From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION TREATY)

(PCT Rule 44bis.1(c))

To:

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Date of mailing *(day/month/year)* 13 June 2024 (13.06.2024)	
Applicant's or agent's file reference AF3993 PCT S3	**IMPORTANT NOTICE**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2022/083929	30 November 2022 (30.11.2022)	01 December 2021 (01.12.2021)

Applicant
UCB BIOPHARMA SRL et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
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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 AF3993 PCT S3	**FOR FURTHER ACTION** See item 4 below	
International application No. PCT/EP2022/083929	International filing date *(day/month/year)* 30 November 2022 (30.11.2022)	Priority date *(day/month/year)* 01 December 2021 (01.12.2021)
International Patent Classification (IPC) or national classification and IPC See relevant information in Form PCT/ISA/237		
Applicant UCB BIOPHARMA SRL		

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 02 May 2024 (02.05.2024)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Nora Lindner e-mail pct.team5@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.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.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2022/083929	30.11.2022	01.12.2021

International Patent Classification (IPC) or both national classification and IPC
INV. A61K39/395 A61K47/60 C07K16/28

Applicant
UCB BIOPHARMA SRL

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 43*bis*.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 notifed the International Bureau under Rule 66.1*bis*(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:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Bernhardt, Wiebke Telephone No. +31 70 340-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2022/083929

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 43*bis*.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.

   b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)),

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4-7, 10-12, 14-16
	No:	Claims	1-3, 8, 9, 13, 17, 18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

see separate sheet

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:

see separate sheet

Re Item V

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

1 Reference is made to the following documents:

D1 US 2020/390705 A1 (BATENS MAARTEN [GB] ET AL) 17 December 2020 (2020-12-17)

D2 WO 2008/118356 A2 (BIOGEN IDEC INC [US]; UCB PHARMA SA [BE] ET AL.) 2 October 2008 (2008-10-02)

D3 WO 2016/119909 A1 (UCB BIOPHARMA SPRL [BE]) 4 August 2016 (2016-08-04)

D4 Zhu Gaozhong ET AL: "Formulation and protein- and peptide-based parenteral products" In: "Parental Medications Third Edition", 1 January 2010 (2010-01-01), XP055874783, pages 222-253,

D5 NICHOLAS W. WARNE: "Development of high concentration protein biopharmaceuticals: The use of platform approaches in formulation development", EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, vol. 78, no. 2, 1 June 2011 (2011-06-01), pages 208-212, XP055534222, ISSN: 0939-6411, DOI: 10.1016/j.ejpb.2011.03.004

D1 discloses formulations comprising Fab'PEG antibody with addition of sucrose, glycine and surfactant in a buffer (examples).

D2 and **D3** both disclose anti-CD40L antibodies comprising antibodies with the sequences according to claim 6 including pegylated Fab fragments.

D4 concerns formulations of protein- and peptide-based parenteral products and discloses the addition of stabilizers (e.g. sucrose and glycine), buffers like histidine and surfactants (e.g. polysorbate 20) in order to generate a product with favorable stability and pharmacokinetic properties (pages 233-249, tables 1, 2, 4-6).

D5 also concerns formulations of protein pharmaceuticals, in particular with high concentration with reference to certolizumab-pegol at 200 mg/ml (page 208, table 1).

2 Industrial applicability (Art. 33(4) PCT)

Claims 1-18 meet the requirements for industrial applicability according to Art. 33(4) PCT.

3 Novelty (Art. 33(2) PCT)

3.1 The present application does not meet the criteria of Art. 33(1) PCT, because the subject-matter of claims 1-3, 8, 9, 13, 17 and 18 is not novel in the sense of Art. 33(2) PCT.

3.2 **D1** discloses a liquid formulation comprising
- 200 mg/ml of a Fab'-PEG antibody,
- 2.5% sucrose and
- 0.25 - 2.5% glycine
- at a pH of 5.5 in a 10 nM histidine buffer

(example 3, paragraphs [0170] - [0171], table 3).

Thus, the subject-matter of claims 1, 8, 9 and 13 lacks novelty over **D1**.

3.3 **D1** further discloses that spray-dried formulations were generated from said formulation (p. [0172]). In view of the fact that it is not clear how a spray-dried formulation can be distinguished from a freeze-dried formulation (see also point 1), the subject-matter of claim 2 is not considered to be novel over **D1** either.

3.4 The same applies to the subject-matter of claim 3, which appears to refer to the components after drying in % w/w of a formulation of clam 1. Thus, the subject-matter of claim 3 is not considered to be novel over D1 either.

3.5 The dried products in **D1** were reconstituted with water (p. [0173]). Hence, the subject-matter of claim 17 is not novel over D1.

3.6 **D1** further refers to a container comprising the dried formulation (p. [0152]). Hence, the subject-matter of claim 18 is not novel.

4 Inventive Step (Art. 33(3) PCT)

4.1 The present application does not meet the criteria of Art. 33(1) PCT because the subject-matter of claims 1-18 does not involve an inventive step in the sense of Art. 33(3) PCT.

4.2 The additional features of claims 4-7 refer to Fab-PEG molecule binding to CD40L and comprising particular sequences.

Such humanized Fab-PEG molecule including PEG-maleimide is well known in the art (e.g. **D2**: Seq ID No. 2, 12, 13, 15; p. [0285] - [0289]; **D3**: Seq ID No. 7, 9, 10) and is now known under its INN designation as dapirolizumab pegol.

Thus, the subject-matter of claims 4-7 cannot establish an inventive step.

4.3 The additional features of claims 10-12 refers to the addition of a surfactant, e.g. polysorbate 20. The addition of such surfactant is standard in the art (see also **D1**: paragraphs [0014] - [0015]; **D4**: page 237, tables 2, 6; **D5**: table 1) and cannot establish an inventive step.

4.4 The additional features of claim 14 refer to a liquid formulation which comprises particular amounts of the Fab'-PEG, buffer, sucrose and glycine.

D1 discloses a composition comprising
- 100mg/ml of the Fab'-PEG,
- 2% glycine and
- 2.5 % sucrose
(paragraph [0174], fig. 8).

Whilst **D1** is silent with regard to the concentration of the buffer in this composition, the use of 20 mM histidine buffer at pH 5.5 is considered standard in the art. The subject-matter of claim 14 is not inventive.

4.5 The considerations under point 4.4 apply *mutatis mutandis* to the subject-matter of claim 15. No inventive step can be derived from the particular formulation according to claim 15.

4.6 Freeze-drying is a standard method for the skilled person and has been also suggested for the pegylated anti-CD40L antibody (see for example D3: pages 16, 20). Hence, in view of the considerations above, no inventive step can be derived from the the method according to claim 16.

Re Item VIII

Certain observation on the international application

1 Claim 2 refers to a freeze-dried formulation obtained by freeze-drying the pharmaceutical composition according to claim 1.

This wording amounts to a formulation in terms of a result to be achieved.

Claims for products defined in terms of processes for their preparation ("product-by-process" claims) are considered to be directed to the product as such and are thus admissible only if the products themselves fulfil the requirements for patentability, i.e. inter alia that they are novel and inventive (see F-IV, 4.12). In particular, novelty can be established only if it is known which particular identifiable characteristics are conferred by the process on the product so that the skilled person can distinguish the claimed product from others and discard any product not having those distinct characteristics.

Accordingly, product-by-process claims are considered to lack clarity if it is not known which particular identifiable characteristics are conferred by the process on the product so that it can be unambiguously identified by the skilled person.

In present claim 2, it is not clear how it can be distinguished whether a certain "dried formulation" has been produced by freeze-drying or, for example, by spray-drying.

Hence, the subject-matter of claim 2 is considered to violate the requirements of Art. 6 PCT. With regard to the implications concerning novelty, reference is made to item V, point 3.3.

2 Although claims 2 and 3 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. Both claims refer to a freeze-dried formulation comprising a Fab-PEG or Fab'-PEG molecule.

The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

3 The term "about" used in many claims is considered vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Art. 6 PCT).