.1.3 The disclosure of this document may be considered to be included in the written disclosure of the present patent application by reference (cf. T 6/84, OJ EPO 1985, 238). It describes human hepatitis A virus, propagated in primary African green monkey kidney cell cultures. Three strains of HAV were used: MS-1, SD-11 and HM-175. The HM-175 strain produced the most intense immunofluorescence and therefore this strain had been serially passaged in cell culture. This strain was obtained from an outbreak in Australia and recovered from a patient (see page 388, right-hand column under "Materials and Methods", 6th and 7th lines). It was thought to prove useful as a source of antigen for serological tests and as a candidate vaccine strain. In this scientific article the special strains MS-1, SD-11 and HM-175 were compared and the authors of the article concluded that the results suggested differences among strains in their ability to grow in vitro. The HM-175 strain, whether isolated directly or after marmoset

passage, consistently produced more viral antigen than either the MS-1 or SD-11 strains (see page 391, right-hand column, "Discussion", second paragraph).

3.1.4 This means that the use of strain HM-175 is not arbitrary but is decisive for the invention and, therefore, the skilled person, when reproducing the invention as claimed in Claims 1 to 6, needs the biological material isolated once from an hepatitis outbreak in Australia.

From these facts the Board concludes that the invention cannot be reproduced from the information given in written form.

3.2 Availability to the public of biological material

3.2.1 The Board examined the question whether or not the invention could possibly be said to have been disclosed sufficiently, as the authors of document (1) may have cultured and kept the strain in question in their laboratory and may possibly have been subject to an irrevocable obligation to supply the strain to each and every person interested in obtaining it, so that the strain HM-175 was in fact available. Strain HM-175 could then be considered as having been made available to the public by analogy with Rule 28(1) EPC.

3.2.2 The Appellants argued along these lines and filed in support of the appeal proceedings an affidavit from Mr Adler, Director of the Office of Technology Transfer, who attested that the authors of the scientific article (document (1)) were also the inventors, named in the present application. They were furthermore employees of the National Institute of Health, being in turn an agency of the Applicant, the United States of America. They were subject to NIH policy for the distribution and public availability of newly developed biological materials.

Mr Adler attested that the NIH supported and encouraged the free interchange of biological material to research workers and the general public. The written policy was delineated in the "NIH Guide for Grants and Contracts" and had been in place at least since 30 March 1984, i.e. before the date of the priority document relating to the present patent application. Accordingly, researchers in the employ of the NIH understood the written policy and routinely released biological material such as viruses. Such a policy had to have regard to patent rights. Thus, such unique biological materials generally would not be made available prior to publication of the associated research findings. However, immediately after this requirement had been met, samples would be released to research workers and the general public upon request.

3.2.3 In the Board's opinion, it would follow from this statement in particular that the biological material mentioned in document (1) was not available to the public as required by Article 83 in conjunction with Rule 28 EPC because, as is illustrated by the present patent application, patent rights had to be respected. As becomes apparent from the paper "NIH policy relating to reporting and distribution of unique biological materials produced with NIH funding", under paragraph B "NIH policy on reporting of newly developed materials", investigators are reminded that unique or novel biological materials and their products are considered to be inventions and therefore are subject to the various laws and regulations applicable to patents. Accordingly, the NIH requires that grantees and contractors adhere to grant regulations and contract clauses, respectively, pertaining to the reporting of inventions to the NIH.

3.2.4 In addition and of equal importance, nowhere is there any obligation on the NIH to ensure that the biological material necessary to carry out the invention in the present case is cultured and kept alive.

3.2.5 Finally, the Board notes that NIH policy of releasing biological material developed within NIH research programmes may be changed at any time in such a manner that the release of newly developed biological material could be restricted in any way whatsoever.

4. Availability through deposit with a recognised depositary institution

4.1 Consequently, the situation as stated in Rule 28(1) EPC exists - namely, the invention concerns a micro-biological process or the product thereof and involves the use of a micro-organism which is not available to the public and which cannot be described in the European patent application in such a manner as to enable the invention to be carried out by a person skilled in the art. In this case, according to Rule 28(1) EPC, the invention will only be regarded as being disclosed as prescribed in Article 83 if the conditions of Rule 28 (1)(a)-(c) EPC are fulfilled.

4.2 The application contains a statement (bridging page 1, lines 33-36, to page 2, lines 1-4) that the HM-175 strain of hepatitis A virus has been deposited with the American Type Culture Collection (ATCC) under the patent procedures prior to the filing of this application, thus affording permanency of the deposit and ready availability to the public upon issuance of the patent. Thus, the requirement of Rule 28(1)(a) EPC is fulfilled. Furthermore, the Board is satisfied that the application as filed gives such relevant information as was available to the Applicant on the characteristics of the micro-organism, as required by

Rule 28(1)(b) EPC. However, the deposit number as issued by the depositary for one defined deposit is not stated in the application.

The Board examined the question whether sufficiency of disclosure could have been given by reference to the "house designation" of the deposited strain, HM-175.

4.3 The Appellants filed on 20 February 1987 documents relating to the deposit of hepatitis A virus strain HM-175. According to a deposit receipt dated 5 December 1985, three sub-strains of hepatitis A virus strain HM-175 were deposited, namely clones 5, 6 and 7 under the ATCC designations VR2097, VR2098 and VR2099. According to a deposit receipt dated 16 August 1984, filed on 23 August 1991, five other hepatitis A virus strains with the "house designation" HM-175 were deposited, namely clones 1 to 4 and one uncloned strain having the deposit numbers ATCC VR2089 to VR2093.

4.4 If a skilled person had recognised that it was possible, according to the description of the originally filed application, to ask the American Type Culture Collection depositary for a hepatitis A virus strain "HM-175", the depositary would not have been able to distinguish between the eight deposited hepatitis A virus strains HM-175 merely by mentioning this "house designation".

4.5 As a Board of Appeal has already ruled in an earlier decision (T 418/89, to be published in OJ EPO) regarding sufficient disclosure in a case where the invention relates to deposited biological material, sufficiency of disclosure within the meaning of Article 83 EPC requires not only that an invention can be carried out at all, but rather that this can be done without undue burden. This is not the situation in this case. In the Board's view it amounts to undue burden to ask the depositary to supply

all the hepatitis A virus strains having the "house designation" HM-175 and then to find out which might be the one necessary to carry out the invention.

4.6 It is thus decisive for sufficiency of disclosure that the public was informed of the deposit number relating to strain HM-175, Pass. 20 uncloned - namely, number ATCC VR2093.

4.6.1 According to Rule 28(1)(c) EPC the depositary institution and the file number of the culture deposit have to be stated in the application. On page 1, line 35, the depositary - American Type Culture Collection - is in fact stated and therefore the first condition of Rule 28(1)(c) EPC is fulfilled. The deposit number, however, was not stated in the application as filed.

4.6.2 Rule 28(2) EPC allows the information referred to in paragraph (1)(c) to be submitted within a period of 16 months after the date of filing of the application or, if priority is claimed, after the priority date. As is evident from the above, in the present case the information regarding the deposit number referred to in Rule 28(1)(c) EPC was not filed until almost seven years after the priority date of the present patent application, i.e. on 23 August 1991 during the appeal proceedings.

4.6.3 In decision J 8/87 (see paragraph II above) the Legal Board of Appeal decided that as an applicant may submit the information relating to a culture deposit (Rule 28(1)(c) EPC) at any time before the end of the 16th month after the date of priority, there is only a deficiency, which he must be given an invitation to correct, when that period has expired. The Board observed an analogy with the situation in one case where certified copies of priority documents were not filed within the 16-

month period provided for in Rule 38(3) EPC, where the Legal Board of Appeal had stated that the applicant must be given an opportunity to remedy that deficiency within a further period. There is an analogy because in both cases the deficiency existed only at the expiration of the time limit. The Board considered, therefore, that a similar solution should be applied in both cases.

This Board is not inclined to follow the rationale of this decision.

4.6.4 The contextual position of Rule 28 within the EPC is such that it prescribes certain conditions which must be fulfilled in order to ensure sufficient disclosure in the case of live material and thus is subordinate to the very principle of the European Patent Convention that an invention has to be described in such a manner that it can be carried out by a skilled person. There is no scope for remedying lack of disclosure of the originally filed application, with the sole exception of the 16-month time limit given in Rule 28(2)(a) EPC. This Board, therefore, shares the view expressed in the decision under appeal. In particular the Board subscribes to the detailed reasoning of the purpose of Rule 28 and in particular Rule 28(2)(c) EPC (see decision of the Examining Division, points 7-9, cited in paragraph II above), where reference is made to the travaux préparatoires to Rule 28(2) EPC. From these documents it is evident that the time limit of 16 months given in Rule 28(2)(a) EPC was introduced to ensure and guarantee that the information about the deposit is filed before the publication of the patent application, i.e. before the public is informed, in all cases. Therefore, if an invention can only be carried out by a skilled person within the meaning of Article 83 EPC by using live material deposited with a recognised depository and only identifiable by the file number of the culture deposit,

this is a precondition for sufficiency of disclosure of a patent application which must already have been fulfilled at the date of filing of the application and not a mere formal requirement of a patent application.

4.6.5 Consequently, the Board is not inclined to follow decision J 8/87 of the Legal Board of Appeal (see paragraph II above).

Order

For these reasons, it is decided that:

The following question shall be referred to the Enlarged Board of Appeal for decision:

"May the information concerning the file number of a culture deposit according to Rule 28(1)(c) EPC be submitted after expiry of the time limit set out in Rule 28(2)(a) EPC?"

The Registrar

P. Martorana

The Chairman

P. Lançon

23.3.93

22.3.93

Beschwerdekammern des Europäischen Patentamts	Boards of Appeal of the European Patent Office	Chambres de recours de l'Office européen des brevets
Geschäftsstelle	Registry	Greffe

Als Anlage erhalten Sie den Leitsatz zur Entscheidung / -

Please find enclosed the headnote of the decision T 815 / 90 - 3. 3. 2

Veuillez trouver en annexe une copie du sommaire de la décision / -

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EPC Article 83 and Rule 28

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Headnote follows.