PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	14 NOV 2018
Applicant's or agent's file reference 2017P19659WO	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US18/50834	13 September 2018 (13.09.2018)	14 September 2017 (14.09.2017)

International Patent Classification (IPC) or both national classification and IPC
IPC - G01N 33/50, 33/53, 33/543; C12Q 1/68 (2018.01)
CPC - G01N 33/50, 33/53, 33/5302, 33/543; C12Q 1/68

Applicant SIEMENS HEALTHCARE DIAGNOSTICS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	26 October 2018 (26.10.2018)	Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 4-20

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 4-20 are so unclear that no meaningful opinion could be formed *(specify)*:

because claims 4-20 are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 4-20

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☐ See Supplemental Box for further details.

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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	3/1-2	YES
	Claims	1-2	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-2, 3/1-2	NO
Industrial applicability (IA)	Claims	1-2, 3/1-2	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by US 2011/0105712 A1 to Jiang et al. (hereinafter 'Jiang').

As per claim 1, Jiang discloses a membrane for an in vitro diagnostic sensor (a polymer monolayer comprising a polymer backbone is utilized on a diagnostic sensor surface, although not explicitly disclosed the surface polymer monolayer would meet the limitation of a membrane; paragraphs [0034], [0036], [0075], [0129]) for detecting the presence of a target analyte in a fluidic biological sample (target molecules (analytes) from a sample can be bound to the polymer monolayer for use as a diagnostic assay, as such the presence of the target analyte would be detected as claimed, the sample may comprise human blood (fluidic biological sample); paragraphs [0036], [0129], [0229]), the membrane comprising: a polymer matrix comprising a polymer that has been modified to contain at least one surface adhesion functional group (the polymer backbone (matrix) comprises one or more catechol groups which allows the polymer to adhere to a surface, as such the polymer has been modified to contain at least one surface adhesion functional group as claimed; paragraphs [0075], [0079]), wherein the at least one surface adhesion functional group enables attachment of the membrane to a substrate of the in vitro diagnostic sensor (the catechol groups (surface adhesion functional group) allow the polymer to adhere (attachment of the membrane) on the surface, the surface is a substrate of the biosensor (diagnostic sensor) for diagnostic assays (in vitro); paragraphs [0033]-[0034], [0079]).

As per claim 2, Jiang discloses the membrane of claim 1, and Jiang further discloses wherein the at least one surface adhesion functional group comprises a catecholic functional group (a catechol (functional) group is utilized with the polymer, the catechol group would meet the limitation of the at least one surface adhesion function group as claimed; paragraph [0079]).

Claims 3/1-2 lack an inventive step under PCT Article 33(3) as being obvious over Jiang, further in view of WO 2016/105503 A1 to Genentech, Inc (hereinafter 'Genentech').

As per claims 3/1-2, Jiang discloses the membrane of claims 1-2, and Jiang further discloses polymer is a polyvinyl (vinyl polymer backbone; paragraph [0083]). Jiang does not disclose wherein the polymer is polyvinyl chloride, carboxylated-polyvinyl chloride, and/or aminated-polyvinyl chloride. Genentech discloses wherein the polymer is polyvinyl chloride (an assay can detect specific biomarkers by binding the biomarkers to a polymer surface, the polymer surface may comprise a polyvinyl chloride; page 43, lines 9-14). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the membrane of Jiang to provide polyvinyl chloride as the polymer material, as taught by Genentech, in order to provide a means for bonding specific biomarkers from a sample in an assay using a well-established binding process (Genentech, page 44, lines 9-18).

Claims 1-2 and 3/1-2 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 2 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claim is indefinite for the following reason(s):

In claim 2, line 2, the phrase "catecholic functional group (1,2-dihydroxybenzene)" is interpreted as being indefinite since it is unclear if (1,2-dihydroxybenzene) is a required limitation of the claim or merely a preferred embodiment. For the purposes of this opinion the phrase has been interpreted as reading -catecholic functional group-.