

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: Nathan Vogler
Morrison & Foerster LLP
2100 L St, NW
Suite 900
Washington, DC 20037
United States Of America

Date of mailing
(day/month/year)

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Applicant's or agent's file reference
777052066240

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US23/68745

International filing date (day/month/year)

20 June 2023 (20.06.2023)

Priority date (day/month/year)

20 June 2022 (20.06.2022)

International Patent Classification (IPC) or both national classification and IPC

IPC - INV. A61K 31/192; A61K 9/20; A61K 47/12; A61K 47/14; A61K 47/26 (2023.01)

ADD. B01F 35/22; B01F 35/71 (2023.01)

CPC - INV. A61K 31/192; A61K 9/2018; A61K 9/2059; A61K 9/2095

ADD. B01F 35/2218; B01F 35/715; B01F 35/7173

Applicant BAYER HEALTHCARE LLC

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/

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

30 September 2023 (30.09.2023)

Authorized officer

Shane Thomas

PCT Help Desk

Telephone No. 571-272-4300

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US23/68745

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 43bis.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.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.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:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US23/68745

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. 4-9, 13-22

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. 4-9, 13-22 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 4-9, 13-22 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. 4-9, 13-22

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

☐ furnish a sequence listing complying with WIPO Standard ST.26, and such listing was not available to the International Searching Authority in the form, language and manner acceptable to it.

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

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US23/68745

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	3, 10-12	YES
	Claims	1-2	NO
Inventive step (IS)	Claims	NAME	YES
	Claims	1-3, 10-12	NO
Industrial applicability (IA)	Claims	1-3, 10-12	YES
	Claims	NAME	NO
2. Citations and explanations:			
Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by WO 2021037874 A1 to DSM IP Assets B.V. (hereinafter 'DSM'). As per claim 1, DSM discloses an oral tablet (oral tablet; page 3, lines 6-9; page 14, line 30) comprising: naproxen sodium (naproxen sodium; page 15, line 8); mannitol (mannitol; page 14, lines 30-32); a superdisintegrant (sodium starch glycolate (superdisintegrant); page 15, lines 1-2); and a lubricant (lubricant; page 15, lines 2-4), wherein the oral tablet does not comprise a glidant (oral tablet does not contain a glidant; page 3, lines 6-9; page 14, lines 30-32, page 15, lines 1-11). As per claim 2, DSM discloses the oral tablet of claim 1, and DSM further discloses wherein the superdisintegrant comprises sodium starch glycolate (sodium starch glycolate; page 15, lines 1-2). Claim 3 lacks an inventive step under PCT Article 33(3) as being obvious over DSM in view of WO 2021/127546 A1 to Bayer Healthcare LLC (hereinafter 'Bayer'). As per claim 3, DSM discloses the oral tablet of claim 1 or 2, but DSM does not disclose wherein the oral tablet comprise 70-80 wt. percent naproxen sodium. However, Bayer discloses wherein the oral tablet comprise 70-80 wt. percent naproxen sodium (oral tablet contains at least 70 wt. percent and less than 80 wt. percent naproxen sodium; paragraphs [0048], [0051]). It would have been obvious to one skilled in the art at the time of the invention to have modified the oral tablet, as disclosed by DSM, to provide the oral tablet wherein the oral tablet comprise 70-80 wt. percent naproxen sodium, as disclosed by Bayer, for the benefit that naproxen sodium is formulated with excipients including disintegrants, mannitol, and optionally without a glidant, to improve formulation for compression into tablets (Bayer; paragraph [0030]). Claims 10-12 lack an inventive step under PCT Article 33(3) as being obvious over DSM in view of the publication entitled "Control Strategy and Methods for Continuous Direct Compression Processes" by Suzuki, et al. (hereinafter 'Suzuki'). As per claim 10, DSM discloses a naproxen sodium tablet (naproxen sodium tablet; page 3, lines 6-9; page 13, line 30-32) formed by the process of (formed by the process of; page 14, lines 30-32; page 15, lines 1-11): mixing naproxen sodium, mannitol, a superdisintegrant, and a lubricant (mixing naproxen sodium, mannitol, sodium starch glycolate (superdisintegrant) and a lubricant; page 15, lines 1-11) to form a tableting mixture (for a tableting mixture; page 14, lines 30-32; page 15, lines 1-11); transferring the tableting mixture to a tablet press (transferring the tableting mixture to a tablet press; page 26, lines 18-22); and pressing the tableting mixture into naproxen sodium tablets (pressing the tableting mixture into naproxen sodium tablets; page 26, lines 18-22; page 27, lines 1-3), but DSM does not disclose a continuous in-line mixer. However, Suzuki discloses a continuous in-line mixer (materials continue to move from upstream process to the downstream process involving blending (continuous in-line mixer) supplied to a blender in-line; figure 1; page 254, right column, bottom paragraph; page 255, left column, top paragraph). It would have been obvious to one skilled in the art at the time of the invention to have modified the tablet, as disclosed by DSM, to provide the tablet wherein the process does not include a granulation step, as disclosed by Suzuki, for the benefit that feeding materials into a continuous blender (in-line mixer) is used to form a drug blend without a granulation step for in-line transfer to a tableting machine to prepare oral tablets, the continuous manufacturing process increases the efficiency of preparing oral tablets (Suzuki; figure 1; page 254, left column, top paragraph; right column, bottom paragraph; page 255, left column, top paragraph; page 261, right column, conclusion). As per claim 11, DSM and Suzuki, in combination, disclose the naproxen sodium tablet of claim 10, but DSM does not disclose wherein the process does not include a granulation step. However, Suzuki discloses wherein the process does not include a granulation step (process does not include a granulation step; figure 1; page 254, right column, bottom paragraph; page 255, left column, top paragraph). It would have been obvious to one skilled in the art at the time of the invention to have modified the tablet, as disclosed by DSM, to provide the tablet wherein the process does not include a granulation step, as disclosed by Suzuki, for the benefit that feeding materials into a continuous blender (in-line mixer) is used to form a drug blend without a granulation step for in-line transfer to a tableting machine to prepare oral tablets, the continuous manufacturing process increases the efficiency of preparing oral tablets (Suzuki; figure 1; page 254, left column, top paragraph; right column, bottom paragraph; page 255, left column, top paragraph; page 261, right column, conclusion). As per claim 12, DSM and Suzuki, in combination, disclose the naproxen sodium tablet of claim 10 or 11, and DSM further discloses wherein mixing naproxen sodium, mannitol, a superdisintegrant, and lubricant (mixing naproxen sodium, mannitol, sodium starch glycolate			
---Continued in Supplemental Box---			

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US23/68745

Supplemental Box

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

Continuation of:

****-Continued From Box V. 2: Citations and Explanations-****

(superdisintegrant) and a lubricant; page 15, lines 1-11) feeding the naproxen sodium, the mannitol, the superdisintegrant, and the lubricant (addition of naproxen sodium, mannitol, sodium starch glycolate (superdisintegrant) and a lubricant; page 15, lines 1-11), but DSM does not disclose in a continuous in-line mixer comprises feeding to the in-line mixer through a loss-in-weight feeder. However, Suzuki discloses in a continuous in-line mixer comprises feeding to the in-line mixer through a loss-in-weight feeder (materials continue to move from upstream process to the downstream process involving blending (continuous in-line mixer) supplied to a blender in-line through a loss-in-weight feeder; figure 1; page 254, right column, bottom paragraph; page 255, left column, top paragraph). It would have been obvious to one skilled in the art at the time of the invention to have modified the tablet, as disclosed by DSM, to provide the tablet in a continuous in-line mixer comprises feeding to the in-line mixer through a loss-in-weight feeder, as disclosed by Suzuki, for the benefit that a loss-in-weight feeder is used to add materials into a continuous blender (in-line mixer) to form a drug blend without a granulation step for in-line transfer to a tableting machine to prepare oral tablets, the continuous manufacturing process increases the efficiency of preparing oral tablets (Suzuki; figure 1; page 254, left column, top paragraph; right column, bottom paragraph; page 255, left column, top paragraph; page 261, right column, conclusion).

Claims 1-3 and 10-12 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.