

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
see form PCT/ISA/220

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/EP2018/070552	International filing date (day/month/year) 30.07.2018	Priority date (day/month/year) 04.08.2017
International Patent Classification (IPC) or both national classification and IPC INV. C07D405/14 C07D413/14 C07D401/04 C07D413/04 C07D417/04 A61P33/00 A61K31/4709		
Applicant BAYER ANIMAL HEALTH GMBH		

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 D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Marzi, Elena Telephone No. +49 89 2399-0
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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 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>1-9, 11-18</u>
	No: Claims	<u>10</u>
Inventive step (IS)	Yes: Claims	<u>1-9, 11-18</u>
	No: Claims	<u>10</u>
Industrial applicability (IA)	Yes: Claims	<u>1-18</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

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

and / or

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

see form 210

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 2015/078800, 4 June 2015
- D2 WO 2013/06446. 10 May 2013
- D3 Hans Suschitzky ET AL: J.C.S. Perkin I 1975,
pages 2409-2413, XP055511143
- D4 LOU SHI ET AL.;
ADVANCED SYNTHESIS & CATALYSIS,
vol. 359, no. 14, 17 July 2017, pages 2457-2470, XP055511432
- D5 JIANRONG LIU ET AL.;
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY,
vol. 136, 19 April 2017, pages 548-560, XP055511441
- D6 GARUDACHARI B ET AL.;
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY 2014,
vol. 74, pages 324-332, XP028623316
- D7 A. ZASK ET AL.;
BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 2003,
vol. 13, no. 8, pages 1487-1490, XP055431371
- D8 US 2012/076732, 29 March 2012
- D9 A1 (BAYER ANIMAL HEALTH GMBH [DE]) 17 May 2018 (2018-05-17)

2. Claims 15, 17-18 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 be 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 use in a first or further medical treatment.

3. Novelty

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty for the present claim 10. Documents D3-D8 represents only a **non-exhaustive list** of novelty destroying documents. These documents discloses compounds encompassed by the present formula II of claim 10 ((D3, page 2411; compound 38; D4, page 2461; compound 3k; D5, page 552; compounds 30a, 30b; D6, page 325; compound 3; page 326; compound 9; D7, Scheme 1, page 1488, compounds 4 and 1 (h, o, p, q, r as defined in Table 1); D8, page 95; compounds 16a, 17a).

Hence claim 10 is not novel.

The present compounds of formulae (I), (III) and (IV) are novel over the compounds of formulae (I) of D1 and D2 at least on account of the present group A.

Therefore claims 1-9 and 11-18 are novel.

4. Inventive step

The application relates to quinoline derivatives for the treatment of helminthic infections.

D1 and D2, which disclose structurally close compounds for the same use, can equally be considered as the closest prior art. The present compounds differ from the compounds of D1 and D2 on account of the present group A.

As this difference does not result in any additional effect, the objective problem to be solved can be seen in the provision of further heterocyclic compounds for the treatment of helminthic infections.

The solution of the applicant, i.e. the provision of compounds of formula (I) which have the desired activity as shown on p. 156-160 of the description, is considered to involve an inventive step. There was no hint in the prior art cited that the modification of the compounds of D1 or D2 in order to arrive at the claimed derivatives would have led to compounds retaining the desired biological activity.

The intermediates of claims 11 and 12 are also inventive. New intermediates which take part in analogy processes for producing new and inventive products, must, in order to qualify as inventive intermediates, provide a structural contribution to the subsequent products. The structural contribution provided by the intermediate must display at least one of those feature which differentiate the product from the closest

prior art. In the present case the structural contribution over the prior art is the present A group. Therefore an inventive step can be acknowledged for the corresponding intermediates of claims 11 and 12 which contain this feature.

Re Item VI

Certain documents cited

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (<i>valid claim</i>) (day/month/year)
WO 2018/087036	17.05.2018	06.11.2017	11.11.2016

D9 discloses quinoline derivatives which can be used for the treatment of parasite infections. The present compounds of formula (I) are novel over the compounds disclosed in D9 on account of the definition of the present substituent Q. D9 discloses compounds encompassed by the present claims 11 and 12 ((D9, Steps 1 and 2, p. 163: step 1, p. 168 step 4, p. 181 step 1, p. 184 steps 2 and 3, p. 185 steps 2,3, p. 186; table 3a; compounds It-1 to It-8).