

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/US2018/063709	International filing date (day/month/year) 04.12.2018	Priority date (day/month/year) 06.12.2017
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International Patent Classification (IPC) or both national classification and IPC
INV. A61K39/09 A61K39/385 A61P31/04 ADD. A61K39/00

Applicant
MERCK SHARP & DOHME CORP.

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:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Scheffzyk, Irmgard Telephone No. +49 89 2399-0	
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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. 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. 3-6, 30, 32, 33, 54-59, 61-93(completely); 1, 2, 7-29, 31, 34-53, 60(partially)

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. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ 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 the whole application or for said claims Nos. 3-6, 30, 32, 33, 54-59, 61-93(completely); 1, 2, 7-29, 31, 34-53, 60(partially)
- ☐ 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

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. 1, 2, 7-29, 31, 34-53, 60(all partially)

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>7, 24, 25, 34-39, 44-46, 50, 51, 60(all partially)</u> |
| | No: Claims | <u>1, 2, 8-23, 26-29, 31, 40-43, 47-49, 52, 53</u> |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | <u>1, 2, 7-29, 31, 34-53, 60(all partially)</u> |
| Industrial applicability (IA) | Yes: Claims | <u>1, 2, 7-29, 31, 34-53, 60(all partially)</u> |
| | 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

Item IV

The problem underlying present application can be seen in the provision of further *S.pneumoniae* polysaccharide-protein conjugate compositions. The problem was solved by providing the compositions as defined in present claims. All the compositions have in common that serotypes 15A,16F,23A,23B,24F,31 and 35B are present. Thus, the common concept underlying presently claimed subject-matter can be seen in the provision of multivalent immunogenic compositions comprising *S.pneumoniae* polysaccharide protein conjugates comprising at least these 7 serotypes. However, such multivalent immunogenic compositions are already taught in the prior art (see e.g. WO2017173415 (D1), e.g. paragraph [0020]). Thus, the common concept linking together presently claimed subject-matter no longer exists. The technical contribution made by presently claimed subject-matter can be seen in the provision of further alternative immunogenic compositions. As the combination of serotypes in the claimed compositions is completely different the compositions do not share any element which would be suitable to unify them. Hence, the common concept does not involve the same special technical feature(s) and so is not a single general inventive concept. The claims define the following groups of invention which are not so linked to form a single general inventive concept:

invention 1 (claims 1,2,7-25,26-29,31,34,35-53,60 all partially,
immunogenic composition comprising 15A,16F,23A,23B,24F,31 and 35B

invention 2 (claims 1,2,7-25,26-29,31,34-53,60 all partially and claim 3 completely
immunogenic composition comprising 15A,16F,23A,23B,24F,31 and 35B, 8, 9N,10A,
11A,12F,15C,17F,20

invention 3 (claims 1,2,7-25,26-29,34-53,60 all partially and claim
4,5,6,30,32,33,61-93 completely,
immunogenic composition comprising 3,7F,19A,22F,33F,15A,16F,23A,23B,24F,31,
35B, 8, 9N,10A,11A,12F,15C,17F,20

invention 4: claim 54-59 completely

Method for preparing a serotype 8 *S.pneumoniae* conjugate

In the present application no further technical feature(s) can be identified that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Consequently, the requirement of unity that there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features is not fulfilled. Depending on the available prior art the defined inventions may be split into further separate inventions.

Item V

Invention 1:

Immunogenic compositions comprising *S.pneumoniae* serotypes 6C,15A,,23A,23B, 24F,31,35B are disclosed in D1 (see e.g. paragraph [0020]). Thus, claims 1 and 2 lack novelty. Novelty of claims 8,9 and 18 cannot be acknowledged either as although D1 fails to disclose the embodiments of these claims the conjugate according to claims 8,9 and 18, respectively is not deemed distinguishable from the conjugates taught in D1. It is noted that claims 8 and 9 are product claims and the product per se must be novel. Moreover, for the time being novelty of claims 10-17 cannot be acknowledged either as it cannot be ruled out that the embodiments of these claims, which are admittedly not expressly mentioned in D1, are intrinsic features of the compositions taught in D1.

The subject-matter of claims 19-23 is disclosed in D1 (see e.g. paragraphs [0064], [0051],[0073],[0102] and [0136]) and thus lacks novelty.

In addition, the compositions according to claims 26-28, which are so-called product-by-process claims, are not deemed distinguishable from the compositions disclosed in D1 and thus are not novel.

Novelty of claims 29,31,40,41,42,43,47,48,49,52 and 53 also is anticipated by D1 (see e.g. paragraph [0020] and examples 10,21, 23 and, 27).

Claims 7,24,25,34-39,44-46,50,51 and 60, which seem to be novel, lack inventive step as the embodiments thereof are only obvious alternatives to a person skilled in the art which are not suitable to establish the presence of an inventive step.

Item VIII

In case present application is pursued as European patent application claims 29-60 and 70-89 would not be patentable relating to medical treatments.