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Datasheet for the decision of 20 November 2012

Case Number: T 0824/08 - 3.3.08

Application Number: 96928446.2

Publication Number: 846181

IPC: C12N 15/86

Language of the proceedings: EN

Title of invention:
cDNA corresponding to the antigenome of nonsegmented negative strand RNA viruses, and process for the production of such viruses encoding additional antigenically active proteins

Patentee:
Crucell Switzerland AG

Opponents:
Akzo Nobel N.V.
MedImmune, LLC
Institut Pasteur
Conzelmann, Karl-Klaus Prof. Dr.

Headword:
Non-segmented negative strand RNA viruses/CRUCELL

Relevant legal provisions:
EPC Art. 56, 83, 84, 123(2)(3)

Keyword:
"Main request - scope of protection (extended)"
"Fifth auxiliary request - added matter (yes)"
"Sixth auxiliary request - requirements of EPC (met)"

Decisions cited:
G 0001/93, T 0371/88, T 0108/91, T 0384/91, T 0190/99, T 0340/00, T 0552/00

Catchword:
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Case Number: T 0824/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 20 November 2012

Appellant I: (Patent Proprietor)
Crucell Switzerland AG
Rehhagstraße 79
CH-3018 Bern (CH)

Representative:
Vossius & Partner
P.O. Box 86 07 67
D-81634 München (DE)

Appellant II: (Opponent 02)
MedImmune, LLC
Corporation Trust Center
1209 Orange Street
Wilmington DE 19801 (US)

Representative:
Ricker, Mathias
Wallinger Ricker Schlotter Tostmann
Patent- und Rechtsanwälte
Zweibrückenstraße 5-7
D-80331 München (DE)

Appellant III: (Opponent 03)
Institut Pasteur
25-28 rue du dr. Roux
F-75015 Paris (FR)

Representative:
Desaix, Anne
Ernest Gutmann - Yves Plasseraud S.A.S.
3, rue Auber
F-75009 Paris (FR)

Appellant IV: (Opponent 04)
Conzelmann, Karl-Klaus Prof. Dr.
Ammerseestr. 34
D-82061 Neuried (DE)

Representative:
Müller, Christian Stefan Gerd
Dr. Volker Vossius
Patent- und Rechtsanwaltskanzlei
Geibelstraße 6
D-81679 München (DE)

Party as of right:
(Opponent 01)

Akzo Nobel N.V.
Velperweg 76
NL-6824 BM Arnhem (NL)

Representative:

van Gent, Marieke
Intervet International B.V.
Wim de Korverstraat 35
NL-5831 AN Boxmeer (NL)

Decision under appeal:

Interlocutory decision of the Opposition Division of the European Patent Office posted 20 February 2008 concerning maintenance of the European patent No. 846181 in amended form.

Composition of the Board:

Chairman: M. Wieser
Members: M. R. Vega Laso
C. Heath

Summary of Facts and Submissions

I. European patent No. 0 846 181 with the title "cDNA corresponding to the antigenome of nonsegmented negative strand RNA viruses, and process for the production of such viruses encoding additional antigenically active proteins" was granted on European patent application No. 96928446.2 (published as WO 97/06270). The patent was granted with 21 claims.

II. Claim 1 of the **patent as granted** read as follows:

"1. A method for the production of an infectious non-segmented negative-strand RNA virus of the family Paramyxoviridae comprising

(a) introducing a cDNA molecule contained in a plasmid, wherein said cDNA molecule comprises the entire (+)-strand sequence of said negative-strand RNA virus operatively linked to an expression control sequence, which allows the synthesis of anti-genomic RNA transcripts bearing the authentic 3'-termini, and wherein said cDNA molecule consists of an integral multiple of six nucleotides, into a helper cell expressing an RNA-polymerase, preferably T7 RNA-polymerase, an N and a P protein, preferably of the virus to be rescued, and, further, an L protein, preferably of the virus to be rescued, encoded by a cDNA either transiently or stably introduced into said cell; and
(b) recovering the assembled infectious non-segmented negative-strand RNA virus."

Claims 2 to 21 related to particular embodiments of the method of claim 1.

III. Four oppositions were filed based on the grounds for opposition of Article 100(a), (b) and (c) EPC, in particular that the claimed subject-matter lacked novelty (Article 54 EPC) and inventive step (Article 56 EPC) and also extended beyond the content of the application as filed, and that the invention as claimed was not disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

IV. In an interlocutory decision under Articles 101(3)(a) and 106(2) EPC posted on 20 February 2008, the opposition division found that the amendments introduced into claim 1 according to the main request contravened Article 123(3) EPC, and that claim 1 according to the first auxiliary request then on file offended against Article 123(2) EPC. However, amended claims 1 to 21 according to the second auxiliary request and a description adapted thereto, and the invention to which they related were considered to fulfil the requirements of the EPC.

V. The patent proprietor (appellant I), opponent 02 (appellant II), opponent 03 (appellant III) and opponent 04 (appellant IV) each lodged an appeal against the decision of the opposition division.

VI. Appellant I submitted together with its statement of grounds of appeal seven sets of claims as main request and first to sixth auxiliary requests. The main request and the fifth and sixth auxiliary requests were

identical to, respectively, the main request and the first and second auxiliary requests underlying the decision under appeal.

VII. Together with their statements of grounds of appeal appellants II and III filed new documentary evidence.

VIII. As a subsidiary request, each of the appellants requested oral proceedings.

IX. In reply to the statements of grounds of appeal of appellants II to IV, appellant I submitted observations and new evidence.

X. Appellants II and III replied to the statement of grounds of appeal of appellant I and submitted observations on the new requests. Neither appellant IV nor opponent 01 (party as of right) submitted any comments.

XI. The parties were summoned to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons, the board drew the attention of the parties to some of the issues to be discussed during the oral proceedings, in particular issues in connection with Articles 123(2) and (3) EPC.

XII. In reply to the board's communication appellant I submitted additional observations.

XIII. Appellants II and IV and the party as of right informed the board that they would not be represented at the oral proceedings.

XIV. At the oral proceedings, which were held on 20 November 2012, only appellants I and III were represented. During the oral proceedings, appellant I withdrew the sets of claims according to its first to fourth auxiliary requests, but maintained the main request and the fifth and sixth auxiliary requests.

XV. Claim 1 according to the **main request** differs from the corresponding claim of the patent as granted (see paragraph II above) in that the wording "*... wherein said cDNA molecule consists of an integral multiple of six nucleotides ...*" in step (a) has been replaced by "*... wherein the replicon specified by said cDNA molecule consists of an integral multiple of six nucleotides ...*" (amendment has been underlined by the board).

XVI. Claim 1 according to the **fifth auxiliary request** differs from claim 1 of the patent as granted (see paragraph II above) in that it reads: "*... a helper cell expressing an RNA polymerase, preferably T7 RNA-polymerase, an N and a P protein, preferably of the virus to be rescued, wherein said proteins are expressed from stably transfected expression plasmids, and, further, an L protein ...*" (wording introduced into the claim has been underlined by the board).

XVII. Claim 1 of the **sixth auxiliary request** differs from claim 1 as granted (see paragraph II above) in that it reads: "*... and wherein said cDNA molecule consists of an integral multiple of six nucleotides, and wherein the replicon specified by said cDNA molecule consists of an integral multiple of six nucleotides, into a*

helper cell expressing an RNA-polymerase, preferably T7 RNA-polymerase, an N and a P protein, preferably of the virus to be rescued, wherein said proteins are expressed from stably transfected expression plasmids, and, further,..." (wording introduced into the claim has been underlined by the board).

XVIII. The following documents are referred to in the present decision:

(4): EP 0 702 085 A1, filed on 14 July 1995 and published 0n 20 March 1996;

(5): P. Calain and L. Roux, August 1993, Journal of Virology, Vol. 67, No. 8, pages 4822 to 4830;

(8): M. J. Schnell et al., 1994, The EMBO Journal, Vol. 13, No. 18, pages 4195 to 4203;

(10): K. Kälin et al., 1994, Ninth International Conference on Negative Strand Viruses, Abstract No. 85;

(27): WO 96/34625, filed on 1 May 1996 and published on 7 November 1996;

(29): F. Radecke et al., 1995, The EMBO Journal, Vol. 14, No. 23, pages 5773 to 5784;

(36): EMBL-EBI database, accession no. K01711, created on 13 June 1985;

(37): I. Ballart et al., 1990, The EMBO Journal, Vol. 9, No. 2, pages 379 to 384;

(39):M. S. Sidhu et al., 1995, Virology, Vol. 208, pages 800 to 807;

(47):C. Combredet et al., November 2003, Journal of Virology, Vol. 77, No. 21, pages 11546 to 11554;

(48):S. Ohno et al., 2004, Journal of General Virology, Vol. 85, pages 2991 to 2999;

(49):P. Devaux et al., 2006, Virology, Vol. xx, pages xxx-xxx (article in press);

(52):Fields Virology, Third edition, 1996, Ed. B. N. Fields et al., page 1294.

XIX. The submissions made by appellant I, orally or in writing, were essentially as follows:

Main request - Article 123(3) EPC

The amendment introduced into claim 1 by replacing the wording "*cDNA molecule*" by "*the replicon specified by said cDNA molecule*" conformed to Article 123(3) EPC. It was apparent from the patent (see, for example, paragraph [0014]) and, as regards Sendai virus, also from document (5) that the rule of six was a consequence of structural requirements of the nucleocapsid protein (NP) binding the single-stranded RNA corresponding to the viral genome. Thus, from a technical point of view there had been no doubt at the priority date that the "rule of six" was not a property of the cDNA molecule, but of the replicon, i.e. the RNA encoded by the cDNA molecule.

The rationale of decision T 108/91 (OJ EPO 1994, 228) was applicable to the present case, because the totality of the disclosure of the contested patent was unambiguous in that the "rule of six" related to the replicon and not to the cDNA molecule. Contrary to the opposition division's view, a requirement that the feature in question had to be meaningless could not be derived from either decision T 108/91 (*supra*) or decision T 371/88 (OJ EPO 1992, 157). Moreover, the opposition division had been wrong in finding that there was no contradiction between the feature in question and the remainder of the disclosure in the patent. As a matter of fact, there was an inconsistency between the claim and the totality of the disclosure of the patent: cDNA molecules which met the "rule of six" were not suitable in those cases where the replicon at the same time did not have a length of 6n, i.e. statistically in five out of six cases. The fact that cDNA molecules having a length of 6n and comprising a replicon of 6n provided workable embodiments was not prejudicial.

Fifth auxiliary request - Article 123(2) EPC

With regard to the feature "*wherein said cDNA consists of an integral multiple of six nucleotides*", which was included also in the claims of the patent as granted, amended claim 1 was not in breach of Article 123(2) EPC. The skilled person read this feature as referring to the replicon specified by the cDNA. As stated in decisions T 190/99 of 6 March 2001, T 340/00 of 9 February 2005 and T 552/00 of 30 October 2003, the claims must be interpreted with synthetic propensity,

i.e. building up, rather than tearing down, to arrive at an interpretation of the claims which is technically sensible and takes into account the whole disclosure of the patent.

Sixth auxiliary request

Article 123(2) and (3) EPC

The amendments introduced into the claims of the sixth auxiliary request did not offend against Article 123(2) and (3) EPC. The rulings of decision G 1/93 (OJ EPO 1994, 541) were applicable to the present case. As the opposition division correctly stated, the feature that the cDNA had to obey a "rule of six" could be viewed as a feature that merely excluded protection for a significant part of the invention, and therefore did not provide any advantage to the patent proprietor. The "rule of six" applied to the family *Paramyxoviridae* had a specific basis in the passage on page 7, end of the first paragraph of the application as filed read in the context of the application as a whole. There was no doubt that the wording "*said proteins*" referred also to the T7 RNA polymerase. This was clear from the passage on page 12, second full paragraph of the application as filed.

Article 83 EPC - Sufficiency of disclosure

The general teaching provided in the patent sufficed to enable the skilled person to practice the invention as claimed. The genetic material required for the preparation of the cDNA had been publicly available at the priority date. For example, cDNA could have been

constructed by reverse transcription of measles vaccine strains available from a number of manufacturers. The skilled person did not encounter any difficulties in interpreting the disclosure content of either Example 3 of the patent or document (39), to which the example referred.

Article 56 EPC - Inventive step

It had not been credibly argued that the method described in document (10) did not require a helper virus. This document provided no suggestion whatsoever of a helper cell expressing four specific proteins, namely the RNA polymerase as well as N, P and L proteins. Moreover, document (10) was not amenable to combination with document (8) which used the Vaccinia virus system and did not provide any incentive to deviate from this well-established system.

XX. The submissions made by appellant II in writing may be summarized as follows:

Main request - Article 123(3) EPC

The amendments introduced into claim 1 "shifted" the scope of protection and contravened Article 123(3) EPC. While claim 1 of the patent as granted required that the cDNA molecule consisted of an integral multiple of six nucleotides, amended claim 1 specified that the number of nucleotides of the replicon was a integral multiple of six. Hence, the additional sequences included in the cDNA molecule could be of variable length. As a consequence, the amended claim encompassed embodiments which were not encompassed by claim 1 of

the patent as granted, namely embodiments where the replicon consisted of a multiple of six nucleotides but the cDNA molecule did not.

Fifth auxiliary request - Article 123(2) EPC

The feature "*said cDNA molecule consists of an integral multiple of six nucleotides*" in claim 1 was neither technically nor formally supported by the application as filed. The feature could not be construed as being "incorrect" or "contradicting the general disclosure of the patent" as in decision T 108/91 (*supra*), because a cDNA that consisted of an integral multiple of six nucleotides could or could not include a replicon that complied with the "rule of six". Thus, Article 123(2) EPC was contravened.

Sixth auxiliary request

Article 123(2) and (3) EPC

The rationale of decision G 1/93 (*supra*) was not applicable to the present case because the underlying situation was distinctively different from the situation outlined in the decision of the Enlarged Board of Appeal. In the present case, the cDNA included - besides the replicon - further sequences which were responsible for the generation of precise 3' ends. Thus, requiring that these additional sequences were a multiple of six represented a technical contribution to the subject-matter of claim 1. Contrary to the opposition division's view, the question whether or not the technical contribution had anything to do with the solution of the technical

problem was not the correct legal standard. By retaining the limitation the proprietor gained an unwarranted advantage because the feature in question placed the claimed subject-matter farther away from the prior art and possibly improved the chances of the proprietor in later proceedings, such as national nullity proceedings.

Article 83 EPC - Sufficiency of disclosure

The working example provided in the patent did not fall under the scope of amended claim 1 because the number of nucleotides of the additional sequences included in the cDNA (i.e. the T7 RNA polymerase terminator and the genomic hepatitis virus ribozyme sequence) was not a multiple of six. These additional sequences were well-defined functional nucleotide sequences whose length could have a significant impact on their function. However, the patent did not teach how to modify the sequences such that their combined nucleotide length was a multiple of six.

Article 56 EPC - Inventive step

The subject-matter of claim 1 was not inventive over document (8). According to this document the virus was rescued by expressing the T7 RNA polymerase and the N, P and L proteins from cDNAs. The "rule of six" requirement in claim 1 was common general knowledge at the time.

XXI. The submissions made by appellant III, orally or in writing, were essentially as follows:

Main request - Article 123(3) EPC

The scope of amended claim 1 went beyond the scope of the patent as granted. Decision G 1/93 (*supra*) did not allow a feature that contravened Article 123(2) EPC to be replaced by a different feature, if the amendment resulted in an offence against Article 123(3) EPC. The rationale of decision T 108/91 (*supra*) was not applicable to the present case because there was no contradiction between the objected feature and the disclosure of the application as a whole. It could not be derived from the application as filed that the "rule of six" applied only to the replicon.

Fifth auxiliary request - Article 123(2) EPC

There was no basis in the application as filed for the feature "*said cDNA molecule consists of an integral multiple of six nucleotides*". Thus, the amendment introduced into claim 1 contravened Article 123(2) EPC.

Sixth auxiliary request

Articles 123(2)(3) and 84 EPC

Contrary to the opposition division's findings, in the present case the requirements established in decision G 1/93 (*supra*) were not fulfilled. While the concept of technical contribution had not been discussed in detail in the decision of the Enlarged Board of Appeal, it was stated in decision T 384/91 of 27 September 1994 that "*... a feature at least then goes beyond providing a mere limitation which does not involve a technical contribution to the invention if it interacts with the*

way in which the other features of the claim solve the technical problem as it is understood from the application as originally filed" (see paragraph 5 of the Reasons). This applied to the contested feature in claim 1. This claim required that two different sequences followed the "rule of six": the cDNA sequence and the specified replicon. Consequently, also the further sequences included in the cDNA - besides the replicon - had to follow the rule of six. This had an influence on the technical solution provided in claim 1 because it limited the choice of sequences to those consisting of an integral multiple of six nucleotides. Thus, the contested feature provided a technical contribution to the claimed subject-matter. Moreover, the combination of the two features concerning, respectively, the cDNA and the replicon was not disclosed in the application as filed.

The rule of six was disclosed in the application as filed only in connection with measles virus. The passage on page 7 on which the opposition division relied, did not allow a generalisation to other members of the family *Paramyxoviridae*. Moreover, since some members of this family did not follow the "rule of six" (e.g. the respiratory syncytial virus), the scope of protection conferred by claim 1 was not clearly defined.

Article 83 EPC - Sufficiency of disclosure

The genetic material required for the preparation of the cDNA specified in claim 1 was not sufficiently disclosed in the application as filed, and a reference to a deposit of biological material under the Budapest Treaty was not provided. In the decision under appeal

(see pages 12 and 13), the opposition division had admitted that Example 3 of the application ("Plasmid constructions") could not be reproduced. In this example, reference was made to documents (39) and (37), and in the latter, document (36) was cited as the source for the RNA required for the preparation of the viral genome. However, the reference to document (36) in document (37) did not reliably identify the required sequence because the version number or the release number of the EMBL database was not given. As reported in document (49), the Edmonton strain used in the experiments of document (37) was incompletely documented and included segments from other strains (see document (52)). Moreover, while it was stated in the application as filed (see legend of Figure 2) that the measles virus sequence used therein differed from the sequence of document (36) in 30 nucleotide positions, neither the specific changes nor their effects were disclosed. Under these circumstances, the skilled person was not able to obtain the genetic material required for carrying out the invention claimed in claims 1 and 16.

The cDNA molecule specified in claim 1 had to include sequences for controlling the expression of the replicon. However, the sole promoter described in the application as filed was the promoter of the T7 polymerase, the sequence of which did not consist of an integral multiple of six nucleotides. There was neither a teaching in the application how to prepare a cDNA molecule following the "rule of six" nor a disclosure of a RNA polymerase which worked with such a construct. It should be noted also that the application as filed disclosed only sequences for preparing cDNA of

measles virus; however, claim 1 encompassed methods for preparing other virus of the family *Paramyxoviridae*, for which no technical information whatsoever was provided.

The lack of sufficient disclosure in the application could not be remedied by the post-published documents cited by the proprietor reporting successful preparation of recombinant measles virus. The genetic material used in the reported experiments had been provided by the inventors of the present patent und was not necessarily the same as described in the application. Moreover, while claim 1 required a cDNA which was suitable for the preparation of a virus of the family *Paramyxoviridae* that could be used as a vaccine, documents(47) and (48) showed that such use was not possible because, when administered to a host, the viruses were eliminated.

Article 56 EPC - Inventive step

When it considered document (8) as the closest prior art, the opposition division disregarded the fact that this document concerned a different family of viruses, namely the *Rhabdoviridae*. Since it had not been shown in the patent that, for a virus of the family *Paramyxoviridae*, a cDNA could be prepared and used for obtaining infectious particles, the claims did not reflect the actual technical contribution provided by the patent in suit and, for the same reasons as set out in connection with Article 83 EPC, the subject-matter of the claims did not solve the technical problem.

Moreover, the claimed subject-matter did not involve an inventive step. Document (5) described the "rule of six" for Sendai virus, a virus of the family *Paramyxoviridae*. As concerns the RNA polymerase, it was stated in document (10) that the enzyme could be either provided by a virus or be produced constitutively by the cell. The fact that in this document a minireplicon was used for producing the virus, was immaterial. Thus, the subject-matter of claim 1 was obvious in view of a combination of documents (8) and (10).

XXII. The submissions made by appellant IV in writing may be summarized as follows:

Sixth auxiliary request

Article 123(2) and (3) EPC

There was no basis in the application as filed for a generalization of the "rule of six" to apply to all members of the family *Paramyxoviridae*. Moreover, the feature "*said cDNA molecule consists of an integral multiple of six nucleotides*" was a technical part of the claimed method and, therefore, the requirement established in decision G 1/93 (supra) for allowing an undisclosed feature in a claim was not fulfilled.

Contrary to the opposition division's view, amended claim 1 encompassed an embodiment in which the RNA polymerase is not expressed from stably transfected expression plasmids, because the reference "*said proteins*" did not unambiguously include the RNA polymerase. Thus, the amendments introduced into claim 1 did not conform to Article 123(2) EPC.

Article 56 EPC - Inventive step

Document (8), which described a method for the generation and manipulation of non-segmented negative strand RNA viruses, was regarded as the closest state of the art. Starting from this document, the problem to be solved was providing a method for rescuing another non-segmented negative strand RNA virus, in particular a virus of the family *Paramyxoviridae*. However, document (8) suggested already that the method described therein for rescuing rabies virus was applicable to other non-segmented negative strand RNA viruses. Moreover, the applicability of the "rule of six" to viruses of the family *Paramyxoviridae* was described in documents (5) and (10) and was part of the common general knowledge at the relevant date. Stable expression of the N and P proteins in the helper cell was an obvious alternative to the transient expression described in document (8) and could not justify an inventive step. If the wording "*said proteins*" had applied also to the RNA polymerase, which was denied, a system stably expressing this enzyme would have been known from document (10). A person skilled in the art, having in mind the drawbacks of the vaccinia virus system, would have replaced the system used in document (8) by a helper cell stably transfected with an expression plasmid encoding an RNA polymerase as described in document (10). Consequently, the combination of document (8) with common general knowledge and document (10) rendered the subject-matter of claim 1 obvious within the meaning of Article 56 EPC. Contrary to the opposition division's view, this combination was not precluded by the fact that the

problem underlying documents (8) and (10) was different, because the skilled person would consider documents in the same or in a closely related technical field. The additional features of dependent claims 2 to 21 were obvious modifications which could not justify acknowledging an inventive step.

XXIII. Appellant I (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or on the basis of the fifth auxiliary request, both filed with the grounds of appeal, or that the appeals be dismissed.

XXIV. Appellants II to IV (opponents 02 to 04) requested, either orally or in writing, that the decision under appeal be set aside and that the patent be revoked.

XXV. The party as of right (opponent 01) did not put forward any request.

Reasons for the Decision

Main request - Article 123(3) EPC

1. The present main request is identical to the main request underlying the decision under appeal. In the decision, the opposition division found that the amendment introduced into claim 1 of this request to replace the wording "*said cDNA molecule consists of an integral multiple of six nucleotides*" by "*the replicon specified by said cDNA molecule consists of an integral*

multiple of six nucleotides" (emphasis added by the board) contravened Article 123(3) EPC.

2. According to decision G 1/93 of the Enlarged Board of Appeal (OJ EPO 1994, 541), where a patent as granted cannot be amended by deleting limiting subject-matter which extends beyond the content of the application as filed within the meaning of Article 123(2) EPC because this would contravene Article 123(3) EPC, such a patent can be maintained "*... if there is a basis in the application as filed for replacing such subject-matter* ***without violating Article 123(3) EPC***" (see Headnote, paragraph 1; emphasis added by the board).

3. In the present case, the amendment in question represents an attempt to overcome an objection under Article 100(c) EPC raised by the opponents with regard to the feature "*said cDNA molecule consists of ...*" in claim 1 of the patent as granted. Since the objected feature cannot be deleted without offending against Article 123(2) EPC, appellant I seeks to replace it by the feature "*the replicon specified by said cDNA molecule ...*", which is undisputedly disclosed in, e.g., the passage on page 7, first paragraph of the application as filed.

4. However, the board considers that, by introducing this amendment into claim 1, the scope of protection conferred by the claim has been extended beyond the scope of protection of the patent as granted, contrary to Article 123(3) EPC. As a matter of fact, the amendment shifts the scope of claim 1, since the amended claim now encompasses methods in which the replicon specified by the cDNA molecule consists of an

integral multiple of six nucleotides, while the number of nucleotides of the cDNA molecule introduced into the helper cell is - other than in claim 1 of the patent as granted - not limited in any way.

5. Contrary to appellant I's view, the rationale of decision T 108/91 (*supra*) is not applicable to the present case. According to this decision, the replacement of an inaccurate technical statement that is in contradiction to the remainder of the patent by an accurate statement of the technical features involved, does not offend against Article 123(3) EPC. In the board's view, there is no contradiction between the feature in claim 1 requiring that the cDNA molecule consists of an integral multiple of six nucleotides, and the statement in the description of the invention that the replicon specified by the cDNA molecule must consist of an integral multiple of six nucleotides. These two requirements are neither incompatible nor exclude each other. Thus, since the circumstances of the present case are different from those in decision T 108/91 (*supra*), the rationale of the cited decision cannot apply.

6. Moreover, appellant I's view that the rationale of decision T 371/88 (*supra*) may be applied to the present case, is not shared by the board. The circumstances under which the competent board in decision T 371/88 (*supra*) allowed a claim to be amended in spite of the scope being broadened (see point 2.5 of the cited decision) are different from those in the present case. In particular, other than in the cited decision the limiting feature in present claim 1 ("*the cDNA molecule consists of an integral multiple of six nucleotides*")

is clear in itself and does not pose any problems when determining the extent of protection conferred by the claim.

7. In sum, the board concludes that the amendments introduced into claim 1 do not conform to Article 123(3) EPC. Consequently, the main request cannot be allowed. In view of this decision, the board does not deem it necessary to decide on further objections raised by the respondents in respect of the main request.

Fifth auxiliary request - Article 123(2) EPC

8. The set of claims according to the fifth auxiliary request was filed together with the statement of grounds of appeal. Claim 1 includes the feature "*... wherein said cDNA molecule consists of an integral multiple of six nucleotides*" which was present also in claim 1 of the patent as granted and was objected by the opponents under Article 100(c) EPC.

9. Even though this specific request was not dealt with in the decision under appeal, it is apparent from the decision (see page 4, lines 6 to 9 from the bottom) that the opposition division considered the objected feature to lack a basis in the application as filed. The board shares the opposition division's view that a method caracterised by the feature in question is not disclosed, either explicitly or implicitly, in the original application.

10. Even though appellant I admitted indirectly the lack of basis in the application as filed when defending its

sixth auxiliary request in appeal proceedings (see below), in connection with the fifth auxiliary request it argued that a person skilled in the art would read the feature in question as referring to the replicon specified by the cDNA molecule, rather than to the cDNA molecule itself. In support of its line of argument, appellant I relied on a number of decisions (see paragraph XIX above) in which the competent boards established that a person skilled in the art, when considering a claim, should rule out interpretations that are illogical or do not make technical sense.

11. In the view of this board, the principle of a "mind willing to understand" established by the boards of appeal can only be applied when the wording of a claim is open to different interpretations, some of which may be technically illogical and are therefore not considered by the skilled person. In the present case, the wording "*... wherein said cDNA molecule consists of an integral multiple of six nucleotides*" is clear in itself and, from the technical point of view, there is no contradiction with the further features of claim 1. Thus, a skilled person with "a mind willing to understand" has no reason to interpret the feature in question other than literally, this interpretation being neither illogical nor evidently wrong from a technical point of view.

12. In the absence of a basis for the subject-matter of claim 1 in the application as filed, in particular with regard to the feature "*... wherein said cDNA molecule consists of an integral multiple of six nucleotides*", Article 123(2) EPC is contravened. Thus, the fifth

auxiliary request cannot serve as basis for the maintenance of the patent in suit.

Sixth auxiliary request

Rule 80 EPC

13. The amendments introduced into the claims according to the sixth auxiliary request, which are identical to those of the second auxiliary request underlying the decision under appeal, are aimed to overcome objections under Article 100(c) EPC raised by the opponents. The board is satisfied that the requirement of Rule 80 EPC is met.

Articles 123(2)(3) and 84 EPC

14. In the decision under appeal, the opposition division considered that, for the same reasons given in connection with the first auxiliary request (see the paragraph bridging pages 4 and 5 of the decision under appeal), the amendments introduced into claim 1 did not contravene Article 123(2)(3) EPC. The opposition division took the view that the amended claims fulfilled the requirements set out in decision G 1/93 (*supra*; see headnote 2 and point 16 of the Reasons) for avoiding a conflict between Article 123(2) and Article 123(3) EPC. In particular, the opposition division held that the limiting feature "*... wherein said cDNA molecule consists of an integral multiple of six nucleotides*", which had not been disclosed in the application as filed but had been added to the application during examination, merely limited the protection conferred by the patent as granted, without

providing a technical contribution to the subject-matter of the claimed invention.

15. Appellants II and III contested this finding arguing that the feature in question made indeed a technical contribution because it interacted with the way the other features of the claim solved the technical problem, and also provided the patent proprietor with an unwarranted advantage.

16. The board disagrees with this view. The undisclosed limitation that the cDNA molecule must consist of an integral multiple of six nucleotides does not necessarily limit the choice of each of further sequences included in the molecule – besides the replicon – to those consisting of an integral multiple of six nucleotides. The sole limitation which arises from the feature in question is that the total number of nucleotides of the further sequences must be a multiple of six. Even if the number of nucleotides of some elements of the cDNA might be subject to certain constraints for the elements to remain functional, this does not exclude the use of these particular elements because the number of nucleotides of other elements which are less "size-constrained" can be adjusted so that the total number of nucleotides of the further sequences meets the "rule of six".

17. Appellants II to IV have not provided a single specific example supporting their argument that a limited choice of a certain element of the cDNA molecule would provide a technical contribution to the claimed subject-matter. Nor have they provided any evidence for an unwarranted specific advantage that the patent proprietor could

gain from the contested feature, other than the vague and theoretical possibility of better chances in national nullity proceedings.

18. When arguing that there is no basis for a combination of cDNA and replicon following the "rule of six" in the application as filed, appellant III seems to overlook that in the situation underlying the present case, if the feature of claim 1 specifying that the cDNA follows the "rule of six" lacks a basis in the application, it cannot be required that the combination of both features does have such a basis.

19. Appellants III and IV objected to the opposition division's findings that the generalisation to a method for the production of an infectious non-segmented negative-strand RNA virus of the family *Paramyxoviridae* had a basis in the first paragraph on page 7 of the application as filed (see page 5, second full paragraph of the decision under appeal). The objection is, however, not justified. The passage indicated by the opposition division ("*The cDNA molecules of the present invention can conveniently be used for the rescue of negative strand RNA viruses of the family Paramyxoviridae*") provides a clear basis for the rescue of RNA viruses of the family *Paramyxoviridae* other than the exemplified measles virus.

20. The board shares the opposition division's views on further issues under Article 123(2) EPC raised in opposition proceedings (see page 5, second paragraph and the paragraph bridging pages 6 and 7 of the decision under appeal). These findings have not been contested in appeal proceedings.

21. As regards Article 84 EPC, the board considers that the fact that some viruses of the family *Paramyxoviridae* may not follow the rule of six does not mean that claim 1 is unclear and that the claimed method cannot be used for producing these viruses. It means only that the claim includes a limiting feature which, as concerns these viruses, is possibly technically unnecessary, but nevertheless clearly delimits the scope of protection conferred by the claim.

22. The board cannot accept appellant IV's argument that the wording "*said proteins*" in amended claim 1 does not include the RNA polymerase, and that, consequently, the scope of protection conferred by the claim has been extended beyond the scope of the patent as granted. Like the opposition division, the board is unable to see any ambiguity in the objected wording. "*Said proteins*" refers clearly to the three proteins mentioned immediately before, i.e. the RNA polymerase, the N and the P protein. Support is found in the passage on page 12, second full paragraph of the application as filed.

23. Summarising the above, the board is convinced that none of the objections raised by appellants II to IV against the findings of the opposition division on Articles 123(2)(3) and 84 EPC is justified.

Article 83 EPC - Sufficiency of disclosure

24. In the decision under appeal, the opposition division found that the claimed invention was disclosed in the application as filed in a manner sufficiently clear and

complete for it to be carried out by a person skilled in the art. In appeal proceedings, appellants II and III contested the opposition division's findings arguing essentially along two lines.

25. In a first line of argument, appellant III maintained that Example 3 could not be reproduced because the genetic material, in particular the source of RNA required for preparing the cDNA was not sufficiently disclosed in the application as filed. Appellant III relied on different documents allegedly showing that a person skilled in the art could not identify the specific genetic material used in Example 3, which is a measles virus derived from the measles virus vaccine strain Edmonston B (see paragraph XXI above).

26. This line of argument fails to convince the board. Article 83 EPC does not require that the examples disclosed in a patent application be reproducible in each detail, but that the technical information provided in the application supplemented with the common general knowledge at the relevant date puts the skilled person in the position to carry out the invention without undue burden of experimentation.

27. The board shares the opposition division's view that, whether or not the specific strain used in the example was readily available and fully characterized at the priority date, and whether or not it had been deposited is immaterial, if the skilled person seeking to carry out the claimed invention had suitable alternative measles virus strains as genetic material to start with. It is undisputed that at the priority date several measles virus vaccine strains were available. And as it

is apparent from e.g. post-published document (47), by applying the method of the invention it is possible to clone and rescue infectious virus from infectious cDNA corresponding to the antigenome of the Schwarz/Moraten strain of measles virus, a widely used measles virus vaccine, or the EdB tag measles virus, a derivative of the Edmonston B vaccine strain, which were both publicly available at the priority date. The low immunogenicity of the latter vaccine in humans is, contrary to appellant III's view, irrelevant to the question whether or not infectious virus of this strain can be obtained from cDNA using the method of the invention.

28. In a second line of argument, it was argued that the working example in the application did not exemplify a method according to present claim 1 because the additional sequences included in the cDNA of Example 3 did not consist of a multiple of six nucleotides, and that, seeking to carry out the method as claimed, the skilled person would not find in the application as filed any information as to how to modify the sequences such that their combined nucleotide length was a multiple of six.

29. In fact, the application does not describe how to modify the additional sequences to otain a number of nucleotides which is a multiple of six. However, the board has no doubt that such modification lies within the normal capabilities of a person skilled in the art, who would be able to find suitable sequences without undue burden of experimentation or applying inventive skills. The same applies to the preparation of

infectious virus of the family *Paramyxoviridae* other than measles virus.

30. Thus, having considered the arguments and evidence put forward by the parties in appeal proceedings, the board concludes that the requirements of Article 83 EPC are fulfilled.

Article 54 EPC - Novelty

31. In the decision under appeal, the opposition division found that, with regard to documents (4) and (27), the claimed subject-matter was novel, and that the content of document (29) did not form part of the state of the art because the priority claimed for the claimed invention was valid (see passage under the heading "Novelty" starting on the bottom of page 7 of the decision under appeal). These findings have not been questioned in appeal proceedings and the board sees no reason to question them of its own motion. Thus, the requirement of Article 54 EPC is regarded as fulfilled.

Article 56 EPC - Inventive step

32. In the decision under appeal, the opposition division regarded document (8) as the closest state of the art. In appeal proceedings all parties agreed with this view. So does the board.

33. Document (8) describes the generation of infectious rabies virus, a non-segmented negative-stranded RNA virus of the *Rhabdoviridae* family, from cloned cDNA by simultaneously expressing in a cell full-length rabies virus antigenome transcripts, and rabies virus N, P and

L proteins expressed from transfected plasmids (see Abstract). The transcripts were generated by T7 RNA polymerase expressed from recombinant vaccinia virus (see page 4196, sentence bridging the left and right-hand columns). It is suggested in document (8) that the method described therein is "*potentially applicable also for other negative-stranded viruses*" (see last sentence of the abstract).

34. Starting from this document, the problem to be solved can be defined as the provision of a method for the production of another non-segmented negative strand RNA virus.

35. As a solution to this problem, the present patent proposes a method according to claim 1, which differs from the method described in document (8) not only in that an infectious virus of the family *Paramyxoviridae* is produced, but also in that the cDNA molecule and the replicon specified by the cDNA consist of an integral multiple of six nucleotides, and that the RNA polymerase is not expressed from recombinant vaccinia virus, but from a stably transfected expression plasmid. In view of the examples in the application and the post-published experimental evidence put forward by appellant I, the board is convinced that the claimed method in fact solves the problem formulated above.

36. The question to be decided is whether or not this solution was obvious to a person skilled in the art. Appellants II to IV argued that the method of claim 1 was an obvious combination of the method of document (8) with the teaching in document (10). The latter document, a short abstract sent to a scientific conference by,

inter alia, some of the inventors of the present patent, concerns artificial measles virus mini- and midi-replicons which contain either CAT or luciferase reporter genes and obey the "rule of six". The longest functional midireplicon contained intact N and P genes followed by a CAT gene and an internally deleted L gene, totalling 5418 nucleotides, about one third of the measles virus genome. It is stated in the abstract that the RNAs were usually synthesized *in vitro*, but that they could also be generated intracellularly by plasmid transfection either of cells infected with vaccinia virus expressing phage T7 RNA polymerase or cells constitutively producing the phage polymerase.

37. Like the opposition division, the board is unable to discern from either document (8) or document (10) an incentive to replace the vaccinia system used in the method of document (8) for a stably transfected plasmid expressing the RNA polymerase. The board is convinced that, if a skilled person, following the suggestion in document (8), had tried to apply the method described therein to other negative-stranded viruses, he/she would not have modified the described method, unless the method turned out not to work for a particular virus. The skilled person might have realized that, if the replicon did not follow the "rule of six", the method of document (8) would not work for, e.g., measles virus. Thus, he/she might have considered modifying the number of nucleotides of the replicon accordingly. However, there is no evidence on file that, by using the vaccinia virus system as described in document (8), the skilled person would not have been able to produce an infectious virus of the family P*aramyxoviridae*.

38. In the light of the content of either document (8) or document (10), the skilled person could not envisage any advantages from the substitution of the vaccinia virus system. While document (10) mentions three different ways of generating the viral RNA, namely by *in vitro* synthesis - which is the approach the authors of document (10) followed -, by using of the vaccinia virus system to express the T7 RNA polymerase - which is the approach in document (8) -, or by constitutive expression by the cell, there is in this document, however, no indication of any advantages of the latter approach that would have motivated the skilled person to depart from the teaching of document (8). The board is, therefore, persuaded that modifying the method of document (8) to replace the expression of the T7 RNA polymerase from recombinant vaccinia virus by the expression from a stable transfected expression plasmid can only be considered to be obvious from the knowledge of the invention.

39. The board thus concludes that the method of claim 1 and its different embodiments according to the dependent claims involve an inventive step within the meaning of Article 56 EPC.

Conclusion

40. Having considered the arguments put forward by the parties in appeal proceedings, the board sees no reason to set aside the decision under appeal.

Order

For these reasons it is decided that:

The appeals are dismissed.

The Registrar: The Chairman:

A. Wolinski M. Wieser