PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	26.06.2018
Applicant's or agent's file reference: FP18-0122-00	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2018/013304	29.03.2018	30.03.2017

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

B01J20/285(2006.01)i, B01D15/36(2006.01)i, B01D15/38(2006.01)i, B01J20/24(2006.01)i, B01J20/281(2006.01)i

Applicant

HITACHI CHEMICAL COMPANY, LTD.

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 or 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/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2018/013304

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:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2018/013304

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

1. Statement

Novelty (N)	Claims	16-19, 24-25	YES
	Claims	1-15, 20-23	NO
Inventive step (IS)	Claims		YES
	Claims	1-25	NO
Industrial applicability (IA)	Claims	1-25	YES
	Claims		NO

2. Citations and explanations:

Document 1: WO 2016/117567 A1 (HITACHI CHEMICAL COMPANY, LTD.) 28 July 2016, entire text, claims 1-8, paragraphs [0010], [0039]-[0082] & EP 3248677 A1 Cl1-8

Document 2: JP 2016-534984 A (GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LIMITED) 10 November 2016, fig. 1, paragraphs [0051]-[0055] & US 2016/0221962 A1 fig. 1, paragraphs [0132]-[0136] & WO 2015/049651 A1 fig. 1 & EP 3052483 A1 fig. 1 & CA 2925862 A1 fig. 1

- Claims 1-15, 20-23

The invention as in claims 1-15 and 20-23 lacks novelty and does not involve an inventive step in light of document 1 cited in the ISR.

Document 1 (entire text, refer particularly to claims 1-8 and paragraphs [0010] and [0039] to [0082]) discloses improvement of the property of liquid permeation by a porous separation material comprising polymer particles ("hydrophobic polymer particles")

having structural units derived from a styrene monomer, and a coating layer that coats a portion of the surfaces of the particles, the coating layer containing a polymer having a hydroxyl group, and the hydrophilic polymer having an epoxy group (refer to paragraph [0045]) of document 1) or a group (refer to paragraphs [0045] and [0082] of document 1) represented by -NH-R-L (where R is a hydrocarbon group and L is a carboxy group or an amino group) such as crosslinked modified agarose (refer to paragraph [0010] of document 1).

In the separation agent disclosed in document 1, the elastic modulus at 5% compressive deformation is 100 to 1000 MPa (refer to paragraph [0075] of document 1), the liquid permeation rate is 800 cm/h or higher when column pressure is 0.3 MPa (refer to paragraph [0071] of document 1), the average particle size is 10 to 300 μm (refer to paragraph [0072] of document 1), the mode diameter in the pore size distribution is 0.05 to 0.6 μm (refer to claim 7 and paragraph [0039] of document 1), the pore volume of the separation material is 30 to 70% by volume (refer to paragraph [0076]) of document 1, the specific surface area of the separation material is 10 m^2/g or greater (refer to claim 6 of document 1), the coefficient of variation of the particle size of the hydrophobic polymer particles is 3 to 15% (refer to paragraph [0037] of document 1), and the amount of the coating layer is about 45 to 591 mg per 1 g of the hydrophobic polymer particles (refer to table 1 in paragraph [0096] of document 1). Document 1 also indicates that the separation material comprising the coating layer can be used for affinity purification, etc., by introducing an ion exchanging group, a ligand

(protein A), etc., via a hydroxyl group, etc., on the surface (refer to paragraph [0056] of document 1). Furthermore, document 1 gives blood proteins, etc., such as immunoglobulin as examples of bio-macromolecules that can be separated using the separation material, and document 1 also indicates the macromolecules are eluted from the separation agent after being made to adsorb on the separation agent (refer to paragraphs [0068] to [0070] of document 1).

In view of this, there are no differences between the invention-specifying matters of the invention as in claims 1-15 and 20-23 and the matters disclosed in document 1.

- Claims 16-19, 24-25

The invention as in claims 16-19 and 24-25 does not involve an inventive step in light of documents 1 and 2 cited in the ISR.

The separation material comprising the coating layer disclosed in document 1 can be used for affinity purification, etc., by introducing a ligand (protein A), etc., via a hydroxyl group, etc., on the surface (refer to paragraph [0056] of document 1).

It is well known that proteins are commonly purified using a separation agent in which a support material and a ligand such as protein A are bonded via a spacer. For example, document 2 (entire text) discloses that in a separation agent for protein purification by affinity chromatography, a ligand (protein A) is bonded by amide bonds (covalent bonds) to a linear spacer and is immobilized on a support body (refer to the

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

"diaminodipropylamine (DADPA) agarose resin" in paragraph [0051] of document 2). It is further indicated that Fc-fusion proteins of immunoglobulin are purified by the separation agent disclosed in document 2 (refer to paragraph [0055] of document 2).

The invention as in claims 16-19 and 24-25 cannot be considered to have any particularly significant effects in comparison to, *inter alia*, the technical matters disclosed in documents 1 and 2 and well-known technologies.

Therefore, a person skilled in the art could easily have conceived of the configuration of the invention as in claims 16-19 and 24-25 on the basis of the matters disclosed in documents 1 and 2 and well-known technologies.