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**Datasheet for the decision  
of 5 April 2022**

**Case Number:** T 2486/18 - 3.3.08

**Application Number:** 09013546.8

**Publication Number:** 2143803

**IPC:** C12P19/34

**Language of the proceedings:** EN

**Title of invention:**

Improved compositions and methods for cDNA synthesis

**Patent Proprietor:**

QIAGEN Beverly, Inc.

**Opponent:**

Leeming, John Gerard

**Headword:**

Storable reagent mixture reverse transcription/QIAGEN

**Relevant legal provisions:**

EPC Art. 76(1), 84, 123(2)

RPBA Art. 12(4)

**Keyword:**

Main request and auxiliary requests 1, 3 to 9, 11 and 13 -  
added subject-matter (yes);

Auxiliary request 2 - admission (no);

Auxiliary requests 6, 7 and 10 to 13 - clarity (no);

New documentary evidence - admission (no);

**Decisions cited:**

R 0011/11, T 0144/09, T 1866/16

**Catchword:**



**Beschwerdekammern**

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Case Number: T 2486/18 - 3.3.08

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.08**  
**of 5 April 2022**

**Appellant:**

(Patent Proprietor)

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**Representative:**

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**Respondent:**

(Opponent)

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**Representative:**

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**Decision under appeal:**

**Decision of the Opposition Division of the  
European Patent Office posted on 24 July 2018  
revoking European patent No. 2143803 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman**

B. Stolz

**Members:**

P. Julià

D. Rogers

## **Summary of Facts and Submissions**

- I. European patent no. 2 143 803 is based on European patent application no. 09 013 546.8 (hereinafter "the patent application"), a divisional application of European patent application no. 03 749 359.0 (published as EP 1 534 850) originally filed under the PCT and published as WO 2004/021986 (hereinafter "the earlier patent application"). The patent was granted with 12 claims. The opposition division considered the claims as granted (main request) to contravene Articles 76(1) and 123(2) EPC and auxiliary requests 1 to 12 not to fulfil the requirements of Article 56 EPC. The patent was revoked (Article 101(3)(b) EPC).
- II. The patent proprietor (appellant) lodged an appeal and, with the statement setting out the grounds of appeal, filed a main request, auxiliary requests 1 to 13, and Exhibit 1.
- III. The opponent (respondent) replied to the appellant's statement of grounds of appeal.
- IV. Both parties requested oral proceedings as an auxiliary measure.
- V. The parties were summoned to oral proceedings. In a communication issued in preparation of the oral proceedings, they were informed of the board's provisional opinion on the issues of the case.
- VI. None of the parties replied in substance to the board's communication. With a letter dated 15 March 2022, the appellant informed the board that neither the representative nor the patent proprietor were to attend

the scheduled oral proceedings. The appellant requested the board to decide on the merits of the case.

VII. The board cancelled the oral proceedings and informed the parties that it intended to issue a decision in line with the provisional opinion as summarised in the conclusions set out in the communication issued in preparation of the oral proceedings.

VIII. Claims 1, 9 and 11 of the main request (claims as granted) read as follows:

"1. A storable reagent mixture suitable for use in a reverse transcription reaction of at least one template nucleic acid, wherein the reagent mixture is ready to use as a mastermix and may be used directly for a reverse transcription reaction without adding additional reverse transcriptase, and wherein said reagent mixture comprises:

(a) glycerol in a concentration between 10% and 40%,  
and

(b) a reverse transcriptase, wherein said reverse transcriptase is selected from the group consisting of AMV RT, RSV RT, MMLV RT, HIV RT, EIAV RT, RAV2 RT, THERMOSCRIPT RTMMLV, ASLV RT and Rnase H-mutants thereof, SUPERScript II RT, and SUPERScript I RT, and

(c) a buffer, wherein said buffer further comprises:

a metal ion necessary for reverse transcriptase activity;  
and nucleoside triphosphates."

"9. The mixture according to claim 1, wherein said metal ion necessary for reverse transcriptase activity is magnesium ion."

"11. The mixture according to claim 1, wherein said buffer comprises a reducing agent."

IX. Claim 1 of auxiliary request 1 reads as claim 1 of the main request except for the replacement of the term "a metal ion" by "metal ions" in part (c) of this claim. Claims 9 and 11 of this auxiliary request read as claims 9 and 11 of the main request except for the replacement of the terms "said metal ion ... is ..." by "said metal ions ... comprise ..." in claim 9.

Claim 1 of auxiliary request 2 reads as claim 1 of auxiliary request 1 except for the deletion of the term "MMLV RT" in part (b) of this claim. Claims 9 and 11 read as claims 9 and 11 of auxiliary request 1.

Claim 1 of auxiliary request 3 reads as claim 1 of the main request except for the preamble which reads "A reagent mixture stable to storage at -20°C and suitable ... [as in claim 1 of the main request]". Claims 9 and 11 read as claims 9 and 11 of the main request.

Claim 1 of auxiliary request 4 reads as claim 1 of the main request except for the preamble which reads "A reagent mixture stable to storage at -20°C for 6.5 months and suitable ... [as in claim 1 of the main request]". Claims 9 and 11 read as claims 9 and 11 of the main request.

Claim 1 of auxiliary request 5 reads as claim 1 of the main request except for part (c) which reads "(c) a buffer suitable for reverse transcriptase reaction, wherein said buffer ... [as in claim 1 of the main

request]". Claims 9 and 11 read as claims 9 and 11 of the main request.

Claim 1 of auxiliary request 6 reads as claim 1 of the main request except for part (c) which reads "(c) a buffer containing all components necessary for cDNA synthesis". Claims 9 and 11 read as claims 9 and 11 of the main request.

Claim 1 of auxiliary request 7 reads as claim 1 of the main request except for part (c) which reads in this auxiliary request as: "(c) a buffer, wherein said buffer comprises: a monovalent cation selected from the group consisting of Li, Na, K and  $\text{NH}_4^+$ ; a magnesium salt; a reducing agent; nucleoside triphosphates; and at least one non-ionic detergent". Claims 9, 10 and 12 of the main request are deleted in this auxiliary request and claim 9 of this auxiliary requests reads as claim 11 of the main request.

Claims 1 of auxiliary requests 8 and 9 are a combination of the amendment introduced into the preamble of claims 1 of auxiliary requests 3 and 4, respectively, with the amendment introduced into part (c) of claim 1 of auxiliary request 5. Claims 9 and 11 of these auxiliary requests read as claims 9 and 11 of the main request.

Claims 1 of auxiliary request 10 and 11 are a combination of the amendment introduced into the preamble of claim 1 of auxiliary requests 3 and 4, respectively, with the amendment introduced into part (c) of claim 1 of auxiliary request 6. Claims 9 and 11 of these auxiliary requests read as claims 9 and 11 of the main request.

Claims 1 of auxiliary request 12 and 13 are a combination of the amendment introduced into the preamble of claim 1 of auxiliary requests 3 and 4, respectively, with the amendment introduced into part (c) of claim 1 of auxiliary request 7. Claims 9, 10 and 12 of the main request are deleted in these auxiliary requests and claim 9 of these auxiliary requests reads as claim 11 of the main request.

X. The following documents are cited in this decision:

(3): US 5,814,502, publication date: 29 September 1998;

(6): WO 2004/021986 (earlier patent application);

(7): V. Goldschmidt *et al.*, Nucleic Acid Research, 2006, Vol. 34, No. 1, pages 42 to 52;

Exhibit 1: "Biochemistry of Reverse Transcription" in Coffin JM *et al.*, editors. Retrovirus, Cold Spring Harbor (NY); Cold Spring Harbor Laboratory Press; 1997 (Taken from the NCBI Bookshelf).

XI. The arguments of the appellant, insofar as relevant to the present decision, may be summarised as follows:

Admission of Exhibit 1 and auxiliary request 2

No reasons were provided why Exhibit 1 and auxiliary request 2 were filed in appeal proceedings and why they could not have been filed during the first instance proceedings.



Main request and auxiliary requests

*Article 100(c) EPC; Articles 76(1) and 123(2) EPC*

Document (7) (in particular, the last sentence of the abstract) showed that, at the priority date of the patent, a person skilled in the art understood that  $Mg^{2+}$ , as a species of metal ion, was necessary for reverse transcriptase (RT) activity. According to page 16, lines 23 and 24, and page 17, lines 1 to 13 of the earlier patent application,  $MgCl_2$  was a component of a typical kit for cDNA synthesis. On page 21, lines 9 to 11 of the earlier patent application, KCl was described as a counterpart to Tris-HCl in the Tris buffer system, not as a metal ion necessary for RT activity. For the same reasons, claim 9 did not contravene Articles 76(1) and 123(2) EPC. In this context, reference was made to Exhibit 1.

- XII. The arguments of the respondent, insofar as relevant to the present decision, may be summarised as follows:

Admission of Exhibit 1 and auxiliary request 2

Exhibit 1 was a late-filed document and no more relevant than other documents already on file, in particular, document (7). Exhibit 1 was only used to confirm information that was already present in the documents on file.

The appellant had ample opportunities before the opposition division to file new claim requests, both in written submissions and during the course of the oral proceedings at first instance. Indeed, the appellant was invited to submit additional auxiliary requests following the finding of the opposition division that auxiliary request 1 lacked inventive step, and the

appellant chose not to present the auxiliary request 2 filed now in appeal.

Main request

*Article 100(c) EPC; Articles 76(1) and 123(2) EPC*

Neither the earlier patent application nor the patent application provided a basis for some features present in claim 1 such as, *inter alia*, (i) storable reagent mixture, and (ii) the buffer components of part (c) of claim 1.

As regards feature (i), the earlier patent application described only a reagent mixture with prolonged stability when stored at  $-20^{\circ}\text{C}$  (page 12, lines 5 to 11; page 17, lines 23 to 26; and claim 16 of the earlier patent application). Therefore, claim 1, as regards the requirements of storability, generalised from this specific disclosure and went beyond it. The reference to mixtures "stably maintained" on page 16, lines 18 and 19 was a general introduction to the section dealing with the disclosed reagent compositions. In this section, reference was made only to the stability of these compositions under prolonged storage at  $-20^{\circ}\text{C}$  (page 17, lines 25 and 26).

As regards feature (ii), there was no basis for the selection of nucleoside triphosphates (NTPs) as a component of the buffer cited in part (c) of claim 1 without the additional components specified on page 12, lines 12 to 14, and in claim 17 of the earlier patent application. Nor was there a basis in the earlier patent application for a buffer containing a single metal ion. Only a buffer containing a plurality of metal ions was disclosed on page 18, lines 2 to 5, and in claim 17 of the earlier patent application. The

typical kit referred to on page 16 was shown on page 17 to include a (Tris-HCl) buffer containing KCl and also MgCl<sub>2</sub> and thus, in line with the disclosure on page 18, lines 2 to 5. The fact that document (7) identified the dependency of RT activity on Mg<sup>2+</sup> concentration did not mean that the reaction was not dependent on other metal ions. Indeed, KCl was also mentioned in the reaction buffer disclosed in this document (page 43, right-hand column of document (7)).

Auxiliary requests

*Articles 76(1) and 123(2) EPC*

The reasons given for the main request to comprise added subject-matter applied also to the auxiliary requests. Moreover, some features introduced into auxiliary requests 3 and 4 were also added subject-matter. In particular, the feature "stable to storage at -20°C for 6.5 months" in claim 1 of auxiliary request 4 represented an intermediate generalisation. This feature was taken from the examples; however, the examples were directed to a specific composition and did not allow to conclude that any reagent mixture having the characteristics set out in auxiliary request 4 would have these storage characteristics.

*Article 84 EPC*

Objections under this article were raised against auxiliary requests 5 and 7. In particular, auxiliary request 7 as a whole lacked clarity in view of the presence of dependent claim 9, since the reference to the buffer for comprising a reducing agent present in that dependent claim had already been introduced into claim 1 of this auxiliary request.

- XIII. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained as granted (main request) or, in the alternative, that the patent be maintained on the basis of any of auxiliary requests 1 to 13.
- XIV. The respondent (opponent) requested that the appeal be dismissed.

### **Reasons for the Decision**

1. The present decision is based on the same grounds, arguments and evidence on which the board's provisional opinion was based. They were neither questioned by the parties, nor did other aspects come up that would require their re-consideration.

#### Procedural issues

##### *Admission of Exhibit 1 into the appeal proceedings*

2. Exhibit 1 was filed by the appellant with the statement of grounds of appeal and was cited under Articles 76(1) and 123(2) EPC for examination of the feature requiring the buffer of the storable reagent mixture in claim 1 to comprise a metal ion necessary for reverse transcriptase (RT) activity. The respondent requested not to admit this document into the appeal proceedings because it was late-filed and not more relevant than other documents already on file, such as document (7).
3. According to the 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 proceedings before any of these divisions (cf. "Case Law of the Boards of

Appeal of the EPO", 9th edition 2019, V.A.1, 1133). By way of Article 25(2) RPBA 2020, Article 12(4) RPBA 2007 states that it is within the board's discretion to hold inadmissible, *inter alia*, evidence which could have been presented in the first instance proceedings.

4. In the Notice of opposition, the opponent raised an objection under Articles 76(1) and 123(2) EPC against, *inter alia*, the feature requiring the buffer in the reagent mixture to comprise a metal ion necessary for RT activity (cf. page 6, point 3.5 of the Notice of opposition). This feature was also addressed by the opposition division in the Summons to attend oral proceedings and considered to contravene Articles 76(1) and 123(2) EPC (cf. page 6, point 2.3.5 of the Summons to attend oral proceedings). At these oral proceedings, the arguments of the parties were heard on the requirements of these articles and the opposition division considered that the feature "a metal ion" had no basis in the earlier patent application (cf. page 1, last paragraph of point 2 of the Minutes).
5. In view of this course of events, the board considers that the appellant had ample time and opportunity to file Exhibit 1 at an earlier stage of the proceedings. The admission of this document in appeal proceedings would be against the primary object and function of an appeal as referred to by the case law cited above. The filing of Exhibit 1 in appeal attempts to re-open the proceedings and not to review the decision under appeal with the evidence on which that decision was based.
6. Thus, the board, in the exercise of its discretion, does not admit Exhibit 1 into the appeal proceedings.

Main request (Claims as granted)

Article 100(c) EPC

7. The opposition division stated that the content of the earlier patent application and that of the patent application were identical except for the incorporation of the claims of the earlier patent application into the description of the patent application. Therefore, the objections under Articles 76(1) and 123(2) EPC were treated together and all references were made to the earlier patent application, i.e. document (6) in these proceedings (cf. page 3, point 1.3.1 of the decision under appeal). Thus, the board will also refer to the earlier patent application hereinafter.
  
8. The opposition division considered that all features of claim 1 had a basis in the earlier patent application except for the feature "a metal ion" (in singular form) comprised in the buffer defined in part (c) of this claim. According to the opposition division, the general teaching of the earlier parent application required this buffer to comprise "metal ions" (in plural form). In line therewith, claim 9 as granted - defining magnesium as the "said metal ion necessary for reverse transcriptase activity" - was considered to contravene Articles 76(1) and 123(2) EPC; none of the other dependent claims were considered to contravene these articles.
  
9. Whilst the appellant contested this decision, the respondent maintained the objections raised at first instance against the features in claim 1 such as, *inter alia*, (i) storable reagent mixture, and (iii) the buffer components of part (c) of claim 1.

10. In the communication issued by the board in preparation of the oral proceedings, the parties' attention was drawn to, *inter alia*, the following issues:

10.1 As regards feature (i), the earlier patent application acknowledges that there was "a widespread prejudice in the art" that the separate components of a complete reaction mix for cDNA synthesis needed to be kept separate for storage purposes (page 16, lines 19 to 23; page 17, lines 18 and 19). Contrary to this prejudice, the earlier patent application discloses a "typical kit for cDNA synthesis" wherein "the components of the cDNA synthesis reaction can be combined and stored as a convenient ready-to-use mix that is stable to prolonged storage at -20°C" (cf. page 17, lines 14 and 15, and lines 23 to 26). This is in line with the general description of this embodiment on page 12, lines 6 to 11, the reference to the stability of the mastermixes in Example III (page 26, lines 2 and 3), and the reagent mixture of claim 16 of the earlier patent application.

The storage stability of all these mixes is directly and unambiguously associated not only with the specific components of these mixes but also with the specific conditions of storage, in particular a temperature of -20°C. There is no indication in the earlier patent application that storage stability is achieved using storage conditions other than the specific conditions disclosed in the earlier patent application.

Thus, the omission of this feature in claim 1 leads to subject-matter that goes beyond what is disclosed in the earlier patent application (cf. "Case Law", *supra*, II.E.1.4, 446, in particular II.E.1.4.3, 447).

10.2 As regards feature (ii), the sentence on page 18, lines 2 to 5 of the earlier patent application clearly refers to the presence in the (suitable) buffer of metal ions necessary for RT activity and, as an example, gives "Mg and a monovalent cation". This is in line with claim 17 of the earlier patent application, wherein the buffer is described as comprising, *inter alia*, a magnesium salt and a monovalent cation. The presence of both, magnesium salt and a monovalent (KCl) cation is also found in the composition described on page 17, lines 1 to 13, for a typical kit for cDNA synthesis and on page 19, lines 1 to 14 of the earlier patent application.

Regardless of whether the presence of the monovalent cation is a counterpart to the Tris-HCl buffer system (as argued by the appellant) or necessary for the RT activity, the disclosure of the earlier patent application always comprises the presence of both "metal ions", namely "Mg and a monovalent cation", as stated on page 18. However, the storable reagent mixture of claim 1 does not necessarily require both metal ions and therefore, the subject-matter of this claim goes beyond the disclosure of the earlier patent application. The references to prior art, such as document (7), for exemplifying the common general knowledge of a skilled person, cannot change the disclosure of the earlier patent application.

11. In view thereof, Article 100(c) EPC prejudices maintenance of the main request.



Auxiliary request 1

12. Auxiliary request 1 is identical to auxiliary request 1 underlying the decision under appeal and thus, it already forms part of these proceedings.

*Articles 76(1) and 123(2) EPC*

13. The amendments introduced into claims 1 and 9 of auxiliary request 1 address the objection concerning feature (ii) of claim 1 of the main request but not those raised against feature (i). Thus, auxiliary request 1 contravenes Articles 76(1) and 123(2) EPC for the same reasons as the main request.

Admission of auxiliary request 2 into the appeal proceedings

14. Auxiliary request 2 was filed by the appellant with the statement of grounds of appeal. Article 25(2) RPBA 2020, in conjunction with Article 12(4) RPBA 2007, states that it is within the board's discretion to hold inadmissible, *inter alia*, requests which could have been presented in the first instance proceedings.
15. Auxiliary request 2 differs from auxiliary request 1 by the deletion of the MoMuLV reverse transcriptase (MMLV RT) in claim 1. This amendment was not present in any of the auxiliary requests filed at the first instance. No reasons were provided by the appellant to explain why auxiliary request 2 was filed at this (late) stage of the proceedings and why it could not have been filed at an earlier stage of the proceedings.
16. The objection for lack of inventive step was raised at the first stage of the opposition, namely in the Notice of opposition. In the Summons to attend oral

proceedings, the opposition division identified document (3) as the closest prior art and considered that the requirements of Article 56 EPC were not fulfilled by the claimed subject-matter. In response thereto, the appellant filed auxiliary requests 1 to 12. According to the Minutes of the oral proceedings at first instance, the appellant filed a new auxiliary request 1 after the opposition division announced that the main request contravened Articles 76(1) and 123(2) EPC. The opposition division also gave the appellant an opportunity to file new requests after announcing that the new auxiliary request 1 and auxiliary requests 2 to 12 then on file did not fulfil the requirements of Article 56 EPC. The appellant waived this opportunity (cf. page 2, point 6 of the Minutes of the oral proceedings).

17. In the light of this course of events, there is no reason that could have prevented the appellant from submitting before the opposition division a request with the amendment introduced into auxiliary request 2 filed in appeal. Both the nature of the amendment and the objection addressed by this amendment are straightforward and the admission of such a request into the proceedings would have been decided by the opposition division. If appealed, this decision would have been then reviewed by the board. The filing of auxiliary request 2 in appeal is an attempt to re-open and continue the opposition proceedings, and not to review a decision taken by the first instance. This is not the purpose or function of an appeal as established in the case law (cf. "Case Law", *supra*, V.A.1, 1133; V.A.4, 1206; and V.A.4.11.3.d), 1233; see also decisions T 144/09 of 4 May 2011, Catchword, points 1.4 and 1.17 of the Reasons, and related R 11/11 of

14 November 2011; T 1866/16 of 11 January 2021, points 1 to 8 of the Reasons).

18. Therefore, the board, in the exercise of its discretion, decides not to admit auxiliary request 2 into the appeal proceedings.

Auxiliary requests 3 to 13

19. Auxiliary requests 3 to 13 correspond to auxiliary requests 1 to 11 filed on 13 April 2018 at first instance, i.e. auxiliary requests 2 to 12 underlying the decision under appeal. Thus, these auxiliary requests already form part of these proceedings.

*Articles 76(1), 123(2) EPC and Article 84 EPC*

20. In the response to the statement of grounds of appeal, the respondent addressed the amendments introduced into auxiliary requests 3 to 5 and 7 and raised, *inter alia*, the following objections: (i) presence of added subject-matter in auxiliary requests 3 to 5 and 7 (Articles 76(1) and 123(2) EPC), and (ii) lack of clarity of auxiliary requests 5 and 7 (Article 84 EPC). As regards auxiliary requests 8 to 13, the respondent considered them to represent combinations of the amendments made to auxiliary requests 3 to 7 and therefore, the objection of added subject-matter (Articles 76(1), 123(2) EPC) applied equally to all these auxiliary requests.

21. In the communication in preparation of the oral proceedings, the board drew the parties' attention to the fact that the objections raised against the main request under Articles 76(1) and 123(2) EPC were also relevant for these auxiliary requests, in particular

for the features concerning the terms (i) "storable" (auxiliary requests 5 to 7) and (ii) "a metal ion" (auxiliary requests 3 to 5, 8, and 9). Moreover, the unallowable intermediate generalisation referred to by the respondent against auxiliary request 4 applies also to auxiliary requests 9, 11 and 13.

22. In this communication, the parties' attention was also drawn to the fact that there is a lack of clarity for these auxiliary requests; in particular the objection raised by the respondent against auxiliary request 5, as well as the references to "said metal ion" in a dependent claim without having any antecedent in claim 1 (auxiliary requests 6, 10 and 11), and the (redundant) reference to a "reducing agent" in claim 1 and in a dependent claim in auxiliary requests 7, 12 and 13.
23. Therefore, none of auxiliary requests 3 to 13 fulfils all the requirements of the EPC.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated