

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference EVOGL-015-PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/IL2022/050450	International filing date (<i>day/month/year</i>) 02 May 2022 (02.05.2022)	Priority date (<i>day/month/year</i>) 06 May 2021 (06.05.2021)	
International Patent Classification (IPC) or national classification and IPC See relevant information in Form PCT/ISA/237			
Applicant LAVIE BIO LTD.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	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 Article 35(2) 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

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis*.2).

	Date of issuance of this report 24 October 2023 (24.10.2023)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Simin Baharlou e-mail pct.team9@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: WEBB & CO. P.O. Box 4177 Ness Ziona 7414003 Israel		Date of mailing (day/month/year) 21 Sep 2022	
Applicant's or agent's file reference EVOGL-015-PCT		FOR FURTHER ACTION See paragraph 2 below	
International application No. PCT/IL2022/050450	International filing date (day/month/year) 02 May 2022	Priority date (day/month/year) 06 May 2021	
International Patent Classification (IPC) or both national classification and IPC IPC (20220101) C12R 1/64 A01P 3/00 A01C 1/06 C12R 1/01 C12N 1/20 A01N 63/20 CPC (20130101) C12R 1/64 A01P 3/00 A01C 1/06 C12R 2001/64 C12R 2001/01 C12N 1/205 A01N 63/20			
Applicant LAVIE BIO LTD.			

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: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Email address: pctoffice@justice.gov.il	Date of completion of this opinion 21 Sep 2022	Authorized officer RAVEH Eli Telephone No. 972-73-3927232
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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/IL2022/050450

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:

WRITTEN OPINION OF THE
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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 International Application does not meet the requirements of unity of invention because it does not relate to one invention, or to a group of inventions so linked as to form a single general inventive concept. (PCT Rule 13.1)

The requirement of unity of invention is only fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. (PCT Rule 13.2). The determination whether a group of inventions is linked, so as to form a single general inventive concept, was made without regard to whether the inventions were claimed in separate claims or as alternatives within a single claim. (PCT Rule 13.3).

The application contains 27 inventions. The reasons for which the inventions are not so linked to form a single general inventive concept are as follows.

Invention group 1 - claims 1-37,39,41-43 and claims 45-46 (partially) - are directed to 26 different isolated bacterial strains or a functional homolog thereof, as listed in claim 1, each strain constitutes a different invention. Therefore, this group of inventions consists of 26 inventions. Claim 45 is affiliated only with invention 1 (following the order of strains listed in claim 1, i.e. strain LAV58567), further defining a selection method by the strain of invention 1 as the end product of the method (regardless of clarity issues concerning the use of a "result to be achieved" language in this claim instead of specifying the starting material (i.e. strain) used in the method to reach the end product). The claims directed to invention 1 (i.e. strain LAV58567) are 1-37,39,41-43, and 45-46.

Invention 2 - Claims 44 (completely) and 45-46 (partially) - are directed to a selection method of obtaining a modified bacterial strain having an improved capability to enable plants to cope with pathogenic fungi and/or oomycetes.

The inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1, since the features of inventions 1-27 are so different that they do not share any same or corresponding special technical feature (Rule 13.2).

Regarding inventions 1-26, each invention is directed to a distinct bacterial strains characterized by unique features; the common technical effect of the different strains is their anti-fungal activity, as taught by the subject application, yet the subject application fails to demonstrate a common structural/molecular element underling this common activity.

Regarding invention 27, the subject matter of this invention is directed to a method of obtaining a modified bacterial strain having an improved capability to enable plants to cope with pathogenic fungi and/or oomycetes The method neither necessarily results in, nor necessarily uses, a starting material (i.e. strain) which is selected from the strains specified in claim 1 and, therefore, is not specially adapted for either obtaining or using the said strains.

It follows that the technical features of inventions 1-27 are different and have different technical effects. Hence, they are not corresponding.

Since the inventions are not linked by a single general inventive concept, the requirements for unity of invention are not met.

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. 1-43,45,46

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IL2022/050450

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 1-37,39,41-43,45,46	YES
	Claims	NO
Inventive step (IS)	Claims 1-37,39,41-43,46	YES
	Claims 45	NO
Industrial applicability (IA)	Claims 1-37,39,41-43,45,46	YES
	Claims	NO

2. Citations and explanations:

2.1. Reference is made to the following documents:

D1: WO2016156164 (A1); (INDUSTRIAS QUÍMICAS DEL VALLÉS, S.A), 2016-10-06;

D2: NCBI GenBank Accession No. CP011130.1, *Lysobacter capsici* strain 55 chromosome, complete genome; [Retrieved from [https://www.ncbi.nlm.nih.gov/nucleotide/CP011130.1?report=genbank&log\\$=nuclalign&blast_rank=2&RID=FVTKUYFR016](https://www.ncbi.nlm.nih.gov/nucleotide/CP011130.1?report=genbank&log$=nuclalign&blast_rank=2&RID=FVTKUYFR016) on 18-08-2022], 16-11-2015;

D3: DE BRUIJN, Irene, et al. Comparative genomics and metabolic profiling of the genus *Lysobacter*. BMC genomics, 2015, 16.1: 1-16. DE BRUIJN, Irene, et al.;

D4: US9756863B2; (FONDAZIONE EDMUND MACH, ; Fondazione Edmund), 2016-03-24;

D5: NCBI GenBank Accession No. LG066239.1, KR 1020150078847-A/1: Novel *Lysobacter capsici* having activity against plant pathogen and use of thereof; [Retrieved from [https://www.ncbi.nlm.nih.gov/nucleotide/LG066239.1?report=genbank&log\\$=nuclalign&blast_rank=3&RID=FVT70CYW016](https://www.ncbi.nlm.nih.gov/nucleotide/LG066239.1?report=genbank&log$=nuclalign&blast_rank=3&RID=FVT70CYW016) on 18-08-2022], 29-06-2016;

2.2. Novelty

The subject matter of claims 1-37, 39, 41-43 and 45-46 appears to meet the criteria of Article 33(2) PCT with respect to novelty.

2.3 Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of (claim 44 and) claim 45 does not involve an inventive step in the sense of Article 33 (3) PCT.

Regarding independent claim 44, **and beyond necessity, since this claim is not included in the examined scope of the first invention**, this claim appears to specify a method which can be, e.g. a routine directed selection method in microbiology. Such a method could have been applied by the person skilled in the art, *inter alia*, for obtaining the modified bacterial strain having the improved capability to confer or enhance the resistance of a plant towards said pathogenic fungi and/or oomycetes, or to protect the plant from a disease caused by said pathogenic fungi and/or oomycetes as compared to the unmodified parent bacterial strain without the need of inventive skills (see, e.g. D1, p. 4, lns. 15-28, which relates to mutants

selection in the context of the field of the present application, i.e. antifungal bacteria for plant protection).

Regarding dependent claim 45, this claim further defines the method by specifying the resulting bacterial strain, LAV58567, i.e., in terms of "results to be achieved", without technically limiting the method so as to define how it is specially adapted to produce the specified strain. Notwithstanding the clarity issues resulting from the "results to be achieved" language, as raised in Box VIII below, it is noted that even if the resulting strain is regarded inventive, it cannot confer with the overtly routine method, as specified, and as long as it does not seem to be specially adapted for obtaining the specified strain, any inventive step. Therefore, the subject matter of both claims 44 and 45 appear to lack an inventive step.

2.2. Allowable subject matter

The subject-matter of claims 1-37, 39, 41-43 and 46 appears to meet the requirements of Articles 33(2) and 33(3) PCT with respect to novelty and inventive step.

Claims 1-37, 39, 41-43 and 46 specify the bacterial strain LAV58567, products comprising said strain and applications or methods making use of this strain for the general purpose of plant protection.

Any one of D2 - D5 may be considered as the closest prior art:

D2 (and D3 to which D2 refers) discloses DNA sequence (at positions 498199-499731) encoding a 16S ribosomal RNA, which is 99% identical with SEQ ID NO:5. D4 and D5 disclose *Lysobacter* strains having antifungal activity for plant protection, with sequences having 91% coverage and 99.7% identity or 92% coverage and 98% identity, respectively, SEQ ID NO:5 (D4, SEQ. ID. No. 5; D5, the whole document).

Nevertheless, none of these documents or of the other documents cited in the search report disclose the specific LAV58567 or any identifying feature of said strain, let alone the use of said strain for plant protection.

Therefore, the subject-matter of claims 1-37, 39, 41-43 and 46 meets the criteria set out in PCT Article 33(2)-(3).

2.5 Industrial applicability

The subject matter of claims 1-37, 39, 41-46 is considered to meet the requirements of industrial applicability under Article 33(4) of the PCT.

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:

claim 45 lacks clarity contrary to article 6 PCT; this claim further defines the method by specifying the resulting bacterial strain, LAV58567, i.e., the method is defined in terms of "results to be achieved", without technically limiting the method so as to define how it is specially adapted to produce the specified strain, rendering the scope of the claim vague and indefinite;

claim 7 lacks clarity with respect to the specified definition of the concentration as exceeding "that found in nature"; this definition appears to be vague and renders the scope of the claim indefinite;

claims 9 and 18 lack clarity contrary to article 6 PCT, with respect to the term "substantially" which renders the scope of this claim indefinite;

claim 21 lacks clarity contrary to article 6 PCT, with respect to the term "optionally"; it is not clear whether the term refers merely to section (ii) of the claim or maybe also to section (iii) of the claim;

claim 33 is not fully supported by the description; the subject description (table 6) positively indicates that the LAV58567 has no antifungal activity against the fungal species *Botrytis cinerea*.

claims 1-8, 10, 12-15, 23-25, 36-41 and all the claims depending therefrom specify, inter alia, "functional homolog" of the claimed strains; the subject description further defines this term (on p. 27, lns. 12-20) as referring, inter alia, to a modification (i.e., mutant, at least one mutation) of the bacterial strains of the invention resulting in a microbial strain that is endowed with substantially the same ensemble of biological activities, particularly anti-fungal and/or anti-oomycete activities; according to the description the term "functional homolog" therefore appears to define the subject matter in terms of "results to be achieved" which is usually considered to lack clarity contrary to article 6 PCT; however, in this instance it seems that claimed scope will be unfairly narrowed absent alternatives to this definition. Therefore, this authority is of the opinion that the term "functional homolog" is to be allowed, however must be strictly limited according to the definition in the description, e.g., must fulfill the proviso "with substantially the same ensemble of biological activities, particularly anti-fungal and/or anti-oomycete activities (+/- 10%, 20%, 40%, 50%, or 60% when tested under the same conditions)".