Print

T 2437/13 (Coronavirus/AMSTERDAM INSTITUTE) of 19.6.2019

URL

https://www.epo.org/law-practice/case-law-appeals/recent/t132437eu1.html

Location

Home > Law & practice > Boards of Appeal > Recent decisions > BoA bibliographic file

European Case Law Identifier:	ECLI:EP:BA:2019:T243713.20190619
Date of decision:	19 June 2019
Case number:	T 2437/13
Application number:	04077342.6
IPC class:	C12N 7/00 C07K 14/165 A61K 39/215 C12Q 1/68 G01N 33/569 C07K 16/10
Language of proceedings:	EN
Distribution:	D
Download and more information:	**Decision text in EN (PDF, 584 KB)** Documentation of the appeal procedure can be found in the **Register** **Bibliographic information is available in:** **EN** **Versions:** **Unpublished**
Title of application:	Coronavirus, nucleic acid, protein and methods for the generation of vaccine, medicaments and diagnostics
Applicant name:	Amsterdam Institute of Viral Genomics B.V.
Opponent name:	Pathofinder B.V.

Board:	3.3.08
Headnote:	-
Relevant legal provisions:	**European Patent Convention Art 113(1)** **European Patent Convention Art 123(2)** **European Patent Convention Art 84** **European Patent Convention Art 83** **European Patent Convention Art 53(c)** **European Patent Convention Art 87** **European Patent Convention Art 54(3)** **European Patent Convention Art 56** **European Patent Convention R 3(3)** Rules of procedure of the Boards of Appeal Art 13
Keywords:	New main request - admission into the proceedings (yes) Admission of documents D12 and D49 to D51 (no) Amendments - allowable (yes) Claims - clarity (yes) Exceptions to patentability - (no) Sufficiency of disclosure - (yes) Priority - (yes) Novelty - main request (yes) Inventive step - main request (yes)
Catchwords:	-
Cited decisions:	**T 0156/91** **T 0727/95** **T 0074/98** **T 0839/01** **T 0820/04** **T 0708/05** **T 1186/05** **T 0871/08** **T 1715/08** **T 1499/09**
Citing decisions:	-

Summary of Facts and Submissions

I. European patent No 1 526 175 is based on European patent application N° 04077342.6 (published as International patent application WO2005/017133; hereinafter "the patent application"). An opposition was filed on the grounds of Article 100(a) EPC in conjunction with Article 54 EPC, 56 EPC and 53 (c) EPC, and Article 100(b) and (c) EPC. The opposition division considered the main request to lack novelty and took the view that auxiliary request 1 (filed during oral proceedings on 12 June 2013), complied with the requirements of the EPC.

II. Both the patent proprietor and the opponent (appellant I and appellant II respectively) lodged an appeal against the decision of the opposition division to maintain the patent in amended form.

III. With its statement of grounds of appeal, appellant I filed a main request and auxiliary requests 1 and 2.

IV. With its statement of grounds of appeal, appellant II submitted arguments as to why the subject-matter of the auxiliary request 1 underlying the decision under appeal, corresponding to the auxiliary request 2 in the appeal proceedings, lacked novelty and/or an inventive step, was insufficiently disclosed within the meaning of Article 83 EPC and contravened Article 123(2) EPC.

V. Appellant I (patent proprietor) replied to appellant II's statement of grounds of appeal with a letter dated 8 July 2014 and submitted auxiliary requests 3 to 5.

VI. The parties were summoned to oral proceedings. In a communication pursuant to Article 17(1) RPBA, the parties were informed of the board's provisional, non-binding opinion on some of the legal and substantive matters of the case.

VII. In reply thereto, appellant I submitted with a letter dated 17 May 2019 further auxiliary requests 6 to 9.

VIII. Oral proceedings were held on 19 June 2019, in the absence of appellant II. At the very end of the oral proceedings, appellant I withdrew its main and auxiliary requests 1 to 5 and made its auxiliary request 6 its new main request.

IX. Independent claims 1 to 3 of the main request read as follows:

- "1. An isolated and/or recombinant nucleic acid having at least 95% sequence identity to a nucleic acid sequence as depicted in table 3 or comprising a sequence having at least 99% sequence identity to a nucleic acid sequence as depicted in figure 19.

- 2. An isolated and/or recombinant nucleic acid according to claim 1, comprising a sequence as depicted in table 3 or figure 19.

- 3. An isolated and/or recombinant proteinaceous molecule that is the ORF-2 Spike protein/S-gene sequence as depicted in figure 22; or that is selected from the group consisting of:

- the ORF 1ab replicase polyprotein sequence as depicted in figure 21;

- the 3ClPro Coronavirus polyprotein processing endoprotease sequence as depicted in figure 21;

- the RNA dependent RNA polymerase (pfam00680) sequence as depicted in figure 21;

- the ExoN 3' to 5' Exonuclease and helicase sequence as depicted in figure 21;

- the XendoU (homolog of) polyU-specific endoribonuclease sequence as depicted in figure 21;

- the 2'-O-MT 2: S-adenosylmethionine-dependent ribose 2'-orthomehyltransferase sequence as depicted in figure 21;

- the ORF-5 pfam01635, Corona_M, Coronavirus M matrix/glycoprotein sequence as depicted in figure 23; and

- the ORF Ia, replicase enzyme complex sequence as depicted in figure 20."

The further claims define embodiments of the invention, which all refer back directly or indirectly to the product of claims 1 or 3.

X. The following documents are cited in this decision:

P1 EP03077602.5 (publication date 18 August 2003);

P2 EP04075050.7 (publication date 7 January 2004)

and US60/535002 (publication date

7 January 2004);

D10 WO 2005/049814 (publication date 2 June 2005);

D11 Nucleic acid and amino acid sequence alignments

of HCoV-NL63 with EMCR-CoV disclosed in

WO 2005/049814;

D12 C.M. van der Hoek et al., Tijdschrift voor

infectieziekten, 2006, vol. 1, Nr.3, pages

108-114;

D13 C. Drosten et al., N Engl J Med, Epub

10 April 2003, vol. 348, pages 1967-1976;

D14 T.G. Ksiazek et al., N Engl J Med, Epub

10 April 2003, vol. 348, pages 1953-1966;

D15 Y. Ruan et al., The Lancet, Epub 9 May 2003,

pages 1-12;

D16 F.Y. Zeng et al., Exp Biol Med, 1 July 2003,

vol. 228, pages 866-873;

D17 P.A. Rota et al., Science, 30 May 2003,

vol. 300, pages 1394-1398;

D23 L. van der Hoek et al.,FEMS Microbiol Rev, Epub

12 June 2006, vol. 30, pages 760-773;

D41 C. B. Stephensen et al., Virus Research, 1999,

vol. 60, issue 2, pages 181-189;

D42 S. S. Chiu et al., CID, 15 June 2005, vol. 40,

pages 1721-1729;

D44 S. M. Poutanen et al., N Engl J Med, Epub

31 March 2003, vol. 348 (20), pages 1995-2005;

D49 E-mail witness of Sylvia Bruisten of the GGD

Amsterdam;

D50 English translation of the E-mail witness of

Sylvia Bruisten of the GGD;

D51 Blanco MTA of the GGD Amsterdam.

XI. The submissions made by appellant I, insofar as they are relevant to the present decision, may be summarized as follows:

Main request

Admission of the main request

The main request was filed in direct response to the board's preliminary opinion expressed in its communication dated 12 April 2019. The deletion of entire claims and of contentious embodiments constituted an attempt to overcome appellant II's objections exposed therein. The main request did not raise new considerations or new objections affecting the procedural efficiency of the proceedings. It should be admitted into the appeal proceedings.

Amendments (Article 123(2) EPC)

The expression "comprising a sequence" in claim 1 of Auxiliary request I underlying the decision under appeal was deleted. This amendment found a basis on page 22, lines 10-12 and 24-28 of the patent application.

The expression ... "has at least 95% sequence identity to a sequence as depicted in table 3 or having at least 99% sequence identity to" ... in claim 3 of Auxiliary request I underlying the decision under appeal was deleted in current claim 3.

These amendments did not raise new considerations or objections and limited the scope of protection claimed.

Article 84 EPC

In the circumstances of the present case, the references to tables and/or figures in the claims were appropriate and concise.

The clarity issue raised against the terms "a virus according to claim 6 or 7 related disease" and "a coronaviral genus related disease" found in claims 19, 20, 23, 26 and 27 of the claim request underlying the decision under appeal - corresponding to current claims 17, 22, 23 respectively - did not result from an amendment to the claims as granted. The granted claims contained already the expression "related disease". As Article 84 EPC was not a ground of opposition under Article 100 EPC and the amendment to the granted claims did not result in non-compliance with Article 84 EPC of the amended claims, these claims could not be examined for compliance with the requirements of Article 84 EPC.

It was clear from reciting a single protein with respect to each sequence in figures 21 - 23 that only one sequence is provided for the ORF 1ab replicase polyprotein, the ORF-2 Spike protein / S-gene sequence and the ORF-5pfam 01635, Corona_M, Coronavirus M matrix/glycoprotein. The reference to the specific proteins shown in figures 20 to 23 did not introduce a clarity issue.

Article 87 EPC

Document P1 disclosed the novel coronavirus comprising nucleic acid sequences and amino acid sequences as depicted in Table 3 (see page 3, line 10 to page 4 line 4) and primers that were specific for this novel virus (see page 8, line 29 to page 9, line 6 and table 7). It disclosed further how the virus could be propagated in cell culture using monkey kidney cells (see page 21, lines 1 20), how the virus could be detected using the HCoV-NL63 specific primers depicted in table 7 (see page 21, line 22 to page 22, line 6) and how the entire virus could be sequenced using the fragments disclosed in the application, i.e. the fragments of Table 3, and random primer JZH2R (see page 18, line 24 to page 19, line 2). Hence, the virus HCoV-NL63 was disclosed and enabled based on document P1.

Document P1 also disclosed nucleic acids, functional parts and equivalents thereof, which were comprising at least 80%, 90% or 95% homology to a nucleic acid of the invention or a part thereof (see page 8, lines 9-27), the use of a nucleic acid sequence as depicted in table 3, or a functional part, derivative or analogue thereof, for different purposes, for instance for detecting a molecule capable of specifically binding said virus in a sample (see page 12, lines 3-8) and for detecting and/or identifying a HCoV-NL63 coronavirus or part thereof in a sample (see page 12, lines 14-18).

Document P1 provided further a basis for the method of claim 23 on page 15, lines 4-8. It described non-limiting examples of how the NL63 virus could be detected, for example by testing its proliferation characteristics, using antibodies or other binding members, using primers and/or probes (see e.g. document P1, page 14, lines 1-25). Thus, claim 23 enjoyed priority rights from priority document P1.

Article 54(3) EPC

Document P1 disclosed nucleic acid sequences and amino acid sequences depicted in Table 3 in an enabling manner. They were derived from the HCoV-NL63 virus full length nucleic acid sequence depicted in figure 19 (see page 3, line 10 to page 4, line 2). Nucleic acid sequences at least 95% identical to a sequence depicted in table 3 were also disclosed on page 8, lines 9-11 and 23-27 of the first priority document P1. Since the filing date of the first priority application of document D10 was later than the filing date of document P1, it was not prior art for subject-matter enjoying priority rights from document P1 under Article 54(3) EPC. Nucleic acid sequences having at least 99% sequence identity to the sequence of figure 19 were not disclosed in document D10. Finally, the rounding up of the percentage of sequence identity was inacceptable in view of the decisions T 74/98 of 19 October 2000 and T 820/04 of 28 September 2006 as this would influence the true disclosure of the prior art. The rounding up of percentage values would imply in the present case an inacceptable change of the disclosure of document D10.

Article 56 EPC

No cited prior art documents disclosed a virus comprising a sequence disclosed in table 3 or figure 19 nor a virus, let alone a coronavirus, responsible for the 7 month old hospitalized child's symptoms. The use of any one of documents D13 to D17, relating to coronaviruses, as closest prior art was based on hindsight.

Even if document D13 was selected to represent the closest prior art, the skilled person would have noted that a cytopathic effect (CPE) was only seen after six days of incubation on Vero cell cultures inoculated with sputum obtained from the index patient collected on day 7 after the start of its illness (see page 1969, col.1, lines 10-14; page 1971, col.1, lines 3-6). The nasopharyngeal clinical sample of the 7 month old child of the patent was inoculated onto a variety of cells but a CPE was exclusively detected on tMK cells and noted at eight days post-inoculation. Additional subculturing on ... Vero cells remained negative for CPE (see page 33, lines 9 to 18 and page 43, lines 1-9 of the patent application). Thus a skilled person following the method of virus detection proposed in document D13 would have failed to isolate the virus infecting the 7 month old hospitalized child.

Even if document D10, published shortly after the effective filing date of granted claim 1 of the patent, applied methods comparable to the ones used in documents D13 to D17 for identifying a previously unknown EMCR-CoV virus, the skilled person had no pointer where to look for the claimed virus and had at best a hope to succeed in finding such a virus in any common cold patient sample but no reasonable expectation of success to do so.

XII. The submissions made by appellant II, insofar as they are relevant to the present decision, may be summarized as follows:

Article 84 EPC

Claims 1 to 3, 8 and 11 referred to figures and tables contrary to Rule 43(6) EPC. The references to the sequences of figures 21 to 23 in claim 3 was unclear because they referred to more than one sequence. The term "related disease" used in claims 17, 22 and 23 was unclear as a skilled person could not determine whether it covered direct and/or indirect diseases caused by the isolated virus or diseases otherwise symptomatically resembling the diseases caused by said virus.

Amended claims 17, 22 and 23 referred to a different set of proteinaceous molecules when compared to claims 20, 27 and 28 as granted. The patent as granted allowed proteins comprising proteinaceous molecules having at least 95% sequence identity to the sequences depicted in figures 20 to 23 or table 3 (see granted claim 4) while the amended claims referred directly or indirectly to the proteinaceous molecules explicitly mentioned in claim 3. Since the term "related disease" had to be reinterpreted with respect to this amended set of proteinaceous molecules, an examination as to whether the amended claims comply with the requirements of Article 84 EPC was possible. The proteinaceous molecules referred to in claims 19, 23, 26 and 27 as granted were not limited to molecules of the HCoV-NL63 virus per se, allowing the term "related disease" to be interpreted as including viral diseases caused by any type of virus as long as it symptomatically resembled the disease caused by the HCoV-NL63 virus. There was however no definition for this term in the patent. For these reasons, claims 1 to 3, 8, 11 and claims 17, 22 and 23 did not comply with the requirements of Article 84 EPC.

Article 87 EPC

The patent claimed priority rights from EP 03077602.5 (document P1), filed on 18 August 2003, and from EP 04075050.7 (document P2) and US60/535002 (document P2') both filed on the 7 January 2004.

In paragraph [0001] of document P1 it was stated that "... the invention relates to the identification of a new coronavirus and to the means and methods associated with a virus such as ...". The reference to nucleic acid or amino acid sequences in document P1 was directed to a virus, a functional part, derivative and/or analogue of said virus. However, the starting material was not deposited under Rule 31(1) EPC and the missing or yet undisclosed sequences of the virus were not directly and unambiguously derivable from the document's content. Document P1 disclosed insufficient information on how to select patients for a successful re-isolation of the virus (see paragraph [0031]). Paragraph [0003] of document P1 stated that a 7 month old child, from whom the virus was isolated, appeared in the hospital with coryza, conjunctivitis, and fever. The chest radiography showed typical features of bronchiolitis, but all these symptoms were not specific for HCoV-NL63 virus infected patients (see post-published documents D42 and D23). Moreover, patients infected with this virus were detected in winter but not in spring or summer (see paragraph [0074] of the patent). As the virus was not omnipresent, its isolation amounted to a chance event (see decisions T 156/91 of 14 January 1993 and T 727/95 of 21 May 1999). In view of decision T 839/01 of 31 March 2004, the virus and the claims directed to or including isolated and/or recombinant nucleic acid sequences and/or recombinant proteinaceous molecules comprising the sequences of table 3 were insufficiently disclosed and not entitled to priority rights from document P1. As claims 1-4, 7, 9, 11 and 16 enjoyed at best priority rights from the second priority document P2, document D10 was prior art for all of them under Article 54(3) EPC.

Claim 9 related to an isolated antibody or fragment thereof capable of specifically binding a proteinaceous molecule according to claim 3 and/or an isolated or recombinant virus according to claims 5 or 6. Antibodies against envelope proteins, for example against the first sequence of Figure 23 (ORF-4), were undoubtedly capable of recognizing the virus according to claims 5 or 6 and as such fell under the scope of claim 9. However, since the envelope protein sequence was not disclosed in document P1, claim 9 encompassed antibodies that were not entitled to priority rights from document P1.

Amended claim 23 was not limited to the method for determining whether an individual suffers from an HCoV-NL63 related disease as claim 44 of document P1 comprising detecting a HCoV-NL63 virus with specific identifying components. Neither the HCoV-NL63 virus nor the yet unknown sequences capable to achieve this detection, encompassed by the claim's wording, were sufficiently disclosed in priority document P1.

Article 54(3) EPC 1973 - Novelty

Since the subject-matter claimed did not enjoy priority rights from priority document P1, document D10 was prior art for all claims within the meaning of Article 54(3) EPC, except for claims 3 and 11.

The patent description underscored that natural variants deviating from the prototype sequence HCoV-NL63 of Figure 19 by at least 5 nucleotides were provided by the invention. They were shown to exist in Figure 16 of the patent application.

Document D10 disclosed an EMCR-CoV virus having 99% overall nucleic acid sequence identity to the HCoV-NL63 virus of the patent (see document D11). It disclosed inter alia an isolated and/or recombinant nucleic acid sequence comprising a sequence as depicted in Table 3, isolated and/or recombinant proteinaceous molecules comprising a sequence as depicted in Table 3, a nucleic acid molecule encoding said proteinaceous molecules, an isolated virus comprising said nucleic acid sequence or proteinaceous molecules, a vector comprising a nucleic acid sequence comprising a sequence as depicted in Table 3, nucleic acid sequences (primers/probes) capable to hybridize with the viral nucleic acid and comprising a sequence as depicted in Table 3, antibodies directed against the EMCR-CoV virus, and the use of EMCR-CoV virus or proteins encoded by the EMCR-CoV virus for detecting specifically binding molecules, use of primers, probes or antibodies in the detection of EMCR-CoV, being a coronavirus comprising a sequence as depicted in Table 3, a vaccine comprising the virus, proteinaceous molecules comprising the sequences depicted in Table 3 or antibodies, a medicament comprising the antibody or fragments thereof as defined above and a EMCR-CoV, essentially identical to HCoV-NL63 virus, for use against a virus according to claims 5 or 6 related disease. All claims, except claims 3 and 11, were deprived of novelty by document D10.

The percentage of sequence identity resulting from a comparison of the sequence disclosed in document D10 and the sequence of figure 19 of the patent had to be rounded up from 98,8% to 99% based on decisions T 1186/05 of 6 December 2007, T 708/05 of 14 February 2007 and T 871/08 of 8 December 2011. The 98.8% sequence identity measured for the nucleic acid sequence disclosed in document D10 satisfied the "at least 99%" identity of claim 1. The available public tools for determining sequence identity between two nucleic acid sequences generated usually a value without decimal spaces (see document D11, 3rd sentence).

Claim 23 related to a method for determining whether an individual suffers from a virus according to claim 5 or claim 6 related disease, standing for any disease whose symptoms are similar to those caused by a HCoV-NL63 virus infection, e.g. a respiratory tract disease (see [0004] of the patent). The methods disclosed in documents D13, D41 and D44 using generic coronaviral primers for detecting the presence of a coronavirus in patients' samples - capable of detecting a HCoV-NL63 virus - were novelty destroying for the method of claim 23.

Article 56 EPC - Inventive step

Any document, such as document D13, teaching how to structurally characterize a common cold virus or a virus in an isolate was considered to represent the closest prior art.

Document D13 described a standard procedure of identifying/characterizing previously unknown coronaviruses in patients with severe acute respiratory syndrome (SARS) comprising the

- Inoculation of cells (e.g. Vero cells) with patient samples containing the virus,

- RNA extraction from cell culture supernatant,

- Reverse transcription with random primers, originally designed against yellow fever virus genome and the polymerase gene of paramyxoviridae under low-stringency conditions, and

- Sequencing.

The patients of document D13 were tested for multiple types of known viruses, including the same viruses the 7 month old patient of the patent was tested for e.g. adenoviruses, rhinoviruses, HCoV-229E, HCoV- OC43, enteroviruses, etc. Since the tests failed to identify the causing viral agent, it was considered that the patients were infected with another, possibly previously unknown virus. Comparable methods for identifying SARS virus were disclosed in documents D14 to D17. The application of such standard methods for identifying unknown viruses was straightforward.

The difference between the closest prior art document D13 and the claimed invention was that the coronavirus strain was characterized by different sequences.

In view of this difference and because standard methods of identifying and characterising coronavirus existed in the prior art, any inventiveness of a virus strain had to derive from an unexpected technical effect going beyond the effects reported for the other virus family members within the viral class.

The problem underlying the present invention was to structurally characterize a further common cold virus or as formulated in the decision under appeal to provide a further coronavirus strain.

Faced with this technical problem and having at hand standard methodologies to identify and characterize coronaviruses, the skilled person had a clear motivation, in this period of SARS coronavirus outbreak, to test if the causing pathogen was a member of the coronavirus family.

The skilled person had a reasonable expectation of success to identify and isolate a further common cold virus rendering the present invention obvious. Even document D10, published shortly after the effective filing date of granted claim 1 of the patent, applied methods comparable to the ones used in documents D13 to D17 for identifying a previously unknown EMCR-CoV virus.

XIII. Appellant I (patent proprietor) requested the decision under appeal to be set aside and the patent to be maintained on the basis of the main request filed at the oral proceedings.

XIV. Appellant II (opponent) requested the decision under appeal to be set aside and the patent to be revoked in its entirety.

Reasons for the Decision

Article 113(1) EPC

1. By its decision not to attend the oral proceedings and not to file substantive arguments in reply to the issues raised in the board's communication pursuant to Article 17(1) RPBA, appellant II waived the opportunity to comment on the board's provisional opinion, either in writing or at the oral proceedings, although this opinion was to the appellant II's disadvantage. According to Article 15(3) RPBA, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying on its written case.

Admission of the main request (Article 13 RPBA)

2. According to the established case law, the function of an appeal is to give a judicial decision upon the correctness of a separate earlier decision taken by an examining or opposition division. Appeal proceedings are not an opportunity to re-run or re-open the proceedings before any of these divisions. The admission of new requests into the appeal proceedings is at the board's discretion (Articles 12(4) and 13 RPBA).

2.1 In its communication in preparation of the oral proceedings, the board, contrary to the opposition division, took the view that the main request and auxiliary requests 1 to 5 extended beyond the content of the patent application. In response to the board's communication, appellant I submitted the current main request, which is a direct attempt to overcome all the objections mentioned in the board's communication. Since the amendments consist only of deletions of contentious subject-matter, neither creating a fresh case nor affecting procedural economy, the board, availing itself of its discretionary power, decided to admit the new main request into the appeal proceedings.

Rule 3(3) EPC - Language in written proceedings

3. Document D12 is in Dutch and was filed during opposition proceedings. The Board, in its communication under Article 17(1) RPBA, requested that the document be translated into an official language if a party wished to rely on it. Since no translation of document D12 in any of the EPO official languages was supplied under Rule 3(3) EPC, the board disregards it. |

Admission of documents D49 to D51

4. With its statements of grounds of appeal, appellant II submitted documents D49 to D51.

4.1 In its communication in preparation of the oral proceedings, the board observed that the prima facie relevance of documents D49 to D51, submitted by appellant II in support of an inventive step attack, was disputed. Document D49, which corresponded to an e-mail, was considered by appellant I to be factually erroneous and document D50, corresponding to its English translation, was claimed to be in part inaccurate. Whether a material transfer agreement (MTA) of the GGD Amsterdam, as shown in document D51, was used for the coronavirus NL63 was also not confirmed.

4.2 Since appellant II did not provide evidence and arguments which established that appellant I's assessment of the relevance of these documents is incorrect, the board concludes that the content of these documents is ambiguous and therefore in the present case not relevant. Under these circumstances the board does not admit documents D49 to D51 into the appeal proceedings.

Main request

The main request is identical to auxiliary request 1 of the decision under appeal filed during oral proceedings in opposition on 12 June 2003, except that:

- claim 1 is directed to an isolated and/or recombinant nucleic acid ... [[deleted: comprising a sequence]] having at least 95% sequence identity to a nucleic acid sequence as depicted in table 3 or comprising a sequence having at least 99% sequence identity to a nucleic acid sequence as depicted in figure 19.

- claim 3 is directed to an isolated and/or recombinant proteinaceous molecule that [[deleted: has at least 95% sequence identity to a sequence as depicted in table 3 or that has at least 99% sequence identity to]] [is] the ORF-2 Spike protein/S-gene sequence as depicted in figure 22; or that is selected from the group consisting of: ...

(emphasis added).

Claims 4, 16, 20, 23 and 44 were deleted and the dependencies of the remaining claims renumbered.

Article 123(2) EPC - Amendments

5. Since the expression "has at least 95% sequence identity to a sequence as depicted in table 3 or having at least 99% sequence identity to the ORF-2 Spike protein/S-gene sequence as depicted in figure 22" ... in claim 3 of the claim request as maintained by the opposition division was deleted in current claim 3, appellant II's objection raised against this subject-matter under Article 123(2) EPC is moot.

5.1 Claim 1 is directed to a "nucleic acid having at least 95% sequence identity to a nucleic acid sequence as depicted in table 3". This embodiment finds basis on page 22, lines 10-12 of the patent application relating to a nucleic acid as depicted in Table 3, and lines 24 to 28 describing an equivalent of a nucleic acid sequence characterized as having, inter alia, at least 95% homology to a nucleic acid sequence of the invention. Claim 1 is further directed at a nucleic acid "comprising a sequence having at least 99% sequence identity to a nucleic acid sequence as depicted in figure 19". This embodiment finds basis in the paragraph bridging pages 6 and 7 of the patent application relating to variants being at least 99% homologous to the prototype HCoV-NL63 nucleic acid sequence provided in figure 19 (see page 6, line 7, of the patent application).

5.2 Since no objection under Article 123(2) EPC was raised by appellant II, neither in its statement of grounds of appeal nor in its subsequent letters, against any other claim of the claim request considered allowable in the decision under appeal, the board sees no reason to query the conclusion drawn by the opposition division in the decision under appeal.

5.3 The main request does not contravene Article 123(2) EPC.

Article 84 EPC - Clarity

6. The claims of the patent may be examined for compliance with the requirements of Article 84 EPC only when, and then only to the extent that, the amendment introduces non-compliance with Article 84 EPC (Decision G 3/14, OJ 2015, 102).

6.1 Appellant II raised a clarity objection under Article 84 EPC against claims 1 to 3, 8, and 11 in that they all referred to figures and tables. Rule 43(6) EPC stipulates that "[e]xcept where absolutely necessary, claims shall not rely on references to the description or drawings in specifying the technical features of the invention".

6.2 Amended claim 1 is directed inter alia at a nucleic acid comprising a sequence having at least 99% sequence identity to a nucleic acid as depicted in figure 19, while the corresponding granted claim 1 related to nucleic acid comprising at least 95% sequence identity to a nucleic acid as depicted in figure 19. Since the amended percentage of sequence identity from 95 to 99% does not have an impact on the clarity of the term "figure 19" itself, the reference to this figure in claim 1 is not open to an objection under Article 84 EPC in combination with Rule 43(6) EPC.

6.3 Amended claim 3 is directed to a proteinaceous molecule selected from the group of molecules depicted in figures 20 to 23, while the corresponding granted claim 4 related to a proteinaceous molecule with at least 95% sequence identity to a proteinaceous molecule comprising a sequence as depicted in figures 20 to 23 or table 3. Since neither the deletion of the at least 95% sequence identity to the proteinaceous molecules depicted in figure 20 to 23 nor the limitation to the proteins expressly recited in figure 20 to 23 have an impact on the clarity of the references themselves, the references to figures 20 to 23 are not open to objections under Article 84 EPC.

6.4 Amended claim 8 is identical to granted claim 10, except that it does not refer to table 10 and figure 18 anymore. The deletion of two references cannot introduce non-compliance with Article 84 EPC of the remaining references. Claims 2 and 11 have not been amended and can therefore also not be examined for compliance with the requirements of Article 84 EPC.

6.5 Appellant II raised a clarity objection under Article 84 EPC against the term "related disease" in claims 17, 22 and 23, because a skilled person could not determine whether this term covered direct and/or indirect diseases caused by the isolated virus or diseases otherwise symptomatically resembling the diseases caused by said virus.

6.6 The board notes that the term "related disease" in amended claims 17, 22 and 23 was present in granted claims 20, 27 and 28. The expression "coronaviral genus" in granted claim 20 was replaced by the expression "virus according to claim 7 or 8" in amended claim 17, while the back-references of granted claims 27 and 28 were renumbered in amended claims 22 and 23. Since the term "related disease" has not been modified in amended claims 17, 22 and 23, the board considers the amendment not to introduce non compliance with the requirements of Article 84 EPC. An exchange of the term "coronaviral genus" by "a virus according to claim 7 or 8" does not alter the fact that the lack of clarity arising from the term "related disease" was not introduced by this amendment.

7. Hence, the main request does not contravene Article 84 EPC.

Article 83 EPC

8. An objection based on Article 100(b) EPC was raised in opposition proceedings against granted claims 3, 17 and 33. The opposition division considered the claimed subject matter to be sufficiently disclosed (see item II.4 of the decision under appeal). Although the appellant mentioned insufficiency of disclosure as one of the reasons for filing its appeal, it did not provide any reasons in this respect. Since the burden of arguing insufficiency of disclosure rests with the appellant, who neither in its statement of grounds of appeal nor in its subsequent letters submitted any arguments, reasons and/or evidence as to why the decision under appeal was incorrect, the board considers the objections under 83 EPC not to be substantiated and sees no reason to deviate from the decision under appeal.

8.1 The main request fulfills the requirements of Article 83 EPC.

Article 53(c) EPC

9. An objection based on Article 100(a) in conjunction with Article 53(c) EPC was raised in opposition proceedings against granted claim 28. In the decision under appeal the opposition division found claim 27 (corresponding to claim 28) not to contravene Article 53(c) EPC (see item II.9). Appellant II's statement of grounds of appeal did not mention Article 53(c) EPC at all. Its reply to the proprietor's statement of grounds of appeal mentions it without however providing any arguments or reasons and/or evidence as to why the decision under appeal was erroneous. The board has therefore no reason to deviate from the conclusion in the decision under appeal.

Article 87 EPC - Priority

10. A European patent application may validly claim a right of priority from a previous first application under Article 87 EPC, if both relate to "the same invention". The concept of "the same invention" expressed in Article 87 EPC has been interpreted by the Enlarged Board of Appeal in decision G 2/98 (OJ EPO 2001, 413, point 9 of the reasons) as meaning subject-matter which the person skilled in the art can derive directly and unambiguously, using common general knowledge, from the previous application as a whole.

10.1 Appellant II contended that document P1 disclosed only fragmentary sequence information. The starting material for isolating those sequences was not made available in document P1 and the missing or yet undisclosed sequences of the virus were not directly and unambiguously derivable from it. Hence, in the light of decision T 839/01 of 31 March 2004, the virus and the claims directed to or including isolated and/or recombinant nucleic acid sequences and/or recombinant proteinaceous molecules comprising the sequences of table 3 were not sufficiently disclosed and accordingly could not enjoy priority rights from document P1. The embodiments of claims 1-4, 7, 9, 11 and 16 enjoyed at best priority rights from the second priority document P2.

10.2 Claim 1 is directed in a first embodiment to a nucleic acid having at least 95% sequence identity to a nucleic acid as depicted in table 3 and in a second embodiment to a nucleic acid sequence having at least 99% sequence identity to the nucleic acid sequence of figure 19.

10.3 The only sequences disclosed in document P1 are the sequences of Table 3. This is accepted by both parties (see point II.5 of the decision under appeal). However, document P1 describes also nucleic acids as depicted in table 3 or a functional part and/or equivalent of such a nucleic acid sequence, wherein "[A]n equivalent of the nucleic acid ... sequence of the invention or part thereof comprises at least ... 95% homology to a nucleic acid ... sequence of the invention" (see first full paragraph on page 8, lines 9 to 13 and lines 23 to 28).

10.4 In the board's view, decisions T 1499/09 and T 1715/08 clarified that ... when the degree of similarity of two nucleotide sequences is expressed quantitatively as a percentage number, "homologous" and "identical" have the same meaning, namely the ratio between the number of identical nucleotides and the total number of nucleotides (see item 7 of both decisions, T 1499/09 of 23 October 2012 and T 1715/08 of 24 October 2012). Thus, even if priority documents P1 and P2 refer to "homology" instead of "identity", both terms, when applied to nucleic acid sequences, have the same meaning.

10.5 The nucleic acid sequences depicted in Table 3 and sequences having at least 95% sequence identity can be generated by standard techniques. There is thus no need for a virus to be deposited under Rule 31(1) EPC in order to disclose the claimed subject matter in an enabling manner.

10.6 The board concludes that the first embodiment of claim 1 is directly and unambiguously disclosed in document P1.

10.7 The second embodiment of claim 1, referring to the specific nucleic acid sequence of figure 19 and sequences 99% identical thereto, however is disclosed for the first time in priority document P2 (see Figure 19). As a result, the second embodiment of claim 1 and of dependent claim 2, referring to the sequence of figure 19, are entitled to priority rights from the second priority document P2 only.

10.8 Appellant II's assessment of priority rights for the subject matter of claims 4, 7, 9, 11 and 16 relied on two arguments. First, the recited claims were not directed to an isolated virus, a functional part, derivative and/or analogue of said virus as disclosed in priority document P1, and second, the virus or starting material and isolated and/or recombinant nucleic acid sequences comprising the sequences of table 3 could not be readily obtained based on the disclosure of priority document P1.

10.9 The board considers that the isolated and/or recombinant nucleic acid having at least 95% sequence identity to a specific sequence depicted in table 3 of claim 1 enjoys priority rights from document P1, irrespective of whether the virus was deposited or its sequence disclosed in full in document P1, and the second embodiment of claim 1 referring to a sequence comprising a sequence which is at least 99% identical to the sequence of figure 19 or a nucleic acid encoding a proteinaceous molecule specifically named in figures 20 to 23 enjoys priority rights from document P2. By the same token claim 4 referring to a nucleic acid encoding a proteinaceous molecule of claim 3, or claim 7 referring to a nucleic acid according to claims 1, 2 or 4 enjoy priority rights of the respective embodiments of claims 1 to 3.

10.10 The board considers further that the subject matter of claims 9, 11 and 16 referring to an isolated or recombinant virus according to claim 5, comprising a nucleic acid sequence at least 95% identical to the nucleic acid sequence of table 3, is disclosed in the paragraph bridging pages 3 and 4 of document P1. The subject matter of claim 5 is not a viral isolate with the sequence of figure 19 but an isolated or recombinant virus comprising one of the nucleic acid sequences of table 3 or a sequence at least 95% identical thereto. Appellant II did not substantiate by verifiable facts that the skilled person using the disclosed sequences was not in a position to isolate a virus comprising such sequences. For these reasons the board does not accept appellant II's argument that claims 5, 9, 11 and 16 enjoy at best priority rights from priority document P2.

10.11 As the proteinaceous molecules of claim 3 were first disclosed in priority document P2, the subject-matter of claims 4, 7, 9, 11 and 16, as far as referring back to claim 3, also enjoys priority rights from document P2.

10.12 Appellant II contended that the method of claim 23 was not disclosed in the first priority document. The method defined in claim 44 of document P1 used specific identifying components, while the use of any means in such a method was not disclosed.

10.13 The board cannot share this view as the method of claim 23 finds a basis on page 15, lines 4-8 combined with page 14, lines 1-25 of the priority document P1. Since the virus of claim 5 is defined as comprising either a nucleic acid sequence having at least 95% identity to a sequence as depicted in table 3, enjoying priority rights from priority document P1, or to a nucleic acid comprising a sequence having at least 99% sequence identity to a nucleic acid as depicted in figure 19 or encoding a proteinaceous molecule specifically named in figures 20 to 23 enjoying priority rights from priority document P2, the method of claim 23 comprising the step of detecting a virus according to claim 5, comprising a nucleic acid sequence having at least 95% identity to a sequence as depicted in table 3, enjoys priority rights from document P1, while the method of claim 23 comprising the step of detecting a virus according to claim 5 or 6 comprising a sequence having at least 99% sequence identity to a nucleic acid as depicted in figure 19 or encoding a proteinaceous molecule specifically named in any of figures 20 to 23 enjoys priority rights from priority document P2.

Article 54(3) EPC

11. Document D10 was filed on 18 November 2004 and claims priority rights from earlier applications filed on 18 November 2003 and 1 December 2003. Thus, it constitutes prior art according to Article 54(3) EPC for subject matter not disclosed at the first priority date (18 August 2003) of the patent in suit. As concluded above, this is the case for claims 1 to 4, 7, 9, 11 and 16 as far as they refer to a nucleic acid sequence having at least 99% sequence identity to a nucleic acid as depicted in figure 19 or encoding one of the proteinaceous molecules specifically defined in any of figures 20 to 23.

12. Based on a sequence comparison submitted as document D11, appellant II argued that the EMCR-CoV virus disclosed in document D10 had 99% overall nucleic acid sequence identity to the HCoV-NL63 sequence shown in figure 19 (see document D11).

In opposition proceedings, appellant II argued, and the opposition division accepted the argument, that the 98.8% sequence identity calculated for the nucleic acid sequence disclosed in document D10 had to be "rounded up to the same number of significant places as mentioned in the claims", i.e. to 99%, "in line with decisions T 1186/05, T 708/05 and T 871/08" which related to direct comparisons of values obtained using a varying degree of accuracy (see point II.6 of the decision under appeal). Besides, publicly available tools for determining sequence identity between two nucleic acid sequences generated usually a value without decimal spaces (see document D11, 3rd sentence).

13. According to the alignment shown in document D11, 27226 nucleotides of the sequence of EMCR-CoV out of 27553 nucleotides matched the sequence set forth in figure 19 of the patent. This leads to a calculated degree of sequence identity of 98.8%.

14. The degree of sequence identity as defined in claim 1 represents the ratio (expressed in %) of identical nucleotides between a query nucleotide sequence that is pairwise aligned with a target nucleotide sequence and the total number of aligned bases. Both numbers are integers which can be counted with absolute precision. Two bases either match or don't. There is no error possible in calling two bases a match or not. The counting of matches can be repeated and leads to the exact same result every time. There is no error of measurement or estimation and no error propagation in the calculated percentage sequence identity and hence no reason for rounding up the calculated ratio when it comes to calculating the degree of sequence identity.

15. It remains to be assessed whether the nucleic acid molecule disclosed in document D10 falls under the definition of a sequence having at least 99% sequence identity.

16. The board takes the view that the definition of a nucleic acid according to claim 1 as a nucleic acid sequence comprising a sequence having at least 99% sequence identity to a nucleic acid sequence as depicted in Figure 19 includes only sequences having a percentage of identity with an integer part of percentage before the decimal separator of "99" or "100". A nucleic acid sequence displaying 98,8% sequence identity to the nucleic acid sequence depicted in figure 19 does not fall under this definition and is therefore not within the scope of claim 1.

17. The decisions mentioned by appellant II as supporting its case concern different technical areas and different facts which do not apply to the present case.

18. Moreover, if the rounding up of the percentage of sequence identity were accepted under the present circumstances, it would expand the subject matter disclosed in document D10 beyond the original content of the document. Indeed, as stated above, the sequence alignment of document D11 reveals 27226 matching nucleotides of the EMCR-CoV sequence disclosed in figure 1 of document D10. Mathematically, a rounded up value of 99% sequence identity is however not limited to 27226 matching nucleotides of the EMCR-CoV but includes sequences with (at least) up to 27278 nucleotides matching the sequence set forth in figure 19. Such sequences are not disclosed in document D10.

19. As the scope of protection of claims 5 and 6, referring back to a nucleic acid of claims 1, 2 or 4 and to a proteinaceous molecule of claim 3 is limited by their back-references and the claim's scope of protection is clear from the claim's own wording, the board sees no reason to interpret claims 5 and 6 based on the patent's description or based on post-published documents D12 or D23, as covering natural variants deviating from the prototype sequence HCoV-NL63 of Figure 19 by at least 5 nucleotides.

19.1 The main request is novel over document D10.

Article 56 EPC

20. The patent provides a virus comprising specific nucleic acid sequences isolated from a child with coryza, conjunctivitis and fever and suffering from bronchiolitis (see e.g. [0004], [0006]). The patent identifies the virus as a new member of the group 1 coronavirus most related to HCoV-229E a common cold virus (see page 4, line 19 and lines 42-44 of the patent specification).

20.1 The technical contribution of the claimed invention can be defined as the provision of a further coronavirus.

20.2 The solution to this technical problem is the virus characterized by the nucleic acid sequences depicted in Table 3 and Figure 19, or the sequences encoding the proteinaceous molecules of Figures 21 to 23 (claims 1 and 3).

20.3 Appellant II considered any document teaching how to isolate and structurally characterize a coronavirus to represent the closest prior art, for instance documents D13 to D17.

21. In the board's view, a skilled person starting from document D13, would not have arrived at the claimed virus in an obvious way.

First, the skilled person had no indication where to find a clinical specimen comprising the infectious agent responsible/causative for the 7 month old hospitalized child symptoms.

Second, the skilled person would have learned from document D13 that for respiratory and blood specimens from three patients in Frankfurt inoculated into Vero, Madin-Derby canine-kidney, and A549 cells a cytopathic effect (CPE) was observed after six days of incubation on Vero cell cultures only (see page 1969, col.1, lines 10-14; page 1971, col.1, lines 3-6).

In contrast, when the nasopharyngeal clinical sample of the 7 month old child was inoculated onto a variety of cells including human fibroblast lung (HFL) cells, tertiary monkey kidney cells (tMK; Cynomolgus) and R-HeLa cells, a cytopathic effect (CPE) was only detected on tMK cells eight days post-inoculation. A more pronounced CPE was observed upon passage onto LLC-MK2 cells. Subculturing on ... Vero cells remained however negative for CPE (see page 33, lines 9 to 18 and page 43, lines 1-9 of the patent application). As a result, even if a skilled person would have applied the methods of document D13 he would have failed to isolate the virus infecting the 7 month old child.

Document D13 further describes that RNA from cell culture supernatant of Vero cells with a CPE was reverse transcribed and randomly amplified using 15 different primer pairs under low stringency conditions. About 20 distinct DNA fragments were obtained, most of which matched human chromosome sequences (see page 1971, left column). Only two of the sequences, when translated in all possible reading frames, showed homology to coronavirus protein sequences. The board concludes from these data that even if the skilled person following the teaching of document D13 would, despite the odds, have found cells showing a cytopathic effect, it would not have had a reasonable expectation of successfully isolating a coronavirus with the structural and pathological properties of the claimed virus.

21.1 The same would have happened had the skilled person started from the teaching of any of documents D14 to D17.

22. The claims directed to viral nucleic acids, proteinaceous molecules, viruses, primers, probes, antibodies and their use involve therefore an inventive step.

23. Consequently the main request meets the requirements of Article 56 EPC.

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 39 of the main request filed at the oral proceedings and a description to be adapted.

Last updated: 07.01.2020