

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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.
PCT/IB2015/059836

International filing date (day/month/year)
21.12.2015

Priority date (day/month/year)
22.12.2014

International Patent Classification (IPC) or both national classification and IPC
INV. A61K39/395 C07K16/24

Applicant
NOVARTIS AG

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 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 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:



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Date of completion of
this opinion

see form
PCT/ISA/210

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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 43bis.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 13ter.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 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.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 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-36</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-36</u>
Industrial applicability (IA)	Yes: Claims	<u>1-36</u>
	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

Ad Section V

Reasoned statement with regard to novelty, inventive step or industrial applicability

The present application relates to a pharmaceutical product comprising particular liquid formulations of IL-17 antibody secukinumab which comprise secukinumab and methionine having a pH of about 5.2-6.2 and wherein the container has a headspace which has reduced oxygen content and wherein the pharmaceutical composition is not reconstituted from a lyophilisate.

1 Documents

D1...WO 2012 059 598

D2...Daugherty & Mrsny (2006) Adv. Drug Delivery Reviews 58: 686-706

2 Art 33(2) PCT

The specific pharmaceutical product as claimed in the independent claims 1, 21 and 36 has not been disclosed in the prior art. The claims are thus considered to meet the requirements of Art 33(2) PCT.

3 Art. 33(3) PCT

An inventive step, however, cannot be acknowledged for the following reasons:

D1 can be regarded to represent the closest prior art. D1 discloses pharmaceutical compositions comprising anti-IL-17 antibody and their use in the treatment of patients suffering from rheumatoid arthritis. The compositions disclosed in D1 comprise 50 mg/ml AIN457 (=secukinumab), histidine buffer at pH 5.8, a surfactant (0.2% polysorbate 80) and a stabilizer (sucrose and mannitol, glycine or arginine). The mixture is lyophilised and reconstituted by adding water.

The difference between the formulations of D1 and the presently claimed compositions lies in the methionine and the requirement that the presently claimed liquid pharmaceutical composition is not reconstituted from a lyophilisate.

The problem to be solved by the present application can thus be seen in the provision of an improved pharmaceutical product comprising a liquid formulation.

The various compounds of the formulation as well as the requirement to reduce the oxygen content in the head space of the vial are well known in the art (see, e.g., discussion in D2, in particular p. 692, right col., 2nd par. - p.694, right col., 1st par. and Table 1). It is furthermore known to the skilled person that the formulation is critically dependent on the (active) protein to be included in the formulation. Furthermore, individual formulations for each substance have to be designed and tested.

It thus appears that an inventive step for a specific formulation could possibly be acknowledged.

The current set of claims, however, defines the compositions in broad terms and wide variations in terms of the concentration of the various ingredients. The subject-matter of the claims as currently worded is thus not considered to solve the above stated problem.

An inventive step can thus not be acknowledged for the claims currently on file.

Ad Section VIII

Certain observations on the international application

The current set of claims is not considered to define the formulation and its ingredients sufficiently clear and precise in order for the skilled person to perform the invention without undue burden. The characterisation of the pharmaceutical product of claim 1, e.g., can only be considered a starting point for testing various formulations of the antibody. Moreover, according to the examples, only very specific parameters of the formulation result in a sufficiently stable product.

The claims are thus objected to under Art. 6 PCT.