

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

09 JUL 2020

Applicant's or agent's file reference
50811-006WO2

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 20/25131

International filing date (day/month/year)

27 March 2020 (27.03.2020)

Priority date (day/month/year)

29 March 2019 (29.03.2019)

International Patent Classification (IPC) or both national classification and IPC

IPC - A61K 39/395, C07K 16/18 (2020.01)

CPC - A61K 39/395, C07K 16/18, A61K 2039/505

Applicant **UNIVERSITY OF MASSACHUSETTS**

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 43bis.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 66.1bis(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
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

24 June 2020

Authorized officer

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International application No.

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Box No. 1 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(b)).
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. 14-51

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. 14-51 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 14-51 are improper multiple dependent claims because they 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. 14-51

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 13ter.1(a) or (b).

See Supplemental Box for further details.

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

1. Statement

Novelty (N)	Claims	<u>1-13</u>	YES
	Claims	<u>NONE</u>	NO
Inventive step (IS)	Claims	<u>1-13</u>	YES
	Claims	<u>NONE</u>	NO
Industrial applicability (IA)	Claims	<u>1-13</u>	YES
	Claims	<u>NONE</u>	NO

2. Citations and explanations:

Claims 1-13 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest to an isolated antibody that specifically binds polymeric immunoglobulin A (pIgA) comprising: CDR-H1 (SEQ ID NO: 1, GFTFSNYG); CDR-H2 (SEQ ID NO: 2, INRGGDRI); CDR-H3 (SEQ ID NO: 3, RGLYYYGSDYYFDY); and CDR-L1 (SEQ ID NO: 4, GNIHNY); CDR-L2 (SEQ ID NO: 5, NAK); CDR-L3 (SEQ ID NO: 6, HHYYSTPYT).

Regarding claim 1, the article "Immunoglobulin A subclass measurement in serum and saliva: sensitivity of detection of dimeric IgA2 in ELISA depends on the antibody used" by de Fijter et al. (hereinafter "de Fijter") teaches an isolated antibody that specifically binds polymeric immunoglobulin A (pIgA) (abstract, We validated IgA and IgA subclass measurements in serum and saliva by sandwich enzyme-linked immunosorbent assay (ELISA). Coating reagents were specific mAbs against IgA (clone 4E8), IgA1 (clone 69- 11.4) or IgA2 (clone 16-512-H5 and clone IF8.58). Pooled normal human serum and purified dimeric IgA1 (d-IgA1) or IgA2 (d-IgA2) myeloma proteins were used to standardize the assays. Polymeric and monomeric forms of IgA in sera from volunteers and patients with myelomatosis were assayed in fractions separated by high performance liquid chromatography (HPLC). Dithioerythritol (DTE) was used to determine the influence of the quaternary structure of IgA on its detection by mAbs. We found that mAbs 4E8, 69- 11.4 and 16-512-H5 reliably measured d-IgA, d-IgA1 and d-IgA2 respectively, independent of the standard employed.). de Fijter does not specifically teach SEQ ID NO: 1-6.

WO 2014/071455 A1 The Macfarlane Burnet Institute for Medical Research and Public Health Ltd (hereinafter "Burnet Inst") teaches an isolated antibody that specifically binds polymeric immunoglobulin A (pIgA) (para [0013], processes and kits, for diagnosing TB in a subject, which assess the level of individual antibody isotypes, including dimeric/polymeric IgA (dIgA).; [0014], the process comprising obtaining a biological sample comprising antibodies from the subject and contacting same with a dIgA binding agent, to allow formation of a test complex between TB antigen specific antibody and antibody binding agent.; [0074], the dIgA binding agent is an antibody or antigen binding fragment thereof or anti-J chain.). Burnet Inst does not specifically teach SEQ ID NO: 1-6.

GenBank AT197782.1 "immunoglobulin heavy chain variable region, partial [Mus musculus]" (hereinafter "AT197782.1") teaches an immunoglobulin heavy chain variable region, wherein:
amino acid residues 27-33 of AT197782.1 is 100% match to SEQ ID NO: 1;
amino acid residues 51-58 of AT197782.1 is 37% match to SEQ ID NO: 2;
amino acid residues 98-110 of AT197782.1 is 71% match to SEQ ID NO: 3.

GenBank: AAA97381.1 "Vk12-13 Ig variable region, partial [Mus musculus]"(hereinafter "AAA97381.1") teaches an immunoglobulin light chain variable region, wherein:
amino acid residues 26-32 of AAA97381.1 is 100% match to SEQ ID NO: 4;
amino acid residues 50-52 of AAA97381.1 is 100% match to SEQ ID NO: 5;
amino acid residues 89-97 of AAA97381.1 is 100% match to SEQ ID NO: 6.

There is no prior art that teaches or fairly suggests to one of ordinary skill in the art, in view of the teachings of de Fijter, Burnet Inst, AAA97381.1 and AT197782.1, to have prepared an isolated antibody that specifically binds polymeric immunoglobulin A (pIgA) comprising: SEQ ID NOs: 1-6.

Regarding claims 2-13, the claims are dependent claims of claim 1, and thus, meet the criteria set out in PCT Article 33(2)-(3), as discussed above.

Claims 1-13 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.