STATE INTELLECTUAL PROPERTY OFFICE OF THE P. R. CHINA

EXAMINATION REPORT

Under Memorandum of Understanding between GCC and SIPO

SIPO’s Reference No.: GCC/CN2011/000512
Filing date (day/month/year) 19 Oct. 2008 (19.10.2008)

FOR FURTHER ACTION Please refer to the Memorandum of Understanding.

Application No.: GCC/P/2008/11961
Priority date (day/month/year) 19 Oct. 2007 (19.10.2007)

Time validity of Priority ☑ Yes ☐ No, See also Box No. II

International Patent Classification (IPC) or national classification and IPC
See Supplemental Box

Applicant
BOEHRINGER INGELHEIM INTERNATIONAL GMBH

1. This report is the FIRST examination report, established by the SIPO (hereinafter referred to as “the Authority”) and transmitted to the GCCPO under the Memorandum of Understanding between the GCC and the SIPO.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.
   ☑ It is also accompanied by a copy of each prior art document cited in this report (See Form GCC/SIPO/611).

3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority.
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ a total of (indicate type and number of electronic carrier(s)), containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing.

4. This report contains indications relating to the following items:
   ☑ Box No. I Basis of the report
   ☑ 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 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 application
   ☑ Box No. VIII Certain observations on the application

Date of receipt of the demand 21 Nov. 2011 (21.11.2011)
Date of completion of this report 20 Feb. 2012 (20.02.2012)

Name and mailing address of the SIPO
The State Intellectual Property Office of the P.R. China,
6 Xitucheng Road, Jimen Bridge, Haidian District,
Beijing, 100088, China
Fax simile No. +86-10-62019451

Authorized officer LIU, Hongyan
Telephone No. +86-10-82246701 Ph. Abir Alsaleem

Form GCC/SIPO/637 (cover sheet)
EXAMINATION REPORT

Box No. I  Basis of the report

1. With regard to the search report(s) used, this examination report is based on:
   - [ ] the search report(s) prepared by the , as selected by the GCCPO.
   - [x] the search report prepared by the SIPO completed on 10 Jan. 2012 (10.01.2012).

2 With regard to the elements of the application, this report is based on:
   - [x] the application as originally filed/furnished
   - [ ] the description:
     - pages received by this Authority on
     - pages received by this Authority on
   - [ ] the claims:
     - pages received by this Authority on
     - pages received by this Authority on
   - [ ] the drawings:
     - pages received by this Authority on
     - pages received by this Authority on
   - [ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/figs
   - [ ] the sequence listing (specify):
   - [ ] any table(s) related to sequence listing (specify):

4. [x] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box.
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/figs
   - [ ] the sequence listing (specify):
   - [ ] any table(s) related to sequence listing (specify):

* If item 4 applies, some or all of those sheets may be marked “superseded.”
EXAMINATION REPORT

Box No. V  Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanation supporting such statement

1. Statement:
   Novelty (N)  
   Claims 1-31  YES  
   Claims None  NO
   Inventive step (IS)  
   Claims 1-31  YES  
   Claims None  NO
   Industrial applicability (IA)  
   Claims 1-31  YES  
   Claims None  NO

2. Citations and explanations

Reference is made to the following documents:

The following explanations are based on the claims reasonably anticipated (see Box No. VIII).  

I. Novelty

D1 (see page 1 line 4 to page 14 line 27) discloses dihydrothienopyrimidines of formula 1, and the pharmacologically acceptable salts,

![Chemical Structure]

which are suitable for the treatment of respiratory or gastrointestinal complaints or diseases, inflammatory diseases of the joints, skin, or eyes, diseases of the peripheral or central nervous system or cancers, as well as pharmaceutical compositions which contain these compounds, wherein X denotes O, S, SO or SO₂.

D2 (see abstract, page 1404 Table 1) discloses thieno[3,2-d]pyrimidines as phosphodiesterase IV inhibitors.

D3 (see column 1 line 14 to column 2 line 16) discloses substitution products of dihydrothieno[3,2-d]pyrimidines and acid addition salts thereof which possess cardiovascular and sedative properties, wherein R is hydrogen, halogen, lower alkyl, aryl or aralkyl.

The subject matter of claim 1 differs from D1 mainly on the piperidine in 2-position.  
The subject matter of claim 1 differs from D2 or D3 mainly on the piperidine in 2-position and the oxidation state of the ring sulphur atom.  
Therefore, the subject-matter of claim 1 and consequently further claims 2-23 is novel in the sense of Article 2/2 of GCC Patent Regulation.

Claims 24-29 are directed to use of compounds according to one of claims 1 to 22 for preparing a medicament. Claims 30-31 are directed to pharmaceutical formulations. According to the comment above, since the compounds are different, these claims are novel in the sense of Article 2/2 of GCC Patent Regulation.

(see Supplemental Box)
<table>
<thead>
<tr>
<th>Box No. VII Certain defects in the application</th>
</tr>
</thead>
<tbody>
<tr>
<td>The following defects in the form or contents of the application have been noted:</td>
</tr>
<tr>
<td>1. Multiple dependent claims 4, 6-9, 11-12, 16, 19-20, 22 shall not refer to the preceding multiple dependent claims.</td>
</tr>
</tbody>
</table>
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:

1. Claim 1 is not supported by the description as required by Article 5/2/4 of Patent Regulation of GCC, as its scope is broader than justified by the description for the following reasons: there are broad definitions for the substituents $R_2^-$-$R_4^+$ in claim 1. However, there are limited examples in the description. A person skilled in the art could not expect that all the compounds of formula 1 in claim 1 can possess the pharmaceutical activity as claimed. Therefore, claim 1 is not supported by the description, and does not meet the criteria set out in Article 5/2/4 of Patent Regulation of GCC.

For the similar reasons, claims 2-21, 23-31 do not meet the criteria set out in Article 5/2/4 of Patent Regulation of GCC.

The explanations in Box No. V have been carried out and based on the actual scope of any one of claims 1-21, 23-31.

2. Claims 3-4, 27, 29 are unclear and do not meet the criteria set out in Article 5/2/4 of Patent Regulation of GCC.

(1) The compounds “methanol” and “ethanol” which are not groups appear in the definition of $R_2^-$, $R_{3-1}$ or $R_5^+$ in claims 3-4.

(2) The term “such as……” in claims 27 and 29 renders the extent of protection of claims 27 and 29 unclear as there are general concept and concrete concept simultaneously.

(3) There are general concept “depression” and concrete concept “bipolar or manic depression” simultaneously in claim 29.

The explanations in Box No. V have been carried out and based on that: The compounds “methanol” and “ethanol” in claims 3-4 are deleted, and all scopes in claims 27, 29 are taken into consideration.

3. Claim 23 includes feature of use, but the feature of use does not imply that the claimed compound has a certain particular structure. Namely, claim 23 has substantially the same extent of protection as any one of claims 1 to 22. Hence, claim 23 is not concise and does not meet the criteria set out in Article 5/2/4 of Patent Regulation of GCC.
2. Inventive step

D1 is considered as the closest prior art. The compounds in claim 1 differ from those of D1 by the replacement of piperazine with piperidine in 2-position. The problem to be solved by present application appears to provide further PDE4 inhibitors. Even though the compounds have been modified only slightly compared to those from D1, none of D1-D3 gives any reason to assume that the compounds also possess the desired activity. Thus, the subject matter of claim 1 and consequently further claims 2-23 involves an inventive step and meets the criteria set out in Article 2/3 of Patent Regulation of GCC.

Since claims 1-22 involve an inventive step, the use for preparing a medicament and pharmaceutical formulations also involve an inventive step. Therefore, the subject matter of claims 24-31 involves an inventive step, and meets the criteria set out in Article 2/3 of Patent Regulation of GCC.

3. Industrial Applicability

Claims 1-31 can be produced or used in pharmaceutical industry, and thus they are industrially applicable in the sense of Article 2/4 of GCC Patent Regulation.