

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

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/EP2016/068890

International filing date (day/month/year)
08.08.2016

Priority date (day/month/year)
12.08.2015

International Patent Classification (IPC) or both national classification and IPC
INV. C07D471/04 A01N43/52

Applicant
SYNGENTA PARTICIPATIONS AG

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:



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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. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☒ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

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, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ 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 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>1-15</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-12, 14, 15</u>
	No: Claims	<u>13</u>
Industrial applicability (IA)	Yes: Claims	<u>1-15</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

Re Item II

Priority

The priority is not valid for the compounds of claim 13, because they are not disclosed in the priority document.

Re Item IV

Lack of unity of invention

Starting from document D2 the problem to be solved by the present application may be regarded to be the provision of further isoquinoline derivatives to be used as antimicrobial agents against plant diseases. The solution of the applicant resides in the compounds of formula I in which the isoquinoline group is substituted with a Q1-Q2-N bicyclic ring system. It is thus the Q1-Q2-N bicyclic ring system which forms a contribution over the prior art. The intermediates of formula XA, XB, XC and XD do not possess the Q1-Q2-N bicyclic ring system and they can therefore not be seen as forming part of the inventive concept. The requirements of unity of invention have therefore not been met (Rule 13 PCT).

Re Item V

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

1 The present application relates to microbiocidal isoquinoline derivatives.

2 Reference is made to the following documents:

D1 DATABASE chemcats, [Online] 1 January 2015 (2015-01-01), XP002753014, retrieved from chemcats Database accession no. 2137532535; ; & "Aurora Building blocks", 1 January 2015

D2 EP 1 736 471 A1, cited in the application

D3 WO 2016/156085 A1 (SYNGENTA PARTICIPATIONS AG [CH])
6 October 2016 (2016-10-06)

Document D3 was published after the filing date and is therefore not regarded as prior art.

3 Novelty

Document D1 discloses isoquinoline derivatives differing from the compounds of formula I in that Ra is hydrogen.

Document D2 discloses isoquinoline derivatives differing from the compounds of formula I in that they are substituted with a quinoline group. The compounds have antimicrobial activity against various plant diseases.

It is noted that document D3 discloses a compound of formula XA and a compound of formula XC.

A compound of formula I is disclosed in none of the cited documents. Claims 1-12 therefore fulfil the requirements of Art 33(2) PCT.

A compound of formula XA, XB, XC or XD is disclosed in none of the cited documents. Claim 13 therefore fulfils the requirements of Art 33(2) PCT.

Claim 14 describes a composition comprising a compound of formula I and is novel by consequence.

Claim 15 describes a method of combating, preventing or controlling phytopathogenic diseases comprising administering a compound of formula I and is novel by consequence.

4 Inventive step (Art 33(3) PCT)

Starting from document D2 the problem to be solved in claims 1-12, 14 and 15 may be regarded to be the provision of further isoquinoline derivatives to be used as antimicrobial agents against plant diseases. The solution of the applicant resides in the compounds of formula I in which the isoquinoline group is substituted with the Q1-Q2-N bicyclic ring system. The applicant shows on pages 91-94 that certain compounds of formula I are effective against various plant diseases. As the structural changes have not been made obvious the solution of the applicant for claims 1-12, 14 and 15 may be regarded to involve an inventive step.

Claim 13 relates to intermediates for the synthesis of compounds of formula I. The compounds of formula X are transformed into compounds of formula IX (see scheme 4). The compounds of formula IX are then reacted with ethynyltrialkylsilane derivatives (scheme 18). Finally the 1-ethynyl derivatives of the compounds of formula IX are reacted with pyridin-1-ium-1-amine derivatives to give the compounds of formula I. The compounds of document D1 in which the Q1-Q2-N ring is an isoquinoline ring are prepared via the route depicted in scheme 13 of the present application (see Method A in document D1). There is thus no analogous process disclosed in the prior art for the route using the intermediates of claim 13. The applicant shows in examples 4, 5 and 6 that using the intermediates XA and XC the compounds

of formula I can be prepared. However, no examples for the use of intermediates XB and XD are present. It has therefore not been made credible that all the intermediates of claim 13 lead to the compounds of formula I. Inventive step can therefore not be acknowledged for claim 13.