Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 20 November 2017

Case Number: T 1957/15 - 3.3.05

Application Number: 09798914.9

Publication Number: 2358906

IPC: C12Q1/68

Language of the proceedings: EN

Title of invention:
SYSTEM AND INSTRUMENT FOR PROCESSING BIOLOGICAL SAMPLES AND MANIPULATING LIQUIDS HAVING BIOLOGICAL SAMPLES

Patent Proprietor:
Tecan Trading AG

Opponent:
Illumina, Inc.

Headword:
Manipulating Liquids/TECAN

Relevant legal provisions:
EPC Art. 54(1), 54(2), 56
RPBA Art. 13(1), 13(3)

Keyword:
Late-filed request - admitted (yes)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1957/15 - 3.3.05

D E C I S I O N
of Technical Board of Appeal 3.3.05
of 20 November 2017

Appellant 1: (Patent Proprietor)	Tecan Trading AG Seestrasse 103 8708 Männedorf (CH)
Representative:	OK pat AG Industriestrasse 47 6300 Zug (CH)
Appellant 2: (Opponent)	Illumina, Inc. 5200 Illumina Way San Diego, CA 92122 (US)
Representative:	Cooley (UK) LLP Dashwood 69 Old Broad Street London EC2M 1QS (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 28 July 2015 concerning maintenance of the European Patent No. 2358906 in amended form.**

Composition of the Board:

Chairman	G. Glod
Members:	A. Haderlein
	O. Loizou

Summary of Facts and Submissions

I. The present appeals of the proprietor (appellant 1) and of the opponent (appellant 2) lie from the opposition division's interlocutory decision finding that European patent No. 2 358 906 in amended form, and the invention to which it relates meet, the requirements of the EPC. The patent in suit concerns a system and instrument for processing biological samples and manipulating liquids having biological samples.

II. The opposition division held *inter alia* that the main request underlying the impugned decision lacked clarity and that the subject-matter of its claims 1 and 30, corresponding to claims 1 and 30 as granted, lacked an inventive step when starting from

E1: WO2007/123908 A2

as the closest prior art.

The following documents among others were cited in the proceedings before the opposition division:

E4: WO 2008/106678 A1
E5: Sista, R., et al., Development of a digital microfluidic platform for point of care testing, Lab on a Chip, 2008, 8, 2091-2104
E12: WO 2007/120240 A2.

III. With its grounds of appeal, appellant 1 filed a main request corresponding to the main request underlying the impugned decision.

IV. With its grounds of appeal, appellant 2 filed the following document:

E13: WO 2007/120241 A2.

V. In its communication pursuant to Article 15(1) RPBA, the board informed the parties of its preliminary opinion according to which claim 16 of the then main request did not comply with the requirement of clarity.

VI. At the oral proceedings before the board, which took place in appellant 2's absence, appellant 1 filed a request titled "Main request" comprising fifteen claims as its sole request (annex 2 of the minutes to the oral proceedings).

VII. Claims 1, 13 and 15 of appellant 1's sole request are identical to claims 1, 13 and 30 of the patent as granted and read as follows:

"1. A biological sample processing system (1) comprising:
- a container (2) for large volume processing having a top side (3) and a base side (4) and comprising at least one well (6) open at the top side (3) for positioning a biological sample (9) and/or a reaction reagent (10) therein, wherein the at least one well (6) comprises a bottom side (8) having at least one opening (11), the container (2) further comprising a channel (12) connecting the opening of the well (11) with an orifice (13) on the base side (4) of the container (2), and wherein the base side (4) of the container (2) comprises protrusions (5) distributed thereon;
- a flat polymer film (14) having a lower surface (15) and a hydrophobic upper surface (16), which is kept at a distance d to the base side (4) of the container (2) by the protrusions (5), the distance d defining at least one gap (17) when the container (2) is positioned

on the film (14), abutting the latter with its protrusions (5); and
- a liquid droplet manipulation instrument (20) comprising:
· at least one electrode array (21) for inducing liquid droplet movements;
· a substrate (22) supporting the at least one electrode array (21); and
· a control unit (23) comprising at least one electrode selector (34) connected with at least one voltage control (29), the at least one electrode selector (34) being accomplished to individually select each electrode (35) of the at least one electrode array (21) and provide the selected electrode (35) with a voltage controlled by a voltage control (29);
wherein the container (2) and the film (14) are reversibly attached to the liquid droplet manipulation instrument (20), the lower surface (15) of the flat polymer film (14) thus abutting the at least one electrode array (21), the system (1) enabling displacement of at least one liquid droplet (19) from the at least one well (6) through the channel (12) of the container (2) onto the hydrophobic upper surface (16) of the flat polymer film (14) and above the at least one electrode array (21); and wherein the liquid droplet manipulation instrument (20) is accomplished to control a guided movement of said liquid droplet (19) on the hydrophobic upper surface (16) of the flat polymer film (14) by electrowetting and to process there the biological sample (9).

13. A cartridge (40) for use in a biological sample processing system (1) according to one of the claims 1 to 12, the cartridge comprising
- a container (2) having a top side (3) and a base side (4) and comprising at least one well (6) open at the

top side (3), wherein the at least one well (6) comprises a bottom side (8) having at least one opening (11), the container (2) further comprising a channel (12) connecting the opening of the well (11) with an orifice (13) on the base side (4) of the container (2), and wherein the base side (4) of the container (2) comprises protrusions (5) distributed thereon and
- a flat polymer film (14) having a lower surface (15) and a hydrophobic upper surface (16), which is kept at a distance d to the base side (4) of the container (2) by the protrusions (5), the distance d defining at least one gap (17) when the container (2) is positioned on the film (14), abutting the latter with its protrusions (5),
wherein the container (2) and the film (14) are attached to one another by gluing or welding.

15. A method for processing a biological sample (9) with a biological sample processing system (1), the system comprising:
- a container (2) for large volume processing having a top side (3) and a base side (4) and comprising at least one well (6) open at the top side (3) for positioning a biological sample (9) and/or a reaction reagent (10) therein, wherein the at least one well (6) comprises a bottom side (8) having at least one opening (11), the container (2) further comprising a channel (12) connecting the opening of the well (11) with an orifice (13) on the base side (4) of the container (2), and wherein the base side (4) of the container (2) comprises protrusions (5) distributed thereon;
- a flat polymer film (14) having a lower surface (15) and a hydrophobic upper surface (16), which is kept at a distance d to the base side (4) of the container (2) by the protrusions (5), the distance d defining at least one gap (17) when the container (2) is positioned

on the film (14), abutting the latter with its protrusions (5); and
- a liquid droplet manipulation instrument (20) comprising:
· at least one electrode array (21) for inducing liquid droplet movements;
· a substrate (22) supporting the at least one electrode array (21); and
· a control unit (23) comprising at least one electrode selector (34) connected with at least one voltage control (29), the at least one electrode selector (34) being accomplished to individually select each electrode (35) of the at least one electrode array (21) and provide the selected electrode (35) with a voltage controlled by a voltage control (29);
wherein the container (2) and the film (4) are reversibly attached to the liquid droplet manipulation instrument (20), so that the lower surface (15) of the flat polymer film (14) is abutting the at least one electrode array, and at least one liquid droplet (19) from the at least one well (6) is displaced through the channel (13) of the container (2) onto the hydrophobic upper surface (16) of the flat polymer film (14) and above the at least one electrode array (21), and wherein the liquid droplet (19) is processed by a guided movement on the hydrophobic upper surface (16) of the flat polymer film (14) by electrowetting controlled by the liquid droplet manipulation instrument (20)."

VIII. Appellant 1's arguments may be summarised as follows:

The subject-matter of all claims was novel in view of the cited prior art. E4 was the closest prior art and in particular did not disclose a container having the features called for in claim 1, claim 13 or claim 15.

None of the cited documents disclosed such a container. Moreover, it was not obvious to penetrate the reference electrode depicted in Figure 13 of E4 which would have been necessary to arrive at the subject-matter of claims 1, 13 and 15.

IX. Appellant 2's arguments may be summarised as follows:

The subject-matter of claim 1 lacked novelty in view of E1 or E5. The subject-matter of claim 13 lacked novelty in view of E5. It also lacked inventive step when starting from any of E1, E4 or E5. When starting from E4, it was obvious to arrive at the subject-matter of claim 13 because it was obvious to provide a reservoir on top of the space where the droplet is manipulated, although such a configuration was not even required by the wording of the claim. Such a configuration was known from E1, E5, E12, or from E13.

X. Requests

Appellant 1 requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the set of claims 1 to 15 of the main request, as its sole request, filed during the oral proceedings of 20 November 2017 (attached to the minutes thereof as "Annex 2").

Appellant 2 requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. Admittance of appellant 1's sole request

Appellant 1's sole request was filed during the oral proceedings. Admitting it into the proceedings was therefore at the board's discretion (Article 13(1), (3) RPBA). This request corresponds to appellant 1's main request filed with its grounds of appeal, wherein claims 14 and 16 to 21 are deleted. The amendments to the main request therefore clearly overcome the clarity objection raised (cf. IV above). They do not raise any new issue and, in particular in view of appellant 1's written submissions concerning patentability, can be said to be clearly allowable. Moreover, the amendments involving only a deletion of claims did not raise issues which the board or appellant 2, had it been present at the oral proceedings, could not reasonably have been expected to deal with without adjournment of the oral proceedings. The board therefore admitted this request into the proceedings.

2. Amendments

The claims correspond to the claims as originally filed and as granted with claims 14 and 16 to 29 being deleted and the remaining claims being renumbered where necessary. Appellant 2 did not raise any objections under Article 123(2) and (3) EPC in the grounds of appeal with respect to the more restricted request held allowable by the opposition division. The board is satisfied that these requirements are met.

3. Novelty

3.1 E1 does not disclose a cartridge suitable for reversibly attaching its container and flat polymer film to a liquid droplet manipulation instrument and wherein the cartridge itself comprises at least one gap between the base side of the container and the flat polymer film (i.e. the gap within which the droplet is manipulated). Rather, in E1 it is the liquid droplet manipulation instrument ("microactuator") which comprises this gap (cf. page 61, lines 2 et seq.: "... and the interior of the droplet microactuator for flowing reagents, sample and/or filler fluid..." (emphasis added by the board). In particular, while the passage on page 61, lines 19 et seq. discloses that the "top-plate" of the microactuator may be provided as a component of the cartridge, this does not mean that the gap is formed between this top-plate and the base of the container, because in E1 the droplet is said to be moved within the gap created by the top plate and the bottom plate of the microactuator (see page 48, lines 24 et seq.; Figure 15: "gap 1506"). Thus, in the event that the cartridge were considered to include the "top-plate" of the microactuator, this configuration would not comprise the gap for droplet manipulation being provided in the cartridge, but this gap would rather be located between the lower surface of the "top-plate" (i.e. a part of the cartridge) and the bottom surface of the microactuator, which is not a part of the cartridge. E1 also foresees the possibility to affix the entire microactuator, onto the cartridge (page 61, lines 11 and 12), but this configuration clearly does not include the reversibility called for in claim 1.

Appellant 2 is furthermore of the opinion that the

passage on page 55, lines 24 et seq. of E1 would clearly disclose a cartridge that was reversibly attachable to a liquid droplet manipulation instrument because it was common general knowledge that the polymer substrates listed in this passage were removable. This argument is however not persuasive. Firstly, said passage refers to the microactuator (cf. lines 16 et seq.), i.e. to a droplet manipulation instrument in the language of the present claims and not to a cartridge. Secondly, even assuming that the materials mentioned in this passage could be considered as "easily removable or replaceable", this does not mean that the container of the cartridge is inevitably "reversibly attached" to the liquid droplet instrument as required in claim 1.

Therefore, E1 is not novelty-destroying for the subject-matter of claim 1. The same reasoning applies *mutatis mutandis* to claims 13 and 15.

3.2 According to appellant 2, the subject-matter of claims 1 and 13 is also not novel in view of E5. In particular, appellant 2 contends that the features "the base side of the container comprises protrusions distributed thereon" and "a flat polymer film..., which is kept at a distance d to the base side of the container by the protrusions" are disclosed in E5.

3.2.1 The board notes that the configuration disclosed in E5, page 2093, section "Digital microfluidic cartridge", and page 2094, section "Cartridge manufacturing", is substantially different from the one called for in claim 1. If one were to consider the bottom surface of the "cover plate" in E5 as the "base side" of the container in claim 1 and the "photolithographically patterned polymer film serv[ing] as the spacer" in E5

as the "protrusions" distributed thereon, then E5 would be missing the "flat polymer film". On the other hand, if one were to consider the "photolithographically patterned polymer film" in E5 as the "flat polymer film" of claim 1, then E5 would be missing the "protrusions".

3.2.2 Moreover, the cartridge according to claim 13 must be suitable for reversibly attaching its container and film to a liquid droplet manipulation instrument. This feature is not disclosed in E5, in particular because the chip in E5 (i.e. the liquid droplet manipulation instrument) is attached to the cover plate (i.e. the container) using an epoxy (page 2094, right-hand column, line 5). Therefore, E5 is also not novelty-destroying for the subject-matter of claim 13.

3.2.3 The same reasoning applies *mutatis mutandis* to independent claims 1 and 15 which also require the feature referred to in 3.2.2 above.

3.3 Thus, the subject-matter of claims 1, 13 and 15 is new (Article 54(1),(2) EPC). Likewise, the remaining (dependent) claims are directed to new subject-matter.

4. Inventive step

4.1 The invention concerns a system and a cartridge for processing biological samples and manipulating liquids having biological samples.

4.2 According to appellant 2, any one of E1, E4 and E5 could serve as the closest prior art.

4.2.1 While all the above documents generally relate to the same purpose as the patent in suit (biological sample

processing systems), E4 is the most promising starting point for assessing inventive step, because E4 discloses a cartridge that is structurally closest to the cartridge according to claim 13, i.e. the broadest independent claim.

E4 discloses (see Figure 13, page 17, lines 22 et seq. and Figure 11, page 15, line 30 to page 16, line 20) a cartridge (1312) comprising a flat polymer film (1110) having a lower surface and a hydrophobic upper surface (page 16, lines 9 and 10), which is kept at a distance to the base side of a substrate (1120) by protrusions (1126). The spacer elements 1126 (page 17, lines 6 and 7) may indeed be considered protrusions in the broadest sense (cf. the patent in suit, column 5, lines 44 et seq.: "...the protrusions may be attached to the base side of the container separately..."). The distance so created defines a gap when the substrate (1120) is positioned on the film (1110) abutting the latter with its protrusions. The cartridge is reversibly attachable (cf. "that is separable from") to a liquid droplet manipulation device (page 17, lines 27 et seq.).

4.2.2 E1 and E5 are less promising starting points for the reasons set out in 3.1 and 3.2 above relating especially to the "reversibly attached" feature.

4.2.3 The board therefore starts from E4 as the closest prior art.

4.3 According to the patent in suit, the problem consisted in suggesting a device which enables the fully integrated handling of biological samples in a simple, automated and rapid manner, starting with the provision of a sample to be analysed for its biological material

into the device and finalising the process with the achievement of a final analysis (paragraph [0012]). With regard to E4, appellant 1 also contends that the problem was to improve handling for the initial provision of biological samples to the analysing device.

4.4 Claim 13 of appellant 1's sole request proposes to solve this problem by a cartridge for use in a biological sample processing system comprising protrusions and a flat polymer film characterised in particular by a container having a top side and a base side and comprising at least one well open at the top side, wherein the at least one well comprises a bottom side having at least one opening, the container further comprising a channel connecting the opening of the well with an orifice on the base side of the container and wherein the base side of the container comprises the protrusions distributed thereon.

4.5 As to the success of the solution, the board is satisfied that the provision of a well in the cartridge of E4 on top of the space where the droplet movement is accomplished, i.e. the "gap" referred to in claim 13, does indeed improve handling. In this way, the sample can be loaded onto the cartridge prior to the cartridge's insertion into the droplet manipulation instrument or, to use the wording of E4, into the droplet microactuator. The problem is therefore solved and does not need to be reformulated.

4.6 As to obviousness, appellant 2 submits that, when starting from E4 as the closest prior art, the solution was suggested in E1, E12 or E13, in particular because E4 referred to E13 in its section 8.5.

While E4 does indeed refer to E13 in its sections 8.5 and 8.6 on page 20, E13 does not disclose the distinguishing features, i.e. "a container having a top side and a base side and comprising at least one well open at the top side, wherein the at least one well comprises a bottom side having at least one opening, the container further comprising a channel connecting the opening of the well with an orifice on the base side of the container and wherein protrusions are distributed on the base side of the container". The distinguishing features indeed require, contrary to appellant 2's opinion, that the well be located above the space for droplet manipulation because the claim requires the channel to be connected to an orifice on the base side of the container. This feature is however not disclosed in E13. For instance, the reservoirs 102, 104 and 106 shown in Figure 1 of E13 are located laterally adjacent to the space (or gap) where droplet manipulation is accomplished (cf. page 16, lines 11 to 17). Similar considerations apply to E12 (see Figure 1; reservoirs 102, 104 and 106). The reservoirs in E1 are also located laterally from the space where droplet manipulation is accomplished (see for instance Figure 1, numerals 112, 114, 116, 118, 122, 124, 126; cf. page 12, lines 17 to 20). For the sake of completeness, the board observes that in Figure 10 of E12 (cf. page 74, lines 22 to 27) and also Figure 10 of E13 (cf. page 77, lines 22 to 27) a loading structure is disclosed that comprises a space 1006 that could be considered a well in the sense of claim 1. This configuration however at least lacks the feature "a bottom side having at least one opening".

What is more, in the cartridge depicted in Figure 13 of E4, the gap where the droplet 1122's movement is accomplished is delimited at its top by a reference

electrode 1120 (cf. page 16, lines 5 et seq. and page 17, lines 23 et seq.). There is no teaching in E4 or in any of E1, E12 and E13 to have a channel penetrate this reference electrode. Put differently, even if the skilled person considered placing a fluid reservoir on top of substrate 1112 in Figure 13 of E4 and dispensing the droplet 1122 into the gap 1114 via a liquid input channel, the skilled person would avoid penetrating the reference electrode 1120, and instead, would provide the channel through the spacer element 1126. By doing so, he or she would arrive at a configuration where the orifice of such a channel would be located at the spacer element 1126, but not at the base side of the container as required in claim 1.

According to appellant 2, E5, page 2093, right-hand column, first paragraph and Figure 1, disclosed a configuration where a well is located above the space for droplet manipulation. The board is not persuaded by this argument. In this passage, reference is made to the "*off-chip reservoir [being] connected to the chip th[r]ough a hole in the cover plate located above the reservoir electrode*". This means that the liquid is provided in a first reservoir located on top of a second reservoir (i.e. the reservoir provided with an electrode) from where it is transferred laterally into the space for droplet manipulation (see also E5, page 2093, right-hand column, second paragraph, lines 8 and 9: "adjacent"). This configuration is thus similar to the one disclosed in E1 where the reservoirs are located laterally from the space for droplet manipulation. E5 therefore does not disclose the distinguishing features.

Appellant 2 also referred to the reasoning provided in the impugned decision according to which the subject-

matter of claim 1 lacked an inventive step when starting from E1 as the closest prior art. As E1 is a less promising starting point than E4 and in particular since E1 is structurally more remote from the subject-matter of claims 1 and 13 than E4 (cf. 3.1 and 4.2.2 above), this argument must fail. A similar reasoning applies to the line of argument taking E5 as the closest prior art.

For these reasons the board concludes that it was not obvious to arrive at the subject-matter of claim 13 in view of the cited prior art. Similar considerations apply to claims 1 and 15, which comprise or refer to a container essentially corresponding to the one having a configuration called for in claim 13.

4.7 Thus, claims 1, 13 and 15 comply with the requirement of inventive step set forth in Article 56 EPC. This reasoning applies equally to the dependent claims, which are directed to particular embodiments of the independent claim upon which they depend.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent in amended form on the basis of claims 1 to 15 of the main request (sole request) as filed during oral proceedings on 20 November 2017 (attached to the minutes thereof as "Annex 2") and a description and drawings to be adapted thereto, if necessary.

The Registrar: The Chairman:

C. Vodz G. Glod

Decision electronically authenticated