

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/US2019/066682

International filing date (day/month/year)
17.12.2019

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19.12.2018

International Patent Classification (IPC) or both national classification and IPC
INV. A61K39/09 A61P31/04

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.

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Date of completion of
this opinion

see form
PCT/ISA/210

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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. 17, 21, 25(completely); 1-16, 18-20, 22-24, 26-34(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. 17, 21, 25(completely); 1-16, 18-20, 22-24, 26-34(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. 1-16, 18-20, 22-24, 26-34(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>1-16, 18-20, 22-24, 26-34(all partially)</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>29, 31(all partially)</u>
	No: Claims	<u>1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)</u>
Industrial applicability (IA)	Yes: Claims	<u>1-16, 18-20, 22-24, 26-34(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

Re Item IV

Lack of unity of invention

1 This Authority considers that the application does not meet the requirements of unity of invention and that there are 54 inventions.

2 The reasons, for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The common matter linking together the alternatives within independent claim 1 is the following: all claimed compositions comprise polysaccharides of each of *S. pneumoniae* serotypes 1, 3, 4, 5, 7F, 9V, 12F, 14, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B, wherein the polysaccharide antigen is conjugated to a carrier protein..

This common matter does not comprise a single general inventive concept, based on same or corresponding special technical features within the meaning of Rule 13.2 PCT, because documents of the prior art disclose vaccine compositions comprising combinations of polysaccharides of *S. pneumoniae* serotypes, wherein the polysaccharides are conjugated to a carrier protein.

WO2018126229 discloses such compositions comprising at least 25 polysaccharides antigens from serotypes 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 9N, 10A, 11A, 12F, 13, 14, 15B, 16, 17F, 18C, 19A, 19F, 20, 22F, 23F, 24F, 31, and 33F (see paragraphs 000136, 000578, claim 35).

WO2015110942 discloses PCV16v, a 16-valent conjugates composition comprising glycoconjugates from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F (16vPnC) all individually conjugated to CRM 97 and PCV20v, a 20 valent conjugates composition comprising glycoconjugates from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F (20vPnC) all individually conjugated to CRM 97 (Example 2).

WO2017085586 discloses 23v a *S. pneumoniae* polysaccharide vaccine comprising polysaccharide antigens of *S. pneumoniae* serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F (see Example 3)

WO2017173415 discloses 65 compositions comprising different combinations of *S. pneumoniae* polysaccharide antigens from different serotypes (see Table 2 in Example 6). In particular, the following compositions comprising *S. pneumoniae* polysaccharide antigens are disclosed:

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (13-valent),
1, 3, 4, 6A, 6B, 6C, 7F, 8, 9N, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 19F,
19A, 20A, 22F, 23A, 23B, 24F, 33F, 35F, 35B and 38 (28-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 19F, 19A,
20A, 22F, 23A, 23B, 24F, 33F, 35F, 35B, and 38 (27-valent),
1, 2, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F,
7F, 19F, 19A, 20A, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (34-
valent),
1, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F,
17F, 18C, 20A, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (32-valent),
1, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20A,
22F, 23A, 23B, 31, 33F, 33A, 34, 35B, 35F, 38 (27-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20A,
22F, 23A, 23B, 24F, 31, 33F, 33A, 34, 35B, 35F, and 38 (29-valent),
1, 2, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F,
17F, 19F, 19A, 20B, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (34-
valent),
1, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F,
17F, 18C, 20B, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (32-valent),
1, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20B,
22F, 23A, 23B, 31, 33F, 33A, 34, 35B, 35F, 38 (27-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20B,
22F, 23A, 23B, 24F, 31, 33F, 33A, 34, 35B, 35F, and 38 (29-valent).

WO2018064444 discloses immunogenic compositions comprising up to 24 *S. pneumoniae* polysaccharide antigens from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15B, 16F, 18C, 19A, 19F, 22F, 23F, 33F, 34, 35B and 38 (see claims 1-24).

The technical feature, representing the difference over the non-inventive common matter, of claim is that different combinations of serotype-specific polysaccharide antigens are claimed, wherein additional polysaccharide antigens from other *S. pneumoniae* serotypes are added to the composition (*e.g.* the polysaccharide antigen from *S. pneumoniae* serotype 23B in the case of WO2018126229).

This feature provides the technical effect of providing compositions which elicit an immune response against additional serotypes, and solves the objective technical problem of providing immunogenic compositions is not inventive because:

The production of *S. pneumoniae* polysaccharides conjugated to a carrier protein is known from the art (see the documents cited above),

S. pneumoniae serotypes 1, 3, 4, 5, 7F, 9V, 12F, 14, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B are known and their polysaccharide antigens have been isolated, conjugated to carrier proteins in view of making immunogenic compositions comprising different combinations of said antigens,

All compositions of the cited prior art are immunogenic and it is expected that any mixture of *S. pneumoniae* polysaccharide antigens conjugated to a carrier protein will have the same effect,

The application does not disclose any experimental data that could make plausible that the claimed compositions, and in particular a composition comprising the polysaccharide antigens of serotypes 1, 3, 4, 5, 7F, 9V, 12F, 14, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B is able to elicit protective immunity against any of the serotypes, the polysaccharide antigens of which are comprised in said compositions,

The application does not disclose any experimental data which shows that the claimed compositions, and in particular a composition comprising the polysaccharide antigens of serotypes 1, 3, 4, 5, 7F, 9V, 12F, 14, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B have unexpected properties that could account for the acknowledgement of an inventive step.

It is therefore considered that the claimed compositions, and in particular a composition comprising the polysaccharide antigens of serotypes 1, 3, 4, 5, 7F, 9V, 12F, 14, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B merely consist of arbitrary mixtures of known *S. pneumoniae* polysaccharide antigens conjugated to a carrier protein that are devoid of any surprising effect.

Hence, the claims comprise neither the same, nor corresponding special technical features, so the technical relationship between the subject matter of the claims required by Rule 13.2 PCT is lacking and the claims are not so linked as to form a single general inventive concept as required by Rule 13.1 PCT.

Consequently the application does not meet the requirement for unity of invention.

3 The inventions are as follows:

1. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates

comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: a) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 10A, 12F, 14, 15A, DeOAcI5B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

2. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of b) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

3. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: c) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, DeOAcI5B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

4. claims: 17(completely); 1-16, 18-20, 22-24, 26-28, 30, 32-34(partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: d) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

5. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: e) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

6. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of f) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, DeOAcI5B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

7. claims: 21(completely); 1-16, 18-20, 22-24, 26-28, 30, 32-34(partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of g) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

8. claims: 25(completely); 1-16, 18-20, 22-24, 26-28, 30, 32-34(partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of h) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

9. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: i) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

10. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of j) 1, 3, 4, 5, 6A, 7F, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

11. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: k) 1, 3, 4, 5, 6B, 7F, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

12. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: l) 1, 3, 4, 5, 6C, 7F, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

13. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: m) 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

14. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: n) 1, 3, 4, 5, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

15. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: o) 1, 3, 4, 5, 6C, 7F, 8, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

16. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: p) 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

17. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: q) 1, 3, 4, 5, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

18. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: r) 1, 3, 4, 5, 6C, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

19. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: s) 1, 3, 4, 5, 6A, 7F, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

20. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: t) 1, 3, 4, 5, 6B, 7F, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

21. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: u) 1, 3, 4, 5, 6C, 7F, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

22. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: v) 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

23. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: w) 1, 3, 4, 5, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

24. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: x) 1, 3, 4, 5, 6C, 7F, 8, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

25. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: y) 1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

26. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: z) 1, 3, 4, 5, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

27. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: aa) 1, 3, 4, 5, 6C, 7F, 8, 9V, 10A, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

28. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: bb) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 12F, 14, 15A, deO-15B,

18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

29. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: cc) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

30. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: dd) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 12F, 14, 15A, deO-15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

31. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: ee) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

32. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the

group consisting of: ff) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

33. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: gg) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 11A, 12F, 14, 15A, deO-15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

34. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: hh) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

35. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: ii) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

36. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include

polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: jj) 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

37. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: kk) 1, 3, 4, 5, 6A, 7F, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

38. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: ll) 1, 3, 4, 5, 6B, 7F, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

39. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: mm) 1, 3, 4, 5, 6C, 7F, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

40. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the

group consisting of: nn) 1, 3, 4, 5, 6A, 7F, 8, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

41. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: oo) 1, 3, 4, 5, 6B, 7F, 8, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

42. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: pp) 1, 3, 4, 5, 6C, 7F, 8, 9V, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

43. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: qq) 1, 3, 4, 5, 6A, 7F, 8, 9V, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

44. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: rr) 1, 3, 4, 5, 6B, 7F, 8, 9V, 11A, 12F, 14, 15A, 15C,

18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

45. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: ss) 1, 3, 4, 5, 6C, 7F, 8, 9V, 11A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

46. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: tt) 1, 3, 4, 5, 6A, 7F, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

47. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: uu) 1, 3, 4, 5, 6B, 7F, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

48. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the

group consisting of: vv) 1, 3, 4, 5, 6C, 7F, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

49. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: ww) 1, 3, 4, 5, 6A, 7F, 8, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

50. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: xx) 1, 3, 4, 5, 6B, 7F, 8, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

51. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: yy) 1, 3, 4, 5, 6C, 7F, 8, 9V, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

52. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: zz) 1, 3, 4, 5, 6A, 7F, 8, 9V, 11A, 12F, 14, 15A, 15B,

18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

53. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: aaa) 1, 3, 4, 5, 6B, 7F, 8, 9V, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

54. claims: 1-16, 18-20, 22-24, 26-28, 30, 32-34(all partially)

A multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: bbb) 1, 3, 4, 5, 6C, 7F, 8, 9V, 11A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F, 35B and 39 and related subject-matter.

Re Item V

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

1 Introduction

The present application relates to compositions comprising 21 to 25 oligosacharrides from different *Streptococcus pneumoniae* serotypes as defined in claim 1.

2 Cited documents

Reference is made to the following documents:

D1 WO 2018/126229 A2 (SUTROVAX INC [US]) 5 July 2018 (2018-07-05)

D2 WO 2015/110942 A2 (PFIZER [US]) 30 July 2015 (2015-07-30)cited in the application

- D3** WO 2017/085586 A1 (PFIZER [US]) 26 May 2017 (2017-05-26) cited in the application
- D4** WO 2017/173415 A2 (LIFFEY BIOTECH LTD [IE]; FORREST BRUCE D [US]; LOVE JACK D [US]) 5 October 2017 (2017-10-05)
- D5** WO 2018/064444 A1 (BIOLOGICAL E LTD [IN]; MATUR RAMESH VENKAT [IN] ET AL.) 5 April 2018 (2018-04-05)

3 Novelty (Art. 33(2) PCT)

3.1 D1 (WO2018126229) discloses immunogenic compositions comprising at least 25 polysaccharides antigens from *S. pneumoniae* serotypes 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 9N, 10A, 11A, 12F, 13, 14, 15B, 16, 17F, 18C, 19A, 19F, 20, 22F, 23F, 24F, 31, and 33F wherein the polysaccharide antigens are conjugated to carrier proteins (see paragraphs 000136, 000578, claim 35).

D2 (WO2015110942) discloses PCV16v, a 16-valent conjugates composition comprising glycoconjugates from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F (16vPnC) all individually conjugated to CRM 97 and PCV20v, a 20 valent conjugates composition comprising glycoconjugates from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F (20vPnC) all individually conjugated to CRM 97 (see Example 2).

D3 (WO2017085586) discloses 23v a *S. pneumoniae* polysaccharide vaccine comprising polysaccharide antigens of *S. pneumoniae* serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F (see Example 3).

D4 (WO2017173415) discloses 65 compositions comprising different combinations of *S. pneumoniae* polysaccharide antigens from different serotypes (see Table 2 in Example 6). In particular, the following compositions comprising *S. pneumoniae* polysaccharide antigens are disclosed:

1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (13-valent),
1, 3, 4, 6A, 6B, 6C, 7F, 8, 9N, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 19F, 19A, 20A, 22F, 23A, 23B, 24F, 33F, 35F, 35B and 38 (28-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 19F, 19A, 20A, 22F, 23A, 23B, 24F, 33F, 35F, 35B, and 38 (27-valent),
1, 2, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 7F, 19F, 19A, 20A, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (34-valent),

1, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 17F, 18C, 20A, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (32-valent),
1, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20A, 22F, 23A, 23B, 31, 33F, 33A, 34, 35B, 35F, 38 (27-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, 33A, 34, 35B, 35F, and 38 (29-valent),
1, 2, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 17F, 19F, 19A, 20B, 22F, 23F, 23 A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (34-valent),
1, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 15C, 16F, 17F, 18C, 20B, 22F, 23F, 23A, 23B, 24F, 31, 33F, 35F, 35B, and 38 (32-valent),
1, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20B, 22F, 23A, 23B, 31, 33F, 33A, 34, 35B, 35F, 38 (27-valent),
1, 3, 4, 6A, 6C, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19F, 19A, 20B, 22F, 23A, 23B, 24F, 31, 33F, 33A, 34, 35B, 35F, and 38 (29-valent).

D5 (WO2018064444) discloses immunogenic compositions comprising up to 24 *S. pneumoniae* polysaccharide antigens from serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15B, 16F, 18C, 19A, 19F, 22F, 23F, 33F, 34, 35B and 38 (see claims 1-24).

- 3.2 None of the cited document discloses the subject-matter of **claim 1a**), *i.e.* a multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: a) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 10A, 12F, 14, 15A, DeOAc15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B and related subject-matter.

4 **Inventive step** (Art. 33(3) PCT)

- 4.1 The closest prior art is any of **D1-D3**.
- 4.2 The difference resides in that the claimed compositions comprise
- 4.3 The technical problem therefore resides in the provision of a immunogenic composition that elicit an antibody immune response against all
- 4.4 The solution resides in the provision of a multivalent immunogenic composition comprising *S. pneumoniae* polysaccharide protein conjugates, wherein each of the conjugates comprises a polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, and wherein the polysaccharide protein

conjugates include polysaccharides of a group of *S. pneumoniae* serotypes selected from the group consisting of: a) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 10A, 12F, 14, 15A, DeOAcI5B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B. The application (see

4.5 The solution is obvious for the following reasons:

- the production of *S. pneumoniae* polysaccharides conjugated to a carrier protein is known from the art,
- serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 10A, 12F, 14, 15A, 15B, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B are known,
- all compositions of the cited prior art are immunogenic and it is expected that any mixture of *S. pneumoniae* polysaccharide antigens conjugated to a carrier protein will have the same effect,
- compositions of the prior art contain combinations of 6A and/or 6B, and 15A and/or 15B and therefore inherently provide cross-reactivity for 6C and 15C,
- the application does not disclose any experimental data that could make plausible that the claimed composition is able to elicit protective immunity against any of the serotypes, the polysaccharide antigens of which are comprised in said composition,
- the application does not disclose any experimental data which shows that the claimed composition has unexpected properties that could account for the acknowledgement of an inventive step.

4.6 It is therefore considered that the claimed composition merely consist of a arbitrary mixture of known *S. pneumoniae* polysaccharide antigens conjugated to a carrier protein that is devoid of any surprising effect.

4.7 None of the independent claims encompassing the claimed subject-matter and none of the dependent claims referring back thereto meet the requirements of Art. 33(3) PCT.

5 **Industrial applicability** (Art. 33(4) PCT)

The claimed subject-matter of **claims 1-34** is industrially applicable.

Claims 1-34 therefore meet the requirements of Art. 33(4) PCT.

Re Item VIII

Certain observations on the international application

- 1 **Claim 16** is directed to a composition comprising 23 distinct *S. pneumoniae* polysaccharide conjugates, wherein each of the conjugates comprises a capsular polysaccharide from a *S. pneumoniae* serotype conjugated to a carrier protein, wherein each distinct polysaccharide protein conjugate comprises a polysaccharide from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 12F, 14, 15A, 15C, 18C, 19A, 19F, 22F, 23B, 23F, 24F, 33F and 35B, respectively, and wherein the carrier protein is CRM197. The claim therefore encompasses compositions that comprise the polysaccharide antigen conjugates from the *S. pneumoniae* serotypes recited in the claims and any additional polysaccharide antigen conjugates from further *S. pneumoniae* serotypes.
- 2 The same observation applies to **claims 20 and 24**.