

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing
(day/month/year)

Applicant's or agent's file reference C1-A0708P2		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/JP2008/067534	International filing date (day/month/year) 26.09.2008	Priority date (day/month/year) 26.09.2007
International Patent Classification (IPC) or both national classification and IPC		
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA		

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 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 66.1bis(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.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

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Box No. I	Basis of this opinion
	<p>1. With regard to the language, this opinion has been established on the basis of:</p> <p><input checked="" type="checkbox"/> the international application in the language in which it was filed</p> <p><input type="checkbox"/> 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)).</p> <p>2. <input type="checkbox"/> 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 43bis.1(a))</p> <p>3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:</p> <p>a. type of material</p> <p><input checked="" type="checkbox"/> a sequence listing</p> <p><input type="checkbox"/> table(s) related to the sequence listing</p> <p>b. format of material</p> <p><input type="checkbox"/> on paper</p> <p><input checked="" type="checkbox"/> in electronic form</p> <p>c. time of filing/furnishing</p> <p><input checked="" type="checkbox"/> contained in the international application as filed</p> <p><input type="checkbox"/> filed together with the international application in electronic form</p> <p><input type="checkbox"/> furnished subsequently to this Authority for the purposes of search</p> <p>4. <input type="checkbox"/> In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.</p> <p>5. Additional comments:</p>

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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
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1. Statement			
Novelty (N)		Claims <u>1-44</u>	YES
		Claims _____	NO
Inventive step (IS)		Claims _____	YES
		Claims <u>1-44</u>	NO
Industrial applicability (IA)		Claims <u>1-44</u>	YES
		Claims _____	NO

2. Citations and explanations:

Document 1: WO 2006/004663 A2 (MedImmune, Inc.),
12 January 2006

Document 2: J. Biol. Regul. Homeost. Agents, 2005,
vol. 19, pages 105-112

Document 3: Cancer Res., 2001, vol. 61, pages 5070-5077

Claims 1-44

The invention as in claims 1-44 does not involve an inventive step in the light of documents 1-3 cited in the ISR.

Document 1 discloses a method for increasing an antibody production level by modifying an amino acid residue at a specific position in the CDR region of the antibody, and also indicates that the feature can be combined with other preferable properties such as an increased serum half-life.

Document 2 indicates that modifying an antibody so as to raise the isoelectric point thereof improves the transitivity thereof to a tissue.

Document 3 indicates that modifying an antibody by amino acid substitution so as to lower an isoelectric point thereof reduces the nonspecific toxicity thereof without decreasing any activities thereof.

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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

Such being the case, as disclosed in documents 2 and 3, imparting preferable properties to an antibody by modifying the isoelectric point thereof had been already performed prior to the priority date of the present application; therefore, in the invention disclosed in document 1, a person skilled in the art could easily conceive of imparting preferable properties such as an increased serum half-life to an antibody by modifying an amino acid residue at a specific position in the CDR region of the antibody so as to modify the isoelectric point thereof.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 43bis.1 and 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 2007/114319 A1 [E, X]	11.10.2007	30.03.2007	31.03.2006

2. Non-written disclosures (Rule 43bis.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC)

C07K16/28(2006.01) i, A61K39/395(2006.01) i,
A61P43/00(2006.01) i, C07K16/46(2006.01) i,
C12N1/15(2006.01) i, C12N1/19(2006.01) i,
C12N1/21(2006.01) i, C12N5/10(2006.01) i,
C12N15/09(2006.01) i, C12P21/02(2006.01) i