

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: AMY KROM
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Date of mailing
(day/month/year) **SEP 28 2022**

Applicant's or agent's file reference
82347-WO-REG-ORG-P-1

FOR FURTHER ACTION
See paragraph 2 below

International application No. PCT/US 22/27372	International filing date (day/month/year) 03 May 2022 (03.05.2022)	Priority date (day/month/year) 04 May 2021 (04.05.2021)
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International Patent Classification (IPC) or both national classification and IPC
IPC - INV. C12N 15/82, C07K 14/325; ADD. A01N 63/23, A01H 5/10 (2022.01)
CPC - INV. C07K 14/325, C12N 15/8286; ADD. Y02A 40/146, C12N 15/8213

Applicant
SYNGENTA CROP PROTECTION 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 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/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Date of completion of this opinion 23 July 2022	Authorized officer Kari Rodriguez PCT Help Desk Telephone No. 571-272-4300
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**WRITTEN OPINION OF THE
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Box No. I Basis of this 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 43*bis*.1(b)).
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 13*ter*.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 13*ter*.1(a)).
☐ on paper or in the form of an image file (Rule 13*ter*.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:

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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, 24-26, 29-30, 37-44

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 22, 24-26, 29-30, 37-44 are so unclear that no meaningful opinion could be formed (*specify*):

claims 22, 24-26, 29-30, 37-44 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 22, 24-26, 29-30, 37-44

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

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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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+, Claims 1-19, 33-36, directed to a nucleic acid molecule. The nucleic acid molecule will be searched to the extent that the nucleic acid molecule encompasses a nucleic acid sequence that is at least 100% identical to SEQ ID NO: 1, or the complement thereof (note, these are the first claimed sequences for the inventive nucleic acid molecule). The first named invention was determined based on the first claimed sequence (claim 3) for the inventive nucleic acid molecule embodiment. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. It is believed that claims 1-19, 33-36 encompass this first named invention, and thus these claims will be searched without fee to the extent that the nucleic acid molecule encompasses a nucleic acid sequence that is at least 100% identical to SEQ ID NO: 1, or the complement thereof, wherein the nucleic acid sequence encodes a polypeptide comprising the sequence of SEQ ID NO: 4. Additional nucleic acid molecule(s) comprising additional sequence(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected nucleic acid molecule(s) comprising additional sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be a nucleic acid molecule comprising a nucleic acid sequence that is at least 100% identical to SEQ ID NO: 8 (claims 1-19, 33-36).

Group II, claims 20-21, 23, directed to methods of producing a transgenic plant or plant product.

Group III, claims 27-28, directed to a method of controlling a lepidopteran pest.

Group IV, claims 31-32, directed to a method of detecting the presence of a nucleic acid molecule in a sample.

The inventions listed as Group I+, II, III and IV do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special technical features

The inventions of Group I+ each include the special technical feature of a unique amino acid and/or nucleic acid sequence. Each nucleic acid sequence encodes a unique peptide, and is considered a distinct technical feature. Each amino acid sequence comprises a unique peptide, and is considered a distinct technical feature.

No technical features are shared between the nucleic acid sequences in each of Group I+ inventions and, accordingly, these inventions lack unity a priori.

Additionally, even if Group I+, II, III and IV inventions were considered to share technical features, these shared technical features are previously disclosed by the prior art, as further discussed below.

----Please see continuation in first supplemental box-----

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

☐ all parts.

☒ the parts relating to claims Nos. 1-19, 33-36, limited to SEQ ID NO:1

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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

1. Statement

Novelty (N)	Claims	1-19, 33-36	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-19, 33-36	YES
	Claims	None	NO
Industrial applicability (IA)	Claims	1-19, 33-36	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-19, 33-36 meet the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed subject matter, specifically SEQ ID NO:1.

Regarding claim 1, WO 2018/111553 A1 to Syngenta Participations AG et al., (hereinafter 'Syngenta'553') teaches Maize optimized *Bacillus thuringiensis* Bt29-Bt22 chimeric gene SEQ ID 7 that is at least 100% identical to instant SEQ ID NO: 3, wherein the nucleic acid sequence encodes a polypeptide comprising the sequence of SEQ ID NO: 4 (Claim 9 - 'The polynucleotide according to claim 8, wherein the polynucleotide comprises a nucleotide sequence that comprises:

(a) a nucleotide sequence of SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 10, SEQ ID NO: 11 or SEQ ID NO: 14 or a toxin- encoding fragment thereof;'; SEQ ID NO 7, nt 1-3510 has 100% identity to instant SEQ ID NO: 3 encoding a polypeptide comprising the sequence of SEQ ID NO: 4). Syngenta'553 fails to teach the remainder of nucleic acid sequence of claimed SEQ ID NO:1.

WO 2020/176412 A2 to Syngenta Crop Protection AG et al., (hereinafter 'Syngenta'412') teaches Vector 25053 DNA sequence, SEQ 533 with 72.4% identity to claimed SEQ ID NO:1 (p28, ln 11 - 'SEQ ID NO: 533 is a nucleotide sequence for vector 25053.'; SEQ ID NO 533, nt 9198-11017 has 72.4% identity to claimed SEQ ID NO:1). Syngenta'412 fails to teach the sequence of claimed SEQ ID NO:1.

There is no prior art of record that, alone or in combination with Syngenta'553, teaches or otherwise makes obvious a nucleic acid molecule comprising a nucleic acid sequence that is at least 100% identical to SEQ ID NO: 1, or the complement thereof. Therefore, claim 1 meets the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed subject matter, specifically SEQ ID NO:1.

Regarding claims 2-19, 33-36, these claims are dependent of claim 1, and as such, claims 2-19, 33-36, also meet the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed subject matter, specifically SEQ ID NO:1.

Claims 1-19, 33-36 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box No. IV. 3. Lack of unity of invention

Common technical features

The feature shared by Groups I+, II, III, and IV is a nucleic acid molecule comprising a nucleic acid sequence wherein the nucleic acid sequence encodes a polypeptide comprising an amino acid sequence.

However, these shared technical features are previously disclosed by US 2019/0194644 A1 to Syngenta Participations AG, (hereinafter 'Syngenta').

Syngenta teaches a nucleic acid molecule comprising a nucleic acid sequence wherein the nucleic acid sequence encodes a polypeptide comprising an amino acid sequence (Abstract - 'Compositions and methods for controlling pests are disclosed. In particular, methods for modulating the activity of Cry1Ba proteins against lepidopteran or coleopteran pests are provided. Further, mutant Cry1Ba proteins having modulated insecticidal activity compared to native Cry1Ba proteins are disclosed.'; Claim 1 - 'A mutant Cry1Ba protein having toxicity to at least European corn borer (*Ostrinia nubilalis*) comprising a Trp (W) or a Phe (F) or a Pro (P) amino acid at an amino acid position corresponding to or at amino acid position 150 of SEQ ID NO: 2.'; para [0019] - 'The invention is further drawn to nucleic acid sequences encoding the eCry1Ba proteins, and to compositions and formulations containing the eCry1Ba proteins, which are capable of inhibiting the ability of insect pests to survive, grow and reproduce, or of limiting insect-related damage or loss to crop plants'; para [0012] - 'Other possible ways to mitigate resistance development include pyramiding multiple Cry proteins in the same transgenic crop plant or replacing existing mature products with new products that produce different Cry proteins. For example, as the current Cry1Ab corn hybrid market matures, new products may be introduced that have Cry proteins other than Cry1Ab or other Cry proteins in addition to Cry1Ab. It would be beneficial for proteins that replace Cry1Ab to have the same or similar specific activity to European corn borer as Cry1Ab.'; para [0044] - 'The present invention further provides a method of controlling insects wherein a transgenic plant comprising a nucleic acid encoding an eCry1Ba protein or vCry1Ba protein further comprises a second nucleic acid sequence or multiple nucleic acid sequences that encode at least one other pesticidal principle. In one aspect, the second nucleic acid sequence encodes a Cry protein different than the eCry1Ba or vCry1Ba proteins of the invention, those that encode a Vegetative Insecticidal Protein, such as those disclosed in U.S. Pat. Nos. 5,849,870 and 5,877,012, which are incorporated herein by reference').

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I+, II, III and IV inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.

Continuation of item 4 above: claims 22, 24-26, 29-30, 37-44 are held unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).