PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/FI2019/050810	14.11.2019	05.12.2018

International Patent Classification (IPC) or both national classification and IPC
INV. G01N33/543

Applicant
TEKNOLOGIAN TUTKIMUSKESKUS VTT OY

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 usually 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 notifed 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:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Gundlach, Björn Telephone No. +31 70 340-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/FI2019/050810

Box No. I Basis of the 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:

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

1. Statement

Novelty (N)	Yes:	Claims	1-12
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-12
Industrial applicability (IA)	Yes:	Claims	1-12
	No:	Claims	

2. Citations and explanations

see separate sheet

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:

see separate sheet

Re Item VIII

Certain observations on the international application

Claim 1 misses features essential for the definition of the claim invention. Without these features the claimed invention would not work:

From figure 1 and also from paragraph [0035] of the description it is clear that the tracer elements are attached to the tracer storage site (10b) using an attachment element (60) (see also figure 1). Without the attachment element (60) all tracer elements would move away from the tracer storage site in phase D in figure 1 and as a consequence in subsequent phase F no tracer element would be present at the tracer storage site (10b) anymore.

Likewise it is clear from figure 1 that the second binder element (20) must be immobilised on the tracer transport site with high affinity (10a). Otherwise the second binder element would not stay in position in phase C in figure 1 and the subsequent phases would not be possible anymore. There appears to be no clear passage in the description describing this feature. Paragraph [0033] merely describes that the tracer transport site (10a) comprises second binder elements "on the surface thereof".

The above applies independent of the "transport" mechanism used (see p. 7, para. 1). Elements (20) and (60) must both be present and attached to sites (10a) and (10b) with higher affinity than to the other elements of the method regardless whether the particles are moved by force or if the assay fluid is pumped.

It follows that claim 1 does not fulfil the requirements of Article 6 PCT. With regard to element (20) it is doubtful whether the requirements of Article 5 PCT are fulfilled, because the application as a whole does not appear to disclose the essential feature.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 WO 2012/016357 A1 (CAPITALBIO CORP [CN]; UNIV TSINGHUA [CN] ET AL.) 9 February 2012 (2012-02-09);

& US 2013/217584 A1 (ZHANG GUANBIN [CN] ET AL) 22 August 2013 (2013-08-22) cited in the application

D2 EP 2 010 321 A2 (INVERNESS MEDICAL SWITZERLAND [CH]) 7 January 2009 (2009-01-07)

The present application meets the criteria of Article 33(2) PCT, because the subject-matter of the claims is new.

D1 discloses:

A method for amplification in a microfluidic assay for analyte detection, comprising binding an analyte to a transport element, wherein the transport element comprises a particle and a first antibody element and the analyte is bound to the first antibody element and the particle comprises a functional group such as avidin (see D1, claims 1, 2, 6-9, 26 and 27).

Claim 1 differs from D1 in that there is transportation of the analyte particle complex to different sites and the affinity of the different binding is chosen to allow binding and detachment of the construct.

Claims 8 and 10 relate to entities specifically adapted for the method of claim 1.

All claims are novel over D1.

D2 discloses a method for detecting an analyte in that magnetic particles carrying a ligand for an analyte are moved by magnetic force within a microfluidic assay format (abstract, claim 1). D2 does not disclose all features of claim 1 or the other claims.

The present application does not meet the criteria of Article 33(3) PCT, because the subject-matter of claims 1-12 does not involve an inventive step.

The technical difference does not result in a new technical effect over D1 as closest prior art: As discussed under item VIII above the subject-matter claimed does not provide a solution to the technical problem defined in the preamble of claim 1. Without the missing essential technical features an amplification of the analyte detection is not possible.

The objective technical problem to be solved is the provision of an alternative method.

The solution provided by claim 1 is considered not to be inventive: In the absence of a working solution the subject-matter of the claims cannot be considered to be non-obvious. The same applies for the other claims for the same reason *mutatis mutandis*.

Subject-matter of all claims is industrially applicable.