

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/EP2019/058891	International filing date (day/month/year) 09.04.2019	Priority date (day/month/year) 10.04.2018
International Patent Classification (IPC) or both national classification and IPC INV. C07D271/06 C07D413/04 A01N43/74 A01P3/00		
Applicant BAYER 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 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 Panday, Narendra 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>4, 5, 8-11</u>
	No: Claims	<u>1-3, 6, 7</u>
Inventive step (IS)	Yes: Claims	<u>4, 5, 8-11</u>
	No: Claims	<u>1-3, 6, 7</u>
Industrial applicability (IA)	Yes: Claims	<u>1-11</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure.

- D1 RASSUKANA YULIYA V ET AL: "Fluorinated NH-iminophosphonates and iminocarboxylates: novel synthons for the preparation of biorelevant [alpha]-aminophosphonates and carboxyl",
TETRAHEDRON,
vol. 70, no. 18, pages 2928-2937, XP028841804,
ISSN: 0040-4020, DOI: 10.1016/J.TET.2014.03.030
- D2 DATABASE CAPLUS [Online]
CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1990,
SOLOSHONOK, V. A. et al.: "Reactions of methyl trifluoropyruvate and its (methoxycarbonyl)imine with pi-rich heterocycles and dipolar compounds",
Database accession no. 1990:459045 ; & SOLOSCHONOK, V. A. ET AL.: "Reactions of methyl trifluoropyruvate and its (methoxycarbonyl)imine with pi-rich heterocycles and dipolar compounds",
ZHURNAL ORGANICHESKOI KHIMII,
vol. 26, no. 2, 1990, - 1990, pages 419-425,
- D3 Rajendra M. Srivastava ET AL: "Synthesis Spectroscopic Studies and the Mechanism of Formation of 4,5-Dihydro-1,2,4-oxadiazoles",
Journal of Heterocyclic Chemistry, 1 February 1987 (1987-02-01), pages 101-105,
XP055492776,
DOI: 10.1002/jhet.5570240121
Retrieved from the Internet:
URL:<https://onlinelibrary.wiley.com/doi/pdf/10.1002/jhet.5570240121>
[retrieved on 2018-07-16]
- D4 WO 2018/029242 A1 (SYNGENTA PARTICIPATIONS AG [CH]) 15 February 2018
(2018-02-15)
- D5 DATABASE CAPLUS [Online]
CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2003,
Pharmacia Corporation: "Preparation of amidine-substituted polycyclic compound prodrugs useful for selective inhibition of serine proteases of the coagulation cascade",
Database accession no. 2003:282399 ; & WO 03/028729 A2 (PHARMACIA CORP [US]; SOUTH MICHAEL S [US]; WEBBER RONALD K [US]; HUANG) 10 April 2003
(2003-04-10)

Re Item V

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

1. Novelty (A. 33(2) PCT)

D1 and **D2** (see passages as indicated in the European search report) disclose compounds falling under the scope of claims 1-3, 7 (**D1**) and 1-3, 6 (**D2**) and which are not excluded by the proviso.

2. Inventive step (A. 33(3) PCT)

Insofar subject-matter lacks novelty, it cannot imply an inventive step.

Regarding the novel part of the claims, the closest prior art is **D4**, which discloses oxadiazoles carrying a trifluoromethyl group and carbonylaminophenyl or pyridyl group. These oxadiazoles are, as present oxadiazolines, disclosed as microbiocidal, especially as fungicidal compounds, for agrochemical use.

Compounds according to present invention coming closest to those of **D1** differ by the partial reduction of the oxadiazole moiety to a oxadiazoline moiety.

In lack of comparative data, the oxadiazolines of present invention, which indeed have fungicidal activity (data on pages 43 to 45 of the application), are to be viewed as alternative fungicidal agrochemicals.

The objective technical problem thus could be formulated as being the provision of alternative fungicidal compounds for agrochemical applications.

D3 teaches that oxadiazolines, in which the trifluoromethyl as present in the oxadiazoles of **D4** is replaced by a methyl, ethyl or phenyl, weakly inhibit the growth of *neurospora crassa* (fungus) and *mycobacterium smegmatis* (bacterium).

It is considered that the rather weak activity observed just against two micro-organism and no activity against other tested micro-organisms would not have motivated the skilled person to change the oxadiazole moiety of the compounds of **D4** to a oxadiazoline in expectation to obtain compounds similarly potent against important fungi parasitical on crop plants.

Claims 8 and 9 (composition including an agriculturally acceptable carrier and the method to combat phytopathogenic fungi) thus implies an inventive step.

The same applies to claims 1 to 7, insofar they fulfill the requirements of novelty.

Inventive step also applies to the process (claims 10/11) of preparing compounds for which inventive step is acknowledged. Insofar claims 10 and 11 also include the preparation of compounds which are part of the state of the art (**D1** and **D2**) they are currently considered as relating to a non-inventive analogy process for the preparation of such known compound. Should the presently claimed process for the preparation of such known compound represent a non-obvious alternative or even improved synthesis compared to the known syntheses, such subject-matter would in any case not share the same inventive concept of the remaining subject-matter causing a lack of unity in the sense of Rule 13.1 PCT. This subject-matter would then have to be assessed in the context of a separate invention.

Re Item VII

Certain defects in the international application

The compounds excluded by means of the proviso appear to be compounds disclosed in **D5**. For the sake of transparency of the patent it would be required to indicate the reason for excluding these compounds: i.e. their accidental anticipation in **D5**. Should the applicant opt for excluding the compounds of **D1** and **D2** by a proviso as well, the reason for such exclusion (accidental anticipation in **D1** and **D2**) should then also be indicated.