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Datasheet for the decision of 21 March 2025

Case Number: T 1554/23 - 3.3.05

Application Number: 18189498.1

Publication Number: 3610947

IPC: B01L7/00, B01L3/00

Language of the proceedings: EN

Title of invention:
MICROFLUIDIC SYSTEM FOR DIGITAL POLYMERASE CHAIN REACTION OF A BIOLOGICAL SAMPLE, AND RESPECTIVE METHOD

Patent Proprietors:
1.F. Hoffmann-La Roche AG
2.Roche Diagnostics GmbH

Opponent:
Bio-Rad Laboratories, Inc.

Headword:
Microfluidic system/ROCHE

Relevant legal provisions:
EPC Art. 56, 83, 84, 123(2)
EPC R. 80
RPBA 2020 Art. 12(4), 13(2)

Keyword:

Decisions cited:
G 0003/14, T 2433/13, T 0792/00, T 1076/21, T 1596/16

Catchword:

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Case Number: T 1554/23 - 3.3.05

D E C I S I O N
of Technical Board of Appeal 3.3.05
of 21 March 2025

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Appellant 1: (Patent Proprietor 2)	Roche Diagnostics GmbH Sandhofer Straße 116 68305 Mannheim (DE)
Representative:	Simmons & Simmons LLP (Munich) Lehel Carré Gewürzmühlstraße 11 80538 Munich (DE)
Appellant 2: (Opponent)	Bio-Rad Laboratories, Inc. 1000 Alfred Nobel Drive Hercules CA 94547 (US)
Representative:	dompatent von Kreisler Selting Werner - Partnerschaft von Patent- und Rechtsanwälten mbB Deichmannhaus am Dom Bahnhofsvorplatz 1 50667 Köln (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 June 2023 concerning maintenance of the European Patent No. 3610947 in amended form.**

Composition of the Board:

Chairman	T. Burkhardt
Members:	J. Roider
	O. Loizou

Summary of Facts and Submissions

I. The appeals by patent proprietors 1 and 2 (appellants 1) and the opponent (appellant 2) lie from the interlocutory decision of the opposition division to maintain European patent EP 3 610 947 B1 in amended form in accordance with auxiliary request 1.

II. The following documents are relevant here:

D1	US 2003/0138819 A1
D5	US 2018/0221875 A1
D7	WO 2018/094091 A1
D10	US 2007/0144253 A1 (referred to as D9 by the opponent)

III. Claim 1 of the main request in the appeal procedure (filed as auxiliary request 1a with the patent proprietors' statement of grounds of appeal) reads as follows (differences with respect to claim 1 of auxiliary request 1 as maintained by the opposition division are underlined or in strikethrough, emphasis added by the board):

"1. A method for digital polymerase chain reaction dPCR of a biological sample in a microfluidic system (1; 1') for digital polymerase chain reaction dPCR of a biological sample,
the microfluidic system (1; 1') comprising:
at least one microfluidic device (2) having an inlet (23), an outlet (24), a flow channel (25) connecting the inlet (23) to the outlet (24), and an array of reaction areas (26) in fluidic communication with the flow channel (25);

a flow circuit (3) connectable to the microfluidic device (2), for flowing liquid through the flow channel (25) of the microfluidic device (2);
a sample liquid source connectable to the microfluidic device (2), for providing the microfluidic device (2) with a sample liquid (27);
a primary sealing liquid source connectable to the microfluidic device (2), for providing the microfluidic device (2) with initial sealing liquid (28) for sealing the sample liquid (27) inside the array of reaction areas (26);
a secondary sealing liquid source (4) connectable to the microfluidic device (2), for providing the microfluidic device (2) with additional sealing liquid (29), and
a pumping means (31) connected to the flow circuit (3) and adapted to pump said additional sealing liquid (29) through the flow channel (25),
and a control unit configured to control the pumping means (31) to pump said additional sealing liquid (29) through the flow channel (25) on demand, for flushing gas bubbles out of the flow channel (25), wherein the method comprises:
a step of streaming a sample liquid (27) through the flow channel (25) of the microfluidic device (2), in particular provided in the form of a microfluidic chip, and filling the array of reaction areas (26) with the sample liquid (27) in a successive manner by pushing the sample liquid (27) through the flow channel (25);
~~characterised in that~~ wherein the method further comprises:
a step of streaming an initial sealing liquid (28) through the flow channel (25) of the microfluidic device (2) for sealing each reaction area of the array of reaction areas (26) after the same has been filled with the sample liquid (27), and for pushing remaining

sample liquid (27) out of the microfluidic device (2), a step of applying a thermocycling temperature profile to the array of reaction areas (26), and a step of pumping additional sealing liquid (29) through the flow channel (25) of the microfluidic device (2), for flushing gas bubbles out of the flow channel (25)."

Dependent claims 2 to 5 concern particular embodiments of claim 1.

IV. The key arguments of the patent proprietors can be summarised as follows:

The amendments in claim 1 of the main request were occasioned by a ground of opposition and a reaction to an objection under Article 84 EPC. The objection under Article 123(2) EPC should not be admitted, and the further objection under Article 84 EPC was not admissible in view of G 3/14.
The patent in suit was moreover sufficiently disclosed and the subject-matter of claim 1 involved an inventive step.

V. The key arguments of the opponent can be summarised as follows:

The main request should not be admitted (Article 12(4) and (6) RPBA) because it was an amendment to the case and did not meet the requirements of Article 84 EPC, Article 123(2) EPC or Rule 80 EPC.
The patent in suit was moreover insufficiently disclosed (Article 83 EPC), and claim 1 of the main request lacked an inventive step (Article 56 EPC) starting from D1, in view of common general knowledge,

D5, D7 or D10.

VI. Substantive requests:

(a) The appellants 1 (patent proprietors 1 and 2) requested that the decision under appeal be set aside and the patent be maintained in amended form according to the set of claims of the main request (previously filed with the statement of grounds of appeal as auxiliary request 1a) or one of auxiliary requests 2-12, filed for the first time with the statement of grounds of appeal or, on the basis of one of auxiliary requests 13-23, resubmitted with the statement of grounds of appeal.

(b) The appellant 2 (opponent) requested that the decision under appeal be set aside and the patent be revoked.

Reasons for the Decision

1. Admission of main request, Article 12(4) and (6) RPBA

1.1 The main request was first filed as auxiliary request 1a with the patent proprietors' statement of grounds of appeal.

Compared with auxiliary request 1 as maintained by the opposition division, the expression "characterised in that the method further comprises" has been replaced by "wherein the method further comprises".

1.2 The opponent requested that the main request not be admitted, under Articles 12(4) and (6) RPBA. Already in its statement of grounds of appeal, it argued with

regard to auxiliary request 1 then on file that the mixture of product and method steps and in particular the step of streaming a sample liquid through the flow channel rendered claim 1 unclear (2nd and 3rd paragraphs of page 5 of the opponent's grounds of appeal), these features also being present in the current main request. In a letter of 21 February 2025 it further argued that the current main request also did not meet the requirements of Article 123(2) EPC. In the oral proceedings, it argued that for these reasons the main request should not be admitted into the proceedings.

1.3 Since the main request was not filed in the proceedings leading to the decision under appeal, it constitutes an amendment of the case and may be admitted only at the discretion of the board.

The board shall exercise its discretion in view of, *inter alia*, the complexity of the amendment, the suitability of the amendment to address the issues, and the need for procedural economy (Article 12(4) RPBA).

1.4 As apparent from points 2. and 3. below, the objection under Article 84 EPC cannot be discussed, in line with G 3/14, and the objection under Article 123(2) EPC is not admitted, under Article 13(2) RPBA.

1.5 It is immediately apparent that the amendment is simple and overcomes an objection under Article 84 EPC relating to the scope of the characterising portion. The opponent raised this objection against the version maintained by the opposition division, the former auxiliary request 1, which was first filed during the oral proceedings before the opposition division (point 5 of the minutes and point II.7 of the decision

under appeal).

1.6 The opponent asserted that the main request should have been filed earlier.

In the present case, this would mean that the main request should have been filed during the oral proceedings before the opposition division, after the opponent's objection under Article 84 EPC had been raised.

However, this is not necessary in the present case.

The requirements of Article 84 EPC on auxiliary request 1 then on file were discussed during the oral proceedings before the opposition division. The opposition division concluded that the requirements were met (point II.7 of the decision under appeal). In view of this outcome of the proceedings, it was not necessary for the patent proprietors to file the request back during the oral proceedings.
Auxiliary request 1a was moreover filed with the patent proprietors' statement of grounds of appeal. Therefore the opponent had sufficient time to reply. It obviously presented its case against auxiliary request 1a in its reply of 6 March 2024. Unfair treatment due to the admittance of auxiliary request 1a cannot be seen.

Hence the main request was admitted into the appeal proceedings (Article 12(4) RPBA).

2. Clarity, Article 84 EPC

The opponent argued that the mixture of system and method features rendered claim 1 of the main request

unclear.

However, the subject-matter of claim 1 is not open to an objection under Article 84 EPC (G 3/14, point 80).

Method claim 1 of the main request is based on method claim 14 as granted, incorporating all the features of system claim 1 as granted.

Method claim 14 as granted related to *"A method for digital polymerase chain reaction dPCR of a biological sample in a microfluidic system (1; 1') according to any one of the preceding claims ..."*, therefore making reference *inter alia* to system claim 1 as granted. According to Rule 43(4) EPC, method claim 14 as granted therefore contained all the features of claim 1 as granted.
Claim 1 of the main request therefore explicitly contains the features which were contained in claim 14 as granted only by reference to claim 1.
Therefore claim 1 of the main request is a claim as granted and as such not open to an objection under Article 84 EPC (G 3/14, point 80).

3. Amendments, Article 123(2) EPC

In the letter of 21 February 2025, i.e. subsequent to the communication under Article 15(1) RPBA, the opponent raised an objection under Article 123(2) EPC. According to its view, method claim 1, by referring to a microfluidic chip, constituted an intermediate generalisation. Claim 1 of the main request resulted from the incorporation of system claim 1 of the patent into method claim 14 of the patent.
However, a microfluidic chip was not mentioned until dependent system claim 8 of the patent, and only in

combination with other features. Claim 14 of the patent referred to a microfluidic chip but did not contain the other features of dependent claim 8 of the patent, which resulted in an intermediate generalisation.

However, an objection under Article 123(2) EPC had been raised neither in the statement of grounds of appeal nor in the subsequent reply, so its admittance is subject to Article 13(2) RPBA.

The opponent argued that this objection ensued implicitly from page 5, second paragraph of the statement of grounds of appeal.

This is however not convincing.

The cited paragraph of the opponent's statement of grounds of appeal is part of an objection under Article 84 EPC. There, the opponent objected that, in its view, auxiliary request 1 was a *"wild mixture"* of a product and method steps. The opponent goes on to state that *"In particular, the step of streaming a sample liquid through the flow channel as being provided in the form of a microfluidic step introduces doubts about the scope of the method claimed."*

In the patent proprietors' view, it was clear that a microfluidic chip was meant in this sentence, not a microfluidic step.
However, nothing in this paragraph suggests that a microfluidic chip was meant. Moreover, there is nothing in this paragraph to suggest that the objection should be applied *mutatis mutandis* to Article 123(2) EPC, in particular with regard to dependent system claim 8. The mere fact that claim 1 comprises both method and product features does not in itself extend the subject-

matter beyond what was originally disclosed. The opponent has not shown that this was the case for claim 1.

It cannot therefore be acknowledged that the objection under Article 123(2) EPC was already implicitly raised in the statement of grounds of appeal.

The opponent did not invoke exceptional circumstances, let alone cogent reasons, for the late submission of the new objection.

Therefore the objection under Article 123(2) EPC is not admitted into the proceedings (Article 13(2) RPBA).

3.1 Rule 80 EPC

Compared with the claims as granted, the main request does not contain system claims. The deletion of the system claims was occasioned by a ground of opposition. Claim 1 of the main request is based on method claim 14 as granted, with the reference to the system claims contained at the outset of method claim 14's text being replaced by the text of system claim 1. Claim 1 of the main request is therefore a combination of claims 14 and 1 as granted.

System claim 1 as granted had included the words "characterized in that". If the system claim had been incorporated into the method claim without modification, the words "characterized in that" would have been placed inappropriately, since the characterising portion would at least have included the step of thermocycling, which is known from D1. Therefore the deletion of these words in the method

claim must be regarded as a consequence of the amendment *as a whole* (T 2433/13, point 1.5).

The amendment complies with Rule 80 EPC.

4. Sufficiency of disclosure, Article 83 EPC

The opponent argued that all the sealing liquids referred to in the patent in suit were generic and covered a vast number of different compounds with different physico-chemical properties. The patent in suit also covered methods utilising two different sealing liquids for the initial sealing liquid and the additional sealing liquid. The patent did not provide any information that would assist the skilled person to select a suitable combination of different sealing liquids. Finding such sealing liquids would require a research project, and was therefore an undue burden. For this reason, the burden to prove that the patent was sufficiently disclosed lay upon the patent proprietors.

In their reply, the patent proprietors argued that the patent in suit provided guidance and indicated some example combinations of different sealing liquids.

For the reasons set out below, the invention is sufficiently disclosed.

The claims of the main request are a combination of claims 1 and 14 of the granted patent. It is therefore incumbent on the opponent to provide facts, arguments and evidence to support the assertion of insufficiency.

Sealing liquids must be suitable to seal the sample

liquid. It is not disputed that such liquids are readily known to the skilled person. Rather, the opponent challenged that the skilled person was not able to suitably select the additional sealing liquid for flushing bubbles. It argued that whether it would be possible to flush bubbles might depend on the exact behaviour of the additional sealing liquid with respect to the first sealing liquid. However, the patent in suit disclosed no example or guidance for the selection of such an additional sealing liquid.

The opponent did not present any evidence to demonstrate that, despite the due consideration of the known physico-chemical properties of the sealing liquids and the sample, the implementation of the invention was unsuccessful for two different sealing liquids. The patent in suit did indeed not disclose requirements for the sealing liquid apart from the immiscibility with the sample liquid. It is however not immediately conceivable that some additional sealing liquids were unsuitable for flushing bubbles when used in combination with another sealing liquid.

T 792/00, cited by the opponent, is not relevant in the present context because the case underlying the above decision relates to a situation where what is claimed is something which, according to prevailing technical opinion at the priority date, would not be possible (see Catchword and point 3 of the decision). The opponent did however not show that, according to the prevailing technical opinion, flushing gas bubbles from the microchannel with an additional sealing liquid different from the first sealing liquid was considered impossible.

The opponent did not show that the selection of the

additional sealing liquid involved an undue burden. It particularly did not present a single example showing that flushing the bubbles from the microchannel using an additional sealing liquid different from the sealing liquid was not successful. Therefore any allegation to this effect appears speculative (see T 1076/21, point 1.1.7; T 1596/16, point 2.2).

The requirements of Article 83 EPC are met.

5. Inventive step, Article 56 EPC

5.1 The patent in suit is directed to a method for digital polymerase chain reaction (dPCR) of a biological sample in a microfluidic system.

5.2 The parties agreed that D1 is to be considered as the most appropriate starting point for an inventive-step objection.

As D1 also relates to a method for PCR (see for example paragraph [0060]), it is indeed a reasonable starting point for assessing inventive step.

5.3 The problem that the patent in suit seeks to solve is to provide an improved method for avoiding and/or removing gas bubbles in microfluidic dPCR systems (patent in suit, paragraph [0013], last sentence).

5.4 It is proposed to solve the problem by the features of claim 1, which differ from D1 at least by *a step of pumping additional sealing liquid (29) through the flow channel (25) of the microfluidic device (2), for flushing gas bubbles out of the flow channel (25).*

The parties agreed that the subject-matter of claim 1

differs from D1 at least in this respect (opponent's statement of grounds of appeal, page 5, penultimate paragraph; patent proprietors' statement of grounds of appeal, page 10, paragraph e) 2.).

5.5 There is no doubt that flushing the bubbles out of the flow channel with the additional sealing liquid solves the problem as stated in the patent in suit. However, D1 also proposes solutions for the avoidance of gas bubbles (see impugned decision, paragraph 10.3.3, referring to D1, paragraphs [0152], [0140] and [0134]), but which are different from the solution of claim 1.

The technical problem as stated in the patent in suit is therefore already solved in D1 and must therefore be reformulated to a less ambitious technical problem, namely the provision of an alternative method.

The opponent argued that the patent did not solve the technical problem as stated above over the whole scope. Apart from the requirement that the first and the additional sealing liquids had to be suitable to provide the sealing function, there was no other requirement for the sealing liquids. It was however not shown that the technical problem as stated above was solved with all imaginable combinations of sealing liquids.

The opponent did not show a single combination of sealing liquids in which the additional sealing liquid could not flush out trapped air bubbles. It is also questionable whether such a combination exists.

5.6 For the reasons set out below, the main request meets the requirements of Article 56 EPC.

5.6.1 Starting from D1, in view of common general knowledge

The opponent argued that D1, paragraphs [0060] and [0140] already led the skilled person to the claimed subject-matter.

It emphasised that the isolation fluid in D1 (which corresponds to the sealing liquid in the patent in suit) was used to purge air (not air bubbles) from the *second* multipurpose channel.
It essentially argued that if there were air bubbles in the *first* multipurpose channel after the displacement of the sample liquid by the isolation fluid, it would have been obvious to the skilled person to flush them out of the first multipurpose channel by supplying isolation fluid again.

This is not convincing.

The second multipurpose channel is completely filled with air before the isolation fluid is introduced. Therefore the air in the *second* multipurpose channel is displaced by the isolation fluid in a similar way to the sample fluid in the *first* multipurpose channel.

The flushing of air bubbles is not rendered obvious by this disclosure.

Moreover, D1 proposes for example bevelled edges to avoid the air bubble formation at 90° edges in the *second* multipurpose channel (D1: paragraph [0152], Fig. 14). If the skilled person were to avoid the formation of air bubbles in the *first* multipurpose channel as well, they would, rather, use the solution proposed for the *second* multipurpose channel.

However, flushing air bubbles in the isolation fluid contained in the *first* multipurpose channel is not rendered obvious by D1.

5.6.2 Starting from D1, in view of D5

D5, paragraph [0008], to which the opponent refers, discloses removing the excess aqueous sample with a displacement fluid. A high-melting sealing agent is subsequently applied to the inlet port only. Paragraph [0054], to which the opponent referred, discloses that both the outlet port and the inlet port are sealed with a solidifying sealing agent.

D5, paragraph [0032] describes the purpose of this seal. The sealing agent melts during the thermocycle and allows for the passage of gases through the inlet port. Paragraph [0044] discloses that pressure on the microfluidic chip from the outside, i.e. by placing it in a pressurised chamber, facilitates the gas exchange.

The opponent could not show a passage in D5 disclosing flushing of gas bubbles. D5 does not disclose flushing bubbles out of the flow channel.

Even if the skilled person were to start from D1 and combine with it the teaching of D5, they would not arrive at the subject-matter of claim 1.

5.6.3 Starting from D1, in view of D7

The opponent argued that the skilled person would recognise from D7 that the elevated temperatures typically applied in the PCR reaction may lead to the formation and/or expansion of air bubbles within the reaction compartments.

It concluded that it would be obvious to the skilled person that the measures in D1 cannot avoid the formation of bubbles in the reaction compartment. Therefore the skilled person would use an isolation medium to flush the bubbles out of the multipurpose channel, all the more so since the isolation medium was immiscible with the sample liquid and could be used to flush air from the second multipurpose channel.

This is not convincing.

The temperatures disclosed in D7 are comparable with the temperature disclosed in D1, paragraph [0115]. There is nothing in D1 to suggest that the measures proposed therein are in sufficient for these temperatures, as alleged by the opponent. Similarly, the conclusion that it was obvious to the skilled person that the isolation medium could also be used to flush the bubbles, because it had certain properties and was used for other purposes, stems from a hindsight consideration.

5.6.4 Starting from D1, in view of D10

Claim 1 corresponds to independent claim 14 as granted.

D10 discloses a dispenser for sample fluid to be dispensed into a cup or a test chip. The dispenser is not a microfluidic device. Air sucked into the dispenser will cause detection errors. If a sensor detects air bubbles, they are flushed out of the dispenser by dedicated means.

Nothing is apparent that would lead the skilled person to consider this document in the context of the microfluidic device of the patent in suit.

The admission of D10 is therefore of no relevance.

5.7 Since the dependent claims contain all the features of independent claim 1, they share the assessment with respect to Article 56 EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside. The case is remitted to the opposition division with the order to maintain the patent in amended form according to the set of claims of the main request (previously filed with the statement of grounds of appeal as auxiliary request 1a) and a description to be adapted.

The Registrar: The Chairman:

C. Vodz T. Burkhardt

Decision electronically authenticated

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Case Number: T 1554/23 - 3.3.05

D E C I S I O N
of the Technical Board of Appeal 3.3.05
of 1 July 2025
correcting an error in the decision
of 21 March 2025

Appellant: (Patent Proprietor 1)	F. Hoffmann-La Roche AG Grenzacherstrasse 124 4070 Basel (CH)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 June 2023 concerning maintenance of the European Patent No. 3610947 in amended form.**

Composition of the Board:

Chairman:	T. Burkhardt
Members:	J. Roider
	O. Loizou

By letter of 25 June 2025, the patent proprietors requested the correction of a sentence in the last paragraph of page 8 of the decision of 21 March 2025.

The sentence for which the correction is requested reads:

> *"In the patent proprietors' view, it was clear that a microfluidic chip was meant in this sentence, not a microfluidic step."*

This sentence is amongst the summary of the opponent's arguments relating to the admittance under Article 13(2) RPBA of the objection under Article 123(2) EPC.

It is therefore immediately evident that the argument was submitted by the opponent.

Based on Rule 140 EPC, according to which obvious mistakes in decisions of the EPO may be corrected, the sentence is corrected in line with the patent proprietors' request so as to read:

> *"In the opponent's view, it was clear that a microfluidic chip was meant in this sentence, not a microfluidic step."*

The Registrar: The Chairman:

C. Vodz T. Burkhardt

Decision electronically authenticated