

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/EP2019/086373	International filing date (day/month/year) 19.12.2019	Priority date (day/month/year) 20.12.2018
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International Patent Classification (IPC) or both national classification and IPC
INV. C07D413/14 C07D403/04 C07D413/04 A01N43/88 C07D237/12 C07D237/14 C07D403/12 C07D417/04
C07D417/14 C07D471/04

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 Papathoma, Sofia 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>1-16</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-16</u>
Industrial applicability (IA)	Yes: Claims	<u>1-16</u>
	No: Claims	

2. Citations and explanations

see separate sheet

This Written Opinion is based on the **following application documents**

Description, Pages

1-302 as originally filed

Claims, Numbers

1-16 as originally filed

The present application relates to compounds of formula (I) useful for controlling phytopathogenic fungi.

Re Item V

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

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

- D1 WO 2007/031213 A1 (BAYER CROPSCIENCE AG [DE]; KRUEGER BERND-WIELAND [DE]; HENSE ACHIM [DE] 22 March 2007 (2007-03-22)
- D2 US 6 251 899 B1 (GERDES PETER [DE] ET AL) 26 June 2001 (2001-06-26)
- D3 US 2006/252755 A1 (SHABER STEVEN H [US] ET AL) 9 November 2006 (2006-11-09)
- D4 WO 2008/089934 A1 (SYNGENTA PARTICIPATIONS AG [CH]; LAMBERTH CLEMENS [CH]; WENDEBORN SEBA) 31 July 2008 (2008-07-31)
- D5 WO 2016/201168 A1 (FORUM PHARMCEUTICALS INC [US]) 15 December 2016 (2016-12-15)

1) Article 33(2) PCT

Document D1 discloses dioxazine- and oxadiazine-substituted arylamides for controlling pests. The entities disclosed therein differ from the presently claimed entities at least in that they lack the pyridazine core moiety characterising the entities of the present application.

Document D2 discloses methoximinomethyloxadiazines as plant-fungicides. The entities disclosed therein differ from the presently claimed entities at least in that they lack the pyridazine core moiety characterising the entities of the present application.

Document D3 discloses 4,5-dihydro-1,2,4-triazin-6-ones as plant-fungicides. The entities disclosed therein differ from the presently claimed entities at least in that they lack the pyridazine core moiety characterising the entities of the present application.

Document D4 discloses pyridazine derivatives as plant-fungicides. The entities disclosed therein differ from the presently claimed entities at least in that they lack the oxadiazine moiety disclosed in the examples or the more generic 5-7-membered heterocyclic moiety defined in claim 1 characterising the entities of the present application.

Document D5 discloses the structurally closest related compounds to those presently claimed (see Table I). Said compounds however lack the pyridazine core moiety characterising the entities of the present application and have a different activity (are useful in the treatment of a neurodegenerative disease).

In view of the above differences, the claimed entities are acknowledged as novel.

By consequence, claim 1 and the dependent thereto claims 2-7 relating to compounds of formula (I), claims 8-10 relating to a process for their preparation and claims 14-16 relating to their compositions and to their use are acknowledged to fulfil the requirements of Article 33(2) PCT.

In addition, the prior art does not disclose compounds of present formulae (3), (4), (7), (20) and (23), and therefore claims 11-13 relating to intermediates of said formulae used in the preparation of compounds of formula (I) are also acknowledged to fulfil the requirements of Article 33(2) PCT.

2) Article 33(3) PCT

The prior art documents D1-D4 disclose compounds useful for controlling phytopathogenic fungi (for D1, see page 20, line 9). As closest prior art is regarded to be document D1.

In view of the closest prior the technical problem underlying the present application is seen in the provision of further compounds useful for controlling phytopathogenic fungi.

As solution are claimed the compounds of present formula (I).

The biological examples on pages 293-302 show that the exemplified entities have the claimed activity.

The presently claimed solution differs from the solution provided in the closest prior art in that the claimed entities are characterised by a pyridazine core moiety which is absent in the entities of the closest prior art.

A pyridazine core moiety is disclosed in the fungicidal compounds of document D4.

However, the structural differences of the compounds disclosed in the closest prior art D1 and in document D4 are so wide that the person skilled in the art would not come up in combining the two documents and even if he would, he would not be able to arrive to the structural design of the claimed entities.

It is therefore considered that the structural design of the claimed entities is not obvious for the person skilled in the art.

However, before a positive opinion on the inventive merit of the presently claimed subject-matter is expressed, it is mentioned that the variation in the substitution pattern of the exemplified entities in the present application does not justify the breadth of the scope claimed:

- as Q is disclosed only a substituted / fused phenyl, and in only 7 examples as Q is disclosed pyridin-3yl, in only 3 thienyl, and in only one pyrazolyl,
- A is in the majority of the examples Ring 1; Rings 6, 7 and 12-17 relate to the same oxadiazine ring substituted with F, Me, Et, OH or OEt. Only example I-007 is with Ring 2 (m=0), only examples I-026, I-062 and I-079 are with Ring 3 (m=2), only examples I-077, I-078, I-185 and I-194 are with Ring 4, only examples I-117, I-118 and I-304 are with Ring 5, only examples I-156 and I-173 are with Ring 8, only example I-181 is with Ring 9, only example I-181 is with Ring 10 and only examples I-184 and I-195 are with Ring 11. In other words from the 348 examples disclosed in the present application, some variation in the core structure is shown in only 17 of them. This variation is however in no relation to the definition of the R¹, R², R³, R⁴, R⁵ and T groups.
- as R¹ is disclosed only hydrogen, methyl and ethyl, as R² only hydrogen, as R³ hydrogen, methyl and ethyl and as R⁴ only hydrogen and methyl,

- none of the R¹ and R², and R³ and R⁴ forms a ring spiro fused to the e.g. oxadiazine core moiety,
- T and R⁵ are always hydrogen,
- m is only 1 and only in example I-007 it is 0 and in examples I-026, I-062 and I-079 it is 2,
- as R⁷ is in the majority of the cases methyl and chloro and only in isolated examples methylamino, cyclopropylamino, 1-ethoxyethen-1-yl, ethyl, vinyl, acetyl pyridin-4-yl, 1-hydroxy-ethyl, 1-fluoroethyl, etc.
- as R⁸ is in the majority of the cases hydrogen and only in isolated examples methoxy, methyl, methylamino, cyclopropylamino, chloro, iodo, 2-methoxyethoxy, pyridin-4-yl, 2-methoxyethyl, cyclopentyl, etc.
- L is absent or methylene, and only in examples I-126, I-131, I-132 and I-133 a variation to methoxy, thio, propan-yl- and ethyl is shown
- R⁶ is in the majority of the cases a substituted phenyl and only in isolated examples it is indolyl, naphthalen-2-yl, furan-2-yl, indanyl, thienyl, pyrrolo[2,3-b]pyridinyl, benzofuranyl and pyridinyl.

In addition, the above mentioned variation is even more limited when it comes to the exemplified compounds of formulae (3), (4), (7), (20) and (23).

The applicant is entitled to claim only obvious modifications of what was described (close related variations), since the claims should represent a reasonable generalisation of the examples given in the description: the technical features stated in the description/ examples as being essential must be the same as those used to define the invention in the claims. The reason for that is that the problem to be solved should be solved by the whole scope of the claimed subject matter (every compound falling within its scope) and not just by individual compounds- especially since the problem may be seen in the provision of compounds acting on a biological system (i.e. on a system depending upon very different parameters). If this were not the case, an invention could arbitrarily be broadened to any limit without consideration, whether the compounds are actually solving the problem underlying the invention (Article 33(3) PCT).

Therefore, it is considered that either further evidence is needed that the problem is solved over the whole breadth claimed or the claims need to be revised and reduced to those compounds that are actually disclosed, and obvious equivalents thereof.

As a final point in this respect reference is made to the use of terms such as aromatic and non-aromatic heterocycles. The use of these terms throughout the claims without further qualification renders the claims obscure in scope. These terms are non-limitative and embrace an infinite number of possibilities not yet explored by the applicant. Therefore it is not clear whether all compounds implied fall within the scope of the present claims and/or represent a solution of the problem underlying the present application. Consequently, for reasons of inventive step and clarity these terms should be limited to the specific meanings given in the description.

In view of the above, no positive opinion can be expressed at the moment with regard to whether the technical problem underlying the present application is solved over the whole breadth claimed and by consequence it is at present considered that the requirements of Article 33(3) PCT are not met.