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**Datasheet for the decision
of 23 January 2019**

Case Number: T 0842/14 - 3.3.08

Application Number: 03767188.0

Publication Number: 1540009

IPC: C12Q1/68

Language of the proceedings: EN

Title of invention:

IMPROVED COMPOSITIONS FOR IN VITRO AMPLIFICATION OF NUCLEIC ACIDS

Patent Proprietor:

QIAGEN Beverly, Inc.

Opponent:

Zwicker, Jörk

Headword:

PCR anti-foam reagents/QIAGEN

Relevant legal provisions:

EPC Art. 54, 83, 84, 114(1), 123(2)

RPBA Art. 13(1), 13(2)

Keyword:

Main request and auxiliary request 1 - Novelty (no);
Auxiliary request 2 - added subject-matter (yes);
Auxiliary request 3 - clarity (no);
Auxiliary request 4 - sufficiency of disclosure (no);
Auxiliary request 5 - admitted into the proceedings (no);
Auxiliary request 6 - clarity (no), sufficiency of disclosure (no);

Decisions cited:

G 0009/91, G 0010/91, G 0001/92, G 0003/14, T 0450/89,
T 0623/91, T 0667/94, T 0728/98, T 0190/99, T 0860/00,
T 0608/07, T 1383/10, T 0270/11, T 0325/13, T 2451/13,
T 1833/14

Catchword:



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Case Number: T 0842/14 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 23 January 2019

Appellant: QIAGEN Beverly, Inc.
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 27 January 2014
revoking European patent No. 1540009 pursuant to
Articles 101(2) and 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. 1 540 009 was granted on the basis of European patent application no. 03 767 188.0, published under the PCT as International patent application WO 2004/013305 (hereinafter "the patent application"). An opposition was filed on the grounds set forth in Articles 100(a) and 100(b) EPC. The opposition division considered the main request (claims as granted) and auxiliary requests 1 to 3 to lack novelty, and auxiliary requests 4 and 5 not to fulfil the requirements of Article 83 EPC. Claim 10 of auxiliary request 1 was also considered to contravene Article 84 EPC. Accordingly, the patent was revoked.
- II. With the statement setting out the grounds of appeal, the proprietor (appellant) filed auxiliary requests 1 to 5 anew.
- III. The opponent (respondent) filed a response to the statement of grounds of appeal.
- IV. The board summoned the parties to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), the board informed the parties of its provisional, non-binding opinion on some of the issues of the case.
- V. Both parties replied to the board's communication. The appellant filed a new auxiliary request 5 and resubmitted its former auxiliary request 5 as auxiliary request 6.
- VI. Oral proceedings were held on 23 January 2019.

VII. Claim 1 as granted (main request) is identical to claim 1 of auxiliary request 1 and reads as follows:

"1. A method for detecting a target nucleic acid in a sample, comprising the step of amplifying the target nucleic acid using a polymerase chain reaction, wherein said polymerase chain reaction is carried out in the presence of a detergent and an effective amount of at least one anti-foam reagent that does not substantially inhibit the action of the polymerase, wherein said polymerase chain reaction is a real-time quantitative polymerase chain reaction."

VIII. Claim 1 of auxiliary request 2 reads as follows:

"1. A method for detecting a target nucleic acid in a sample, comprising the step of amplifying the target nucleic acid using a polymerase chain reaction, wherein said polymerase chain reaction is carried out in the presence of a detergent stabilizing said polymerase and an effective amount of at least one anti-foam reagent preventing the formation of foam that suppresses foaming/bubble formation and does not substantially inhibit the action of the polymerase, wherein said polymerase chain reaction is a real-time quantitative polymerase chain reaction."

IX. Claim 1 of auxiliary request 3 reads as follows:

"1. A method for detecting a target nucleic acid in a sample, comprising the step of amplifying the target nucleic acid using a polymerase chain reaction, wherein said polymerase chain reaction is carried out in the presence of a detergent stabilizing said polymerase and an effective amount of at least one anti-foam reagent preventing the formation of foam by the detergent that

suppresses foaming/bubble formation to an extent necessary to permit accurate optical analysis of the reaction mixture or accurate fluid handling and does not substantially inhibit the action of the polymerase, wherein said polymerase chain reaction is a real-time quantitative polymerase chain reaction."

X. Claim 1 of auxiliary request 4 reads as follows:

"1. A method for detecting a target nucleic acid in a sample, comprising the step of amplifying the target nucleic acid using a polymerase chain reaction, wherein said polymerase chain reaction is carried out in the presence of a detergent and an effective amount of at least one anti-foam reagent selected from the group consisting of 1520-US, AF, FG-10, 0-30, SE-15, and Antifoam B that does not substantially inhibit the action of the polymerase, wherein said polymerase chain reaction is a real-time quantitative polymerase chain reaction.

XI. Claim 1 of auxiliary request 5 is identical to claim 1 of auxiliary request 4 except for the deletion of the anti-foam reagents "AF, FG-10, 0-30, and SE-15".

XII. Claim 1 of auxiliary request 6 reads as follows:

"1. A method for detecting a target nucleic acid in a sample, comprising the step of amplifying the target nucleic acid using a polymerase chain reaction, wherein said polymerase chain reaction is carried out in the presence of a detergent stabilizing said polymerase and an effective amount of at least one anti-foam reagent preventing the formation of foam by the detergent, wherein the at least one anti-foam reagent is selected from the group consisting of 1520-US, AF, FG-10, 0-30,

SE-15, and Antifoam B, wherein said effective amount suppresses foaming/bubble formation to an extent necessary to permit accurate optical analysis of the reaction mixture or accurate fluid handling and does not substantially inhibit the action of the polymerase, wherein said polymerase chain reaction is a real-time quantitative polymerase chain reaction."

XIII. The following documents are cited in this decision:

- (2): Entry "Surfactant" in Wikipedia, print out dated 25 June 2012;
- (3): J.J. Bikerman *et al.*, "Foams: Theory and Industrial Applications", Chapter 15, C.C. Currie, Reinhold Publishing Corp., N.Y., 1953, 297 to 329;
- (4): WO-A1-93/04195 (publication date: 4 March 1993);
- (6): US-B1-6,300,542 (publication date: 9 October 2001);
- (7): U. Reischl *et al.*, J. Clin. Microbiol., July 2002, Vol. 40, No. 7, 2555 to 2565;
- (18): Dow Corning, Product information, "Silicone Antifoams", Antifoam 1520-US;
- (19): Sigma, Product information, "Antifoams", Antifoam B Emulsion;
- (24): Sigma, Product information sheet, Triton X-100;
- (25): Entry "Triton X-100" in Wikipedia, print out dated 14 February 2013;

(32): Entry "Real-time polymerase chain reaction" in Wikipedia, print out filed on 4 November 2013;

(33): C.A. Heid *et al.*, Genome Research, 1996, Vol.6, 986 to 994.

XIV. The submissions made by the appellant, insofar as relevant to the present decision, may be summarised as follows:

Admission of the ground for opposition under Article 100(b) EPC and of documents (32) and (33) into the appeal proceedings

The objection under Article 100(b) EPC was not substantiated in the Notice of opposition. The reasons given therein were all related to the clarity of the claims and not to sufficiency of disclosure. The case law and the decisions of the Boards of Appeal cited in the decision under appeal all concerned Article 84 EPC and not Article 83 EPC. From the beginning of the opposition procedure, no evidence was provided that a person skilled in the art could not have reproduced the invention. On the contrary, evidence was on file that the products referred to by trademarks in the claims were commercially available and thus, that a skilled person could reproduce the invention.

Documents (32) and (33) were admitted into the proceedings because they were considered to be relevant for the novelty discussion. However, none of the objections raised for lack of novelty was based on any of these documents. Thus, they were not highly relevant and should not have been admitted into the proceedings.

*Main request (claims as granted); Auxiliary request 1
Article 100(a) EPC/Article 54 EPC*

According to the case law, for acknowledging lack of novelty, the claimed subject-matter had to be directly and unambiguously disclosed in the prior art, beyond any doubt and not merely probably (*inter alia*, T 450/89 of 15 October 1991).

Document (7) identified Triton X-100 and Tween 20 as components of a lysis buffer used to prepare a template DNA which was directly transferred to a PCR assay, but none of these compounds was described as having anti-foaming activity. This activity was known in the art to be highly dependent on the type of sample and the conditions used. Therefore, in the absence of any indication in document (7), a skilled person would give these compounds the meaning common in the art, namely acting as detergents (documents (24) and (25)). In document (3), Tween 20 was identified as a detergent, even though under some specific reaction conditions - which were different from those described in document (7) - it could have anti-foam activity. The sample (pure bacterial culture with heaviest growth) and PCR reaction conditions described in document (7) were very specific and thus, in the absence of any indication, it was impossible to know beyond doubt whether Triton X-100 and Tween 20 acted as anti-foam reagents in the system described in document (7).

Although the use of a buffer comprising Triton X-100 was described in one of the methods disclosed in document (6), it was also explicitly stated that the bubbles were removed from PCR plates by physical means (brief spin in centrifuge). None of the methods disclosed in this document relied on Triton X-100 as an

anti-foaming reagent. Moreover, since the activity and efficiency of Triton X-100 as anti-foam reagent was highly dependent on the specific sample and the conditions used, the information provided by document (6) did not directly apply to the system described in document (7).

Likewise, document (4) was not concerned with PCR and DNA amplification, but with spheres containing the reagents necessary for analyzing biological products, a system and purpose completely different from those described in document (7). In a generic reference to the use of surfactants for inhibiting bubble formation non-ionic detergents in general were cited, but neither Triton X-100 nor Tween 20 were mentioned. Although in the mixtures described in Examples 2 and 3 of document (4) Triton X-100 was used for controlling bubbles during dissolution, these mixtures contained other compounds (HEPES, sodium chloride in Example 2; HEDTA, glycerol in Example 3) that were not present in the lysis buffer and PCR mixtures described in document (7). Moreover, the concentrations of Triton X-100 in the systems described in documents (4) and (7) were not comparable. These documents described different systems and the information provided by document (4) did not directly apply to the system described in document (7).

Neither document (7) itself nor any other prior art document, provided evidence beyond any doubt that in the system (sample, PCR reaction mixture and conditions) described in document (7), Triton X-100 or Tween 20 were acting as anti-foam reagents. Thus, the claimed subject-matter was not anticipated by document (7).

*Auxiliary request 2 (Article 123(2) EPC),
Auxiliary request 3 (Admissibility of the objection
raised under Article 84 EPC; Article 84 EPC)*

No submissions were made in appeal proceedings on any of these issues.

Auxiliary request 4 (Article 83 EPC)

The sole argument put forward for substantiating the objection raised under Article 83 EPC was an alleged ambiguity arising from the use of trademarks for designating the anti-foam reagents cited in claim 1. According to decision T 608/07 of 27 April 2009, an ambiguity could lead to an insufficiency objection only if it deprived the skilled person of the promise of the invention. Care had to be taken that an insufficiency objection arising out of an ambiguity was not merely a hidden objection under Article 84 EPC, itself not a ground of opposition. In the present case, the objection raised under Article 83 EPC was in fact an objection under Article 84 EPC. The case law cited in connection with this issue, such as decisions T 623/91 of 16 February 1993 and T 270/11 of 6 June 2013, confirmed this.

According to the case law, the requirements of Article 83 EPC were fulfilled if at least one way for practicing the invention was available to a skilled person at the filing and priority dates of the patent. There was evidence on file that the products designated by trademarks in the claims were all commercially available at these dates. The commercial availability of these products rendered their chemical composition part of the state of the art (decisions T 667/94 of 16 October 1997; G 1/92, OJ EPO 1993, 277). Their

chemical composition could be analysed and there was no evidence on file that these analyses required undue burden from a skilled person. The fact that the trademark products and their exact composition were identified as being "proprietary", did not imply any difficulties for analysing these products. This merely meant that they were the property of, or belonged to, the companies supplying and/or commercialising them. Furthermore, there was no evidence on file that the chemical composition of the trademark products could actually change during the lifetime of the patent.

Admission of auxiliary request 5 into the appeal proceedings

The request was filed in reply to the board's communication. The amendment introduced into this request, namely the deletion of four anti-foam reagents, was straightforward and in accordance with the board's indications given in its communication. According thereto, some of the anti-foam reagents designated by trademarks in claim 1, such as those based on the disclosures of documents (18) and (19), could fulfil the requirements of Article 83 EPC. The deletion of four anti-foam reagents did not introduce any complexity into the case and did not result in the respondent being faced with new arguments for which it could not have been prepared.

Auxiliary request 6

No submissions were made in appeal proceedings on this request other than those made for the corresponding subject-matter of auxiliary requests 3 and 4.

XV. The submissions made by the respondent, insofar as relevant to the present decision, may be summarised as follows:

Admission of the ground for opposition under Article 100(b) EPC and of documents (32) and (33) into the appeal proceedings

The objection raised under Article 100(b) EPC was substantiated in the Notice of opposition. Substantiation was not to be confused with the merits of the objection and required only that the opposition division could understand the objection without further research. The objection in the Notice of opposition was based on the use of trademarks in the claims, which led to a lack of clarity that resulted in an insufficiency of disclosure because a skilled person could not reproduce the invention without undue burden. As shown by the decision under appeal, the objection was clearly understood by the opposition division at the beginning of the opposition procedure.

Documents (32) and (33) were filed in reply to the preliminary opinion of the opposition division for elucidating the terms "real-time PCR" and "quantitative real-time PCR". Based thereupon, the opposition division changed its opinion on document (7) and considered it to be novelty destroying.

Main request (claims as granted); Auxiliary request 1 Article 100(a) EPC/Article 54 EPC

The anti-foam reagent in claim 1 was functionally defined and its concentration range limited by an upper and a lower end, the upper end defined as the concentration not inhibiting polymerase activity

substantially and the lower end as the concentration providing anti-foam activity. Complete suppression of foaming/bubble formation was not required but only the presence of an effective amount of anti-foam reagent. Effective concentrations of these anti-foam reagents, including an optimal range, were disclosed in the patent.

A skilled person would not have considered Triton X-100 in the PCR mixture described in document (7) to be a mere detergent, because Triton X-100 was known in the art to have anti-foaming activity in many different assays and conditions, including in PCR assays. Although not concerned with PCR, document (4) described Triton X-100 acting as anti-foaming reagent within the range of concentrations given in the patent. Document (6) disclosed the contribution of low concentrations of Triton X-100 - within the range given in the patent - for eliminating bubbles in a PCR assay. When reading document (7), a skilled person understood, based on its knowledge of the art, that Triton X-100 - in a concentration within the range indicated in the patent - acted as anti-foam reagent. Thus, document (7) disclosed a PCR method with all features of claim 1.

Auxiliary request 2 (Article 123(2) EPC)

Claim 1 required the anti-foam reagent to suppress foaming/bubble formation. The term "suppress" was used in the patent application as a relative term qualifying a level of suppression that was inextricably linked to the extent necessary to permit accurate optical analysis of the reaction mixture or accurate fluid handling. The criteria referred to in decision T 860/00 of 28 September 2004 for acknowledging an implicit disclosure did not apply to the present case because

there was no disclosure in the patent application, neither explicit nor implicit, of a PCR method wherein an effective amount of the anti-foaming reagent provided a complete suppression of foaming/bubble formation.

Auxiliary request 3 (Admissibility of the objection under Article 84 EPC; Article 84 EPC)

An objection for lack of clarity arising from the introduction of the feature "suppresses foaming/bubble formation" into claim 1 was put forward in opposition. This feature was intrinsically linked to two other features both characterized by the term "accurate", namely "accurate optical analysis" and "accurate fluid handling". There was thus a contextual relationship between the objection raised in opposition and the objection raised against the term "accurate" in the appeal proceedings. The submissions made in response to the statement of grounds of appeal provided a further argument to support the objection for lack of clarity already raised in opposition.

According to the case law (*inter alia*, T 728/98, OJ EPO 2001, 319), the requirement of legal certainty implied that a claim was not clear if it comprised a technical feature for which no unequivocal generally accepted meaning existed in the art. The term "accurate" in claim 1 was ambiguous and neither the patent nor the state of the art provided information that could allow a skilled person to know when an optical analysis and/or fluid handling was "accurate". Therefore, it remained unclear what "an effective amount of at least one anti-foam reagent" was.

Auxiliary request 4 (Article 83 EPC)

In order to fulfil the requirements of Article 83 EPC, the disclosure of the patent application had to enable the skilled person to perform the invention at the filing and priority dates of the patent as well as during the lifetime of the patent. Thus, the anti-foam reagents designated by trademarks in claim 1 had to be available during the lifetime of the patent. Since, for trademark products, changes in their composition could not be excluded, there was no certainty that the invention could be performed during the lifetime of the patent, unless chemical/structural information about the anti-foam reagents was provided by the patent application.

This was in line with the case law on trademarks, such as decisions T 623/91 and T 270/11, *supra*. In the cases underlying these decisions evidence was provided that the changes in the chemical compositions would have resulted in a corresponding change in the trademarks. No such evidence had been provided in the present case. The close relationship between Articles 84 and 83 EPC was acknowledged in the case law (*inter alia*, decision T 608/07, *supra*) which stated that an insufficiency objection could arise out of an ambiguity if that ambiguity resulted in the skilled person being deprived of the promise of the invention. This applied in the present case.

In decision T 667/94, *supra*, the board, with reference to decision G 1/92, *supra*, considered that a trademark product was commercially available to the public on the priority date of the patent and thus, it could be analysed and its chemical composition formed part of the state of the art. However, in the present case, the

patent acknowledged that the products designated by trademarks in claim 1 were proprietary formulations. Documents (18) and (19) described the commercial anti-foam reagents 1520-US and Antifoam B as emulsions of silicon-based polymers. As proprietary formulations, the exact composition of these reagents was not made available to the public. Moreover, contrary to the product referred to in decision T 667/94, it was known in the polymer field that the nature of the catalyst system, the type of reaction system and process conditions significantly affected the properties of the produced polymer. As stated in decision T 1833/14 of 7 December 2017, for polymers, sufficiency of disclosure was met only if the patent application disclosed all this information, when necessary supported by common general knowledge. In view thereof, it could not be concluded that the chemical composition of the trademark products cited in claim 1 could be easily determined by merely analysing the commercial products. Such analysis required an undue amount of work from the skilled person. This situation was similar to that of the case underlying decision T 325/13 of 25 March 2014.

Admission of auxiliary request 5 into the appeal proceedings

The request was late-filed, it had not been filed after issuance of the board's communication but just one day before the oral proceedings. The amendments introduced into the request were not directly derivable from documents (18) and (19). Whilst some of the anti-foam reagents disclosed in document (19) were deleted in this request, others with similar properties were not. The respondent could be confronted with new arguments for which no preparation had been possible.

Auxiliary request 6

Claim 1 combined the amendments introduced into claim 1 of auxiliary requests 3 and 4. The objections raised against said requests equally applied to auxiliary request 6.

XVI. The appellant (patent proprietor) requested, as a main request, that the decision under appeal be set aside and the patent be maintained as granted, or alternatively, that the patent be maintained upon the basis of one of auxiliary requests 1 to 4, filed under cover of a letter dated 6 June 2014, or further upon the basis of one of auxiliary requests 5 to 6, filed under cover of a letter dated 21 January 2019. The appellant further requested that the ground for opposition set forth in Article 100(b) EPC and documents (32) and (33) not be admitted into the proceedings.

XVII. The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

Admission of the ground of opposition under Article 100(b) EPC and documents (32) and (33) into the appeal proceedings

1. According to the case law, if the way in which the opposition division has exercised its discretion when deciding on a procedural matter is challenged in an appeal, it is not the function of the board to review all the facts and circumstances of the case as if it were in the place of the opposition division, and to decide whether or not it would have exercised such

discretion in the same way as the opposition division. The board will only overrule the way in which the opposition division has exercised its discretion, if the board concludes that it has done so according to the wrong principles or in an unreasonable way (cf. "Case Law of the Boards of Appeal of the EPO", 8th edition 2016, III.K.5, 761, and the case law referred to therein).

2. In points 3.2 and 4.2 (see also point 4.2.1) of the decision under appeal, the opposition division provided the reasons for admitting documents (32) and (33) and the ground for opposition under Article 100(b) EPC into the opposition proceedings. Although the appellant contests the reasons given by the opposition division, it has not argued that the opposition division exercised its discretion according to the wrong principles or in an unreasonable way. All its arguments relate to the merits of the objections.
3. As regards documents (32) and (33), the board agrees with the appellant that there is no novelty objection based on any of them. However, as stated by the respondent, these documents were cited for establishing that the real-time PCR assay described in document (7) is a real-time quantitative PCR assay as required in claim 1 of all requests. Only when this fact had been established, did the opposition division consider the disclosure of document (7) to anticipate the claimed subject-matter. The admission of these documents into the opposition proceedings was thus fully justified and not unreasonable.
4. Since the board does not consider that the opposition division exercised its discretion in an unreasonable way or according to the wrong principles, the ground of

opposition under Article 100(b) EPC and documents (32) and (33) form part of the appeal proceedings.

The main request and the auxiliary requests 1 to 4 and 6

5. The main request (claims as granted) and auxiliary requests 1 to 4 and 6 are identical to the main request and auxiliary requests 1 to 5, respectively, underlying the decision under appeal. Thus, all these requests are part of the appeal proceedings.

Main request (claims as granted) and auxiliary request 1

Article 100(a) EPC/Article 54 EPC

6. Claim 1 is directed to a real-time quantitative polymerase chain reaction (PCR) amplification method for detecting a target nucleic acid in a sample, wherein the polymerase chain reaction is carried out in the presence of a detergent and "an effective amount of at least one anti-foam reagent that does not substantially inhibit the action of the polymerase". Apart from the presence of a detergent and an "effective amount" of an anti-foam reagent, there is no limitation in claim 1 as regards the presence/absence of any other compounds, the type of sample and the conditions under which the real-time quantitative PCR is carried out. Nor does the patent describe any of these factors as essential for performing the claimed method. Moreover, the term "effective amount" must be given a broad meaning, i.e. any amount providing an anti-foaming effect, no matter how small this effect may be. Claim 1 requires the anti-foam reagent not to substantially inhibit the action of the polymerase but it does not require an optimal amount of anti-foam

reagent (cf. page 9, lines 31 to 35; and page 11, lines 54 to 58 of the patent).

7. Document (7) discloses a real-time fluorescence PCR assay which the opposition division, in the light of documents (32) and (33), acknowledged to be a quantitative PCR assay. The preparation of the template DNA relies on a lysis buffer that comprises 1% Triton X-100 and 0.5% Tween 20. After carrying out the lysis and a centrifugation step, the template DNA is directly transferred to the PCR mixture - by 10-fold dilution. Thus, the concentrations of Triton X-100 and Tween 20 in the PCR mixture are 0.1% and 0.05%, respectively (cf. page 2556, right-hand column, first paragraph). Since neither Triton X-100 nor Tween 20 need to be removed for carrying out the PCR assay, it is understood that none of these compounds inhibits the action of the polymerase. The concentration of Triton X-100 and Tween 20 in the PCR mixture falls within the range of "effective concentrations" defined in the patent (0.0001% to 10%) and, more particularly, in the range wherein "many reagents will work optimally", namely 0.0001% to 0.1% (cf. page 9, lines 31 and 32 of the patent).

8. In the board's view, the skilled person is well aware of the surfactant nature of Triton X-100 and that it may thus act both as a detergent (foaming) as well as an anti-foaming reagent - as known in the art to be the case for all surfactants (cf. *inter alia*, page 2, last paragraph of document (2)). Indeed, there is a large body of prior art on file showing that Triton X-100 acts as an anti-foam reagent in several systems and under different conditions such as, for instance, documents (4) and (6). Although document (4) is not concerned with PCR amplification assays, it refers

nevertheless to the detrimental effect of bubbles by their interference with optical measurements and the use of surfactants for inhibiting their formation (cf. page 10, lines 4 to 11). In Examples 2 and 3, the non-ionic detergent Triton X-100 is explicitly stated to be used "for controlling bubbles" (cf. page 17, lines 6 and 7; and page 19, lines 8 and 9). Document (6), concerned with PCR assays performed in wells of microtiter plates, refers also to the problems arising from the formation of bubbles due to the small volumes of the solutions used in the PCR, and to the importance of preventing bubble formation during PCR (cf. column 6, lines 55 to 64). Although several measures are taken for preventing bubble formation (such as use of degassed water and a brief spin in centrifuge), it is explicitly acknowledged in Example 2 that 0.01% Triton X-100 "contributes greatly to elimination of bubbles" (cf. column 10, lines 63 to 65).

9. In view of this prior art, the board has no doubts that Triton X-100 in the PCR mixture described in document (7) has anti-foam properties. Moreover, in view of the different systems and conditions referred to above, the board is also convinced that none of the factors referred to by the appellant (type of sample, PCR conditions, etc.) would have led the skilled person to think otherwise.

10. The appellant also argued that due to several factors, in particular the specific sample (pure bacterial culture with heaviest growth) and PCR conditions used in the PCR assay described in document (7), it could not be ascertained beyond doubt that Triton X-100 acted as an anti-foam reagent in said PCR assay. In this context, the appellant referred to the established case law that, for acknowledging lack of novelty, required a

prior art document to directly and unambiguously disclose all necessary features. The board agrees with the appellant that, for the purpose of assessing novelty, a much stricter standard than the so-called "balance of probabilities" has to be applied. However, in the board's view, the standard to apply is not absolute certainty. What is required is not "beyond any (possible) doubt" but "beyond any reasonable doubt" (cf. "Case Law" *supra*, I.C.3.5.2.a), 100; see, for instance, T 2451/13 of 14 January 2016, point 3.2.4 of the Reasons in relation to the publication date of a document).

11. As stated above, claim 1 does not define any particular amount of anti-foam reagent but only an "effective amount". Nor does claim 1 require the anti-foam reagent to provide any particular level or extent of suppression of foaming/bubble formation, let alone an optimal one. Therefore, any amount providing a suppression, no matter how small this suppression may be, has to be considered as an "effective amount" within the meaning of claim 1. In view thereof and of the disclosure of document (7), the board is convinced - beyond any reasonable doubt - that the surfactant Triton X-100 present in the PCR assay described in document (7) acts as an anti-foaming reagent as defined in claim 1.

12. It follows from the above considerations, that the subject-matter of claim 1 of the main request and of auxiliary request 1 lacks novelty over the disclosure of document (7).

Auxiliary request 2

Article 123(2) EPC

13. Claim 1 of this request requires the presence of "an effective amount of at least one anti-foam reagent" that "suppresses foaming/bubble formation" and "does not substantially inhibit the action of the polymerase". The disclosure on page 12, lines 19 and 22 of the patent application has been cited as providing the basis for all these features.

14. According to the passage on page 12, an "effective amount" of an anti-foam reagent in a reaction mixture is defined as "an amount or concentration that suppresses foaming/bubble formation to an extent necessary to permit accurate optical analysis of the reaction mixture or accurate fluid handling, especially of small volumes of reaction mixture, but that does not substantially inhibit enzyme activity in the reaction mixture" (cf. page 12, lines 20 to 24 of the patent application). In view of this disclosure, the board considers that:
 - 14.1 The new features of claim 1 have been taken from the description of the patent application but, whilst they are of a relative nature in the description, i.e. the foaming/bubble formation is suppressed to a certain extent, this is not the case for claim 1 which requires the effective amount of anti-foaming reagent to provide a complete suppression of foaming/bubble formation. The introduction into claim 1 of only part of the definition of an effective amount of at least one anti-foam reagent results in an amendment that introduces subject-matter which, as such, is not disclosed and has no basis in the patent application.

- 14.2 As a consequence of the amendment, the anti-foam reagents referred to in claim 1 are limited to those achieving a complete suppression of foaming/bubble formation while not substantially inhibiting the action of the polymerase. These requirements may not be fulfilled by all possible anti-foam reagents and thus, claim 1 defines a subgroup of anti-foam reagents that, as such, is not disclosed in the patent application. Moreover, even if this subgroup of anti-foam reagents may be comprised within the group of more generally defined anti-foam reagents disclosed in the patent application, the amount or concentration of any reagents required for achieving a complete suppression of foaming/bubble formation is different from the amount required to achieve only a partial suppression still permitting accurate optical analysis of the reaction mixture or accurate fluid handling. Thus, claim 1 defines a subrange of concentrations that, as such, is not disclosed in the patent application.
15. Therefore, claim 1 of auxiliary request 2 contravenes Article 123(2) EPC.

Auxiliary request 3

Admission of the objection raised under Article 84 EPC

16. In its communication, the board observed that the arguments on which the respondent based its objection under Article 84 EPC in appeal proceedings, were different from those on which the objection under this article was based at first instance proceedings. As a consequence thereof, there was neither a decision of the opposition division nor any arguments from the appellant on this issue on file. Moreover, no reasons were provided by the respondent why these arguments

were not put forward at an earlier stage of the proceedings.

17. In reply thereto, the respondent provided reasons for admitting the objection of lack of clarity into the appeal proceedings. The appellant provided neither written nor oral submissions on this issue, even though the board informed the parties at the beginning of the oral proceedings that it intended to admit the objection into the proceedings.
18. There are several reasons for the board to admit the objection for lack of clarity based on arguments that were not put forward before the opposition division.
 - 18.1 First, although other arguments were taken into consideration, the objection for lack of clarity and the decision thereupon are part of the first instance proceedings. The new arguments on which the objection for lack of clarity is based, have been filed at the earliest stage of the appeal proceedings, namely in reply to the appellant's statement of grounds of appeal (Articles 12(1)(b) and 12(2) RPBA).
 - 18.2 Second, the feature objected to for lack of clarity in opposition proceedings and that objected to in appeal proceedings have the same basis on page 12, lines 19 to 24 of the patent application. The term "accurate", considered unclear by the respondent in appeal proceedings, qualifies the two properties, namely optical analysis and fluid handling, that define the effective amount of anti-foam reagent which the respondent considered unclear in opposition proceedings. In this sense, the features objected to in opposition and in appeal proceedings are directly related and in a contextual relationship.

18.3 Third, claim 1 does not result from a simple combination of granted claims but it has been amended by the introduction of a feature taken from the description of the patent application. According to decisions G 9/91 and G 10/91 (OJ EPO 1993, 408 and 420), for this type of amendments, the formal requirements, in particular those of Articles 123(2) and 84 EPC, for subject-matter arising directly from these amendments must always be examined (see also G 3/14, OJ EPO 2015, A102, points 14 to 17 of the Reasons).

19. In view thereof, the board, in the exercise of its discretion (Article 114(1) EPC), admits the new arguments and thus, the objection for lack of clarity based thereupon, into the appeal proceedings.

Article 84 EPC

20. The objection for lack of clarity arises from the use of the term "accurate" in claim 1.

20.1 "Accurate" is a relative term qualifying a technical feature or property. In the board's view, the term may be unclear, ambiguous or open to interpretation, depending on said feature or property and the technical field associated therewith. Whilst for some properties, the meaning of "accurate" may be well established in a particular technical field, for the same properties in other technical fields or for other properties in the same or other technical fields, the term may not be so well established. Thus, a certain degree of ambiguity may arise even for a skilled person reading the claim with a mind willing to understand (cf. T 190/99 of

6 March 2001, Catchword and point 2.4 of the Reasons; see also "Case Law", *supra*, II.A.6.1 *et seq.*, 287).

20.2 The term "accurate" qualifies two properties in claim 1, namely optical analysis and fluid handling. These properties limit the extent of suppression of foaming/bubble formation that may be achieved by an effective amount of the anti-foam reagent. The board is not convinced that the level of "accuracy" for these two properties is so well established in the technical field under consideration that no ambiguity arises from the wording of this claim. There is no information in the patent application concerning the (standard, common) level of accuracy for any of these properties. Nor is this information directly and unambiguously derivable from the prior art on file.

20.3 Moreover, the wording of claim 1 ("to an extent necessary to permit accurate optical analysis ... or accurate fluid handling") does not require the use of anti-foam agents in such amounts that both conditions are met. Whilst one of them must be "accurate", the other need not. Thus, the amount of anti-foam reagent may, for example, suppress foaming/bubble formation to an extent necessary to permit "accurate" fluid handling but not necessarily to permit an "accurate" optical analysis of the reaction mixture. In the board's view, such a method would not be suitable for optical detection, in particular when using fluorescent (nucleic-acid binding) dyes as specified in the dependent claims. Since both properties are essential features for performing the method of claim 1, the proposed amendment insufficiently defines the claimed invention (cf. "Case Law", *supra*, II.A.3.2, 272).

21. For these reasons, claim 1 does not fulfil the requirements of Article 84 EPC.

Auxiliary request 4

Article 83 EPC

22. Claim 1 of this request requires the "anti-foam reagent" to be selected from a group of anti-foam reagents designated by trademarks, namely "1520-US, AF, FG-10, 0-30, SE-15, and Antifoam B". This group of anti-foam reagents was already defined in claims 8 and 9 as granted. Thus, claim 1 of auxiliary request 4 results from a simple combination of granted claim 1 with granted dependent claims 8 and 9.
23. With reference to decisions T 270/11 and T 623/91, *supra*, the opposition division decided that, since the chemical composition of the products designated by trademarks was not available to the skilled person and there was no evidence on file that their composition remained constant during the lifetime of the patent, the skilled person could not readily reproduce the claimed subject-matter. Therefore, the requirements of Article 83 EPC were not fulfilled (cf. page 20, points 17.3 and 17.4 of the decision under appeal).
24. The decisions cited by the opposition division are concerned with Article 84 EPC and not Article 83 EPC. This is also the case for most of the decisions of the case law dealing with the issue of trademarks or trade names in the claims (cf. "Case Law", *supra*, II.A.3.1, 271, third paragraph). However, the case law acknowledges that there is a relationship between both articles (cf. "Case Law", *supra*, II.C.7, 356) and that an ambiguity can lead to an objection of insufficiency

of disclosure if, as stated in decision T 608/07, *supra*, this ambiguity deprives the skilled person of the promise of the invention.

25. Indeed, some decisions - cited at first instance and in appeal proceedings - explicitly refer to Article 83 EPC (cf. T 667/94, *supra*, point 4 of the Reasons; T 325/13, *supra*, point 2 of the Reasons; and T 1383/10 of 24 June 2014, point 12.1.ii) of the Reasons). In these cases, the competent board considered that, when the products designated by trademarks are essential for carrying out the invention, the requirements of Article 83 EPC are fulfilled, if these products are available to the skilled person not only at the priority and filing dates of the patent but also during its whole lifetime. In fact, the public availability of a product essential for reproducing an invention during the whole lifetime of a patent is a well acknowledged requirement of Article 83 EPC. For inventions involving the use of a biological material which cannot be described in such a manner as to enable the invention to be carried out by a person skilled in the art, a deposit of this biological material with a recognised depositary institution is always required (Rule 31 EPC) and must be available to the public during the whole lifetime of the patent (cf. Rules 32 to 34 EPC, see the reference to twenty years in Rule 32(1)(b) EPC).
26. In the present case, it is common ground between the parties that the method of claim 1 provides different effects and results depending on the specific anti-foam reagent selected from the group of reagents mentioned in the claim (cf. *inter alia*, Tables 2 and 3 of the patent). Therefore, in order to reproduce the claimed method, each one of the anti-foam reagents is essential and must be available during the whole lifetime of the

patent. Whilst it is common ground between the parties that all of them were commercially available at the priority and filing dates of the patent, their availability up to the end of the patent term was disputed.

27. Documents (18) and (19) are product information sheets from Dow Corning and Sigma for the trademark products "Antifoam 1520-US" (document (18)), "Antifoam B", "O-30", and "SE-15" (document (19)). "Antifoam 1520-US" is described as "a 20 percent-active, food grade, silicone emulsion", and the active ingredient of the silicone anti-foam emulsions "Antifoam B" and "SE-15" is "a silicone-based polymer that has a molecular weight range of 3.200 to 16.500 Da". Document (19) refers to the presence of "non-ionic emulsifiers" in these silicone emulsions. However, no specific information is provided on the nature and amount of these emulsifiers which, moreover, are indicated to be different for each of the described silicone emulsions.

28. The chemical composition of the anti-foam reagents designated by trademarks is thus not directly and unambiguously derivable from any of these documents. Indeed, the exact composition of these anti-foam emulsions or reagents is explicitly said to be "proprietary" in document (19). In the board's view, this indication does not merely signal to the public that this information belongs to the commercial supplier of these reagents, but that the exact chemical composition of these reagents is deliberately not described and intended to be kept under lock and key. In view thereof, the board considers that there can be no certainty that the composition of these anti-foam reagents will remain unchanged for the whole lifetime of the patent. Contrary to the case underlying decision

T 623/91, *supra*, there is no evidence on file to support the argument that a change in the exact composition of these anti-foam reagents necessarily results in a change of the corresponding trade name.

29. With reference to decision G 1/92, *supra*, the appellant further argued that, even if the exact composition of the anti-foam reagents cited in claim 1 was not described in documents (18) and (19), their composition was made available to the skilled person by the availability of the commercial products. The skilled person could easily analyse them by conventional techniques.
30. Decision G 1/92 is concerned with novelty (Article 54 EPC) and it is within the assessment of this article that the discussion arose whether or not "a product put on the market" is "made available to the public". According to this decision, the information as to the chemical composition of a commercially available product is considered to be available if direct and unambiguous access to such information is possible by means of analytical techniques well-known and easily available to the skilled person, i.e. without undue burden or excessive experimentation, irrespective of whether or not particular reasons can be identified for analysing said composition (cf. "Case Law", *supra*, I.C.3.2.4.d), 88).
31. Article 83 EPC requires the patent application to be sufficiently clear and complete for the invention to be carried out by a person skilled in the art. The skilled person may use its common general knowledge to supplement the information contained in the patent application (cf. "Case Law", *supra*, II.C.3, 330). This common general knowledge has been defined by the Boards

of Appeal in the context of Articles 54 and 56 EPC (cf. "Case Law", *supra*, I.C.2.8, 75, and I.D.8.3, 195). The board considers that the chemical composition of a commercially available product, here the anti-foam reagents designated by the trademarks in claim 1, may be part of the common general knowledge of a skilled person, only and exclusively, if all the conditions set out in decision G 1/92 are fulfilled.

32. It is common ground between the parties that the chemical composition of the anti-foam reagents cited in claim 1 is made available to the skilled person, if at all, only by being commercially available. It is thus necessary to assess whether the conditions set out in decision G 1/92 are fulfilled in the present case. Documents (18) and (19) provide only a partial characterization of these reagents and, for some of them, the active ingredient is stated to be "a silicone-based polymer". In the polymer field, the requirements of sufficiency of disclosure must be analysed with particular care. In decision T 1833/14 (*supra*), with reference to decision G 1/92, the board considered these requirements and, in view of the relevance of the nature of the catalyst system, the type of reaction system and the process conditions for the properties of the produced polymer, concluded that, in the absence of a disclosure of the method of preparation of the polymer, the mere disposal of a sample was not sufficient for a skilled person to be able to prepare it (cf. T 1833/14, *supra*, point 1 of the Reasons, in particular point 1.6).
33. In the present case, the board is convinced that the commercial availability of the anti-foam reagents mentioned in claim 1 does not make available the methods of preparation of these anti-foam reagents nor

is their chemical composition available to the public because information about the chemical composition of these reagents is "proprietary". Moreover, in line with the above cited case law, undue burden and excessive experimentation is required for analysing the exact chemical composition of these silicone polymer and emulsifier based anti-foam reagents.

34. Since the conditions set out in decision G 1/92 are not fulfilled, claim 1 does not fulfil the requirements of Article 83 EPC.

Auxiliary request 5

Admission into the appeal proceedings

35. This request was filed in reply to the board's communication and shortly before the date of the oral proceedings. Thus, auxiliary request 5 represents an amendment of the appellant's case and, according to Articles 13(1) and 13(3) RPBA, its admission into the proceedings is at the board's discretion.
36. Except for the deletion of the anti-foam reagents "AF, FG-10, O-30, and SE-15", claim 1 of this request is identical to claim 1 of auxiliary request 4. The anti-foam reagents in claim 1, namely "1520-US" and "Antifoam B" (described in documents (18) and (19), respectively), are silicone-based polymers of synthetic origin. In the board's view, the amendment introduced into auxiliary request 5 is based on an arbitrary selection of anti-foam reagents which cannot be regarded as the direct and unambiguous consequence of the discussion of auxiliary request 4 and the disclosure of documents (18) and (19). In this sense, the amendment comes as a surprise to the respondent - shortly before the oral proceedings. Moreover, the

amendment seems unsuitable to overcome the objection raised under Article 83 EPC against auxiliary request 4. The admission of auxiliary request 5 at this stage of the proceedings may therefore result in the respondent being confronted with arguments that have not been put forward at an earlier stage of the appeal proceedings.

37. Thus, the board, in the exercise of its discretion (Articles 13(1) and 13(3) RPBA), does not admit auxiliary request 5 into the appeal proceedings.

Auxiliary request 6

38. Claim 1 of this request combines the amendments introduced into claim 1 of auxiliary requests 3 and 4. Therefore, the board's conclusions in respect of the objections raised under Article 84 EPC against claim 1 of auxiliary request 3 and under Article 83 EPC against claim 1 of auxiliary request 4 equally apply to claim 1 of auxiliary request 6.

39. Thus, claim 1 of auxiliary request 6 does not fulfil the requirements of Articles 84 and 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



L. Stridde

B. Stolz

Decision electronically authenticated