

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

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/IB2015/059631	International filing date (day/month/year) 15.12.2015	Priority date (day/month/year) 16.12.2014
International Patent Classification (IPC) or both national classification and IPC INV. C07D413/06 A61K31/42 C07D413/12 C07D261/08		
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:  European Patent Office Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Rufet, Jacques Telephone No. +49 30 25901-0
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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 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	<u>1-25</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-25</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-25</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

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

1 Reference is made to the following documents:

D1 WO 2012/137094 A1 (PFIZER [US]) 11 October 2012 cited in the application

D2 WO 2011/073845 A1 (PFIZER [US]) 23 June 2011 cited in the application

D3 WO 2010/032147 A2 (PFIZER [US]) 25 March 2010 cited in the application

2 Method for treatment of the human or animal body by therapy

Claims 16 to 19 and 25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv)/67.1(iv) PCT.

The patentability can also dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for in a first or further medical treatment.

3 Novelty

The present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1 to 25 is considered to be new over the prior art D1 to D3 in the sense of Article 33(2) PCT for the following reasons:

D1 refers to structurally very close isoxazole hydroxamic acid derivatives (see especially claim 1, formula I and examples 2, 5, 6, 8, etc..) also useful as antibacterial agents which differ only by the nature of linker L according to present formula (I).

D2 refers to oxo-pyridine hydroxamic acid derivatives (see especially claim 1; examples 65 and 67) also useful as antibacterial agents. The distinguishing feature should be seen in the oxo-pyridine ring instead of the mandatory isoxazole ring according to present formula (I).

D3 describes aryl hydroxamic acid derivatives also useful for treating bacterial infections.

The distinguishing features should be seen in the absence of the isoxazole ring (aryl) and the nature of present variable X (oxygen in stead of NH or CH₂).

4 Inventive step

The present application addresses the problem of providing compounds useful for treating bacterial infections.

4.1 D1 is considered to represent the closest prior art, since it refers also to isoxazole hydroxamic acid derivatives useful as antibacterial agents.

The structural distinguishing feature should be seen in the nature of linker L, which is not -C≡C- or -CR₅=CR₅- as claimed.

4.2 There is no comparative data in the present application showing that the distinguishing feature as mentioned above is responsible for an unexpected effect, thus the objective technical problem solved by the subject-matter of claim 1 should be seen in the provision of an alternative linker in order to provide further isoxazole hydroxamic acid derivatives useful as antibacterial agents.

In view of the examples and the biological data given in tables A and B it is credible that the distinguishing feature solve the above-mentioned problem. Furthermore taking into account the structural diversity of the examples and the biological results the scope of protection conferred by formula (I) of claim 1 represents a legitimated (fair) scope of protection.

4.3 There is no technical link in D2 nor in D3 which would have incited the skilled worker to replace the linker L of D1 with the linker -C≡C- or -CR₅=CR₅- as described for examples 65 and 67 of D2 (see also D2, claim 1, definition of L), and thus arriving to the claimed compounds. Indeed, there is no indication in D2 nor in D3 that the oxopyridine ring and the isoxazole ring are interchangeable.

The subject-matter of claims 1 to 25 meets thus the requirements of Art. 33(3) PCT.

5 Before the entry into the European phase, claims 23 and 24 should be deleted in accordance with the decision G2/08; the Enlarged Board of Appeal held that the use of Swiss-type claims is permissible in applications having a priority date earlier than 29 January 2011, Art. 54(5) EPC (see G2/08, paragraph 7.1.4 of the reasons for the decision).