PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

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/IB2005/000971	International filing date *(day/month/year)* 13.04.2005
Priority date *(day/month/year)* 16.04.2004	
International Patent Classification (IPC) or both national classification and IPC C07C229/48, A61K31/196, A61P31/10, C07C227/42	
Applicant PLIVA-ISTRAZIVACKI INSTITUT D.O.O.	

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 or 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"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed 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 three 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.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Bedel, C Telephone No. +49 89 2399-2506

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2005/000971

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, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 22,42,44,50,56,63

because:

☒ the said international application, or the said claims Nos. 22,42,44,50,56,63 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ not paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos.

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	
	No:	Claims	1-64
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-64
Industrial applicability (IA)	Yes:	Claims	1-21,23-41,43,45-49,51-55,57-62,64
	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

I Claims 22,42,44,50,56,63 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

For the assessment of the present claims 22,42,44,50,56,63 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

IV The present application concerns the solid state forms ($\alpha,\beta,\delta,\epsilon,\zeta$ defined by specific parameters) of an already known compound the (-)-(1R,2S)-2-amino-4-methylene-cyclopentanecarboxylic acid and their use as pharmaceutical in particular in the treatment of fungal infection in human. This compound is already known from the prior document D1 and D2 to exhibit the same antifungal activity.

The present application lacks unity since the common feature, namely the above mentioned compound, is already known, as well as its use. Consequently, there is no common new and inventive feature linking together all the different inventions.

Therefore, the application must be split in different applications according to the different solid state forms (alpha, beta...)

V Reference is made to the following documents:

D1: MITTENDORFJ ET AL: "NOVEL ANTIFUNGAL BETA-AMINO ACIDS: SYNTHESIS AND ACTIVITY AGAINST CANDIDA ALBICANS" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 13, no. 3, 10 February 2003 (2003-02-10), pages 433-436, XP002317979 ISSN: 0960-894X

D2: J.MITTENDORF: "Efficient Asymetric Synthesis of beta-Amino Acid BAY 10-8888/PLD-118, a Novel Antifungal for the Treament of Yeast Infections" SYNTHESIS, no. 1, 2003, pages 136-140, XP002344848

1. None of the cited documents disclose the different solid state forms nor the parameters used to define them. Therefore the present application could be considered as novel.

2. However, the isolation of a particular solid state form of a known compound is generally considered as a routine procedure for the skilled person merely wishing to get alternative compounds exhibiting the same activity.
Such a subject-matter cannot be regarded as inventive unless **some new and unexpected properties** (biological or pharmacological) linked to the different solid state forms are **proven** over the previously known compound for which no particular solid state form was identified.

   In the absence of such proof, the subject-matter of claims 1-64 cannot be considered as complying with the requirements of Article 33 (3) PCT.

VIII Further remarks :

1. There is a spelling mistake all through the claims and in the description in the chemical formula of the compound. It should read "(1R,2S)" instead of "(1R,1S)", according to the name icofungipen and the title which is correct.

2. The vague and imprecise statement in the description on page 11 (l.5-12) implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.