

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43*bis*.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/EP2016/067614

International filing date (day/month/year)
25.07.2016

Priority date (day/month/year)
27.07.2015

International Patent Classification (IPC) or both national classification and IPC
INV. C07D235/30

Applicant
BAYER PHARMA AKTIENGESELLSCHAFT

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 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 66.1*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:



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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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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>1-16</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>6-16</u>
	No: Claims	<u>1-5</u>
Industrial applicability (IA)	Yes: Claims	<u>1-16</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

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

Reference is made to the following document:

D1 WO 2010/151441 A1 (WANG TONG [US]; GATELY STEPHEN [US];
TRANSLATIONAL GENOMICS RES INST []) 29 December 2010
(2010-12-29)cited in the application

Re Item V

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

Novelty

The document D1 discloses a process for the preparation of 2-phenylaminobenzimidazoles from which the process of claim 1 formally differs in that the starting compound 1,2-phenylene diamine is structurally different from the starting compounds of D1 (see page 1, lines 9-15; page 25, Scheme 1; page 20, Examples 3, 5; page 24, Example 23; claim 3).

Consequently, the subject-matter of independent claims 1 and 12-16 and dependent claims 2-11 is deemed novel by this Authority.

Inventive step

The *subjective* problem underlying the novel subject-matter may be regarded as the provision of a *further* process for the production of 3-(2-anilino-1-cyclohexyl-1H-benzimidazol-5-yl)propanoic acid (see description, page 1).

The distinguishing feature between the novel process of claim 1 and the process according to D1 is to be seen as the particular starting material.

In the absence of any experimental evidence either in the application or D1 that this feature brings about technical advantages compared to the process disclosed in D1, the *objective* problem underlying the novel subject-matter equals the *subjective* problem.

However, the use of the particular 1,2-phenylene diamine derivative according to claim 1 as solution to such a very general problem cannot contribute to inventive activity, since the skilled person searching a solution to this problem had a clear incentive from D1 to modify the process of D1 in order to arrive at the desired 2-phenylaminobenzimidazole molecular skeleton so that the subject-matter of independent claim 1 and dependent claims 2-5 is deemed by this Authority to lack inventive step.

This applies even more, since the document D1 likewise addresses the preparation and use of 2-phenylaminobenzimidazoles as medicaments for the treatment of cancer.

Notwithstanding this, this Authority is of the opinion that the subject-matter of dependent claim 6 and claims 7-16 insofar as the subject-matter of claim 6 is concerned, involves an inventive activity, since D1 is entirely silent on the use of enantiomerically pure educts in order to arrive at the corresponding enantiomerically pure products.

Consequently, the presence of inventive step could have been acknowledged for a the subject-matter of a Main Claim directed to the particular embodiment of present claim 6.

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)
WO2015121210	20/08/2015	10/02/2015	11/02/2014

Re Item VIII

Certain observations on the international application

In claim 12, it should possibly have read "obtainable".