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(54) **Title:** CONJUGATION OF STREPTOCOCCAL CAPSULAR SACCHARIDES TO CARRIER PROTEINS

(57) **Abstract:** Three conjugation methods for use with the capsular saccharide of Streptococcus agalactiae. In the first method, reductive animation of oxidised sialic acid residue side chains is used, but the aldehyde groups are first aminated, and then the amine is coupled to a carrier via a linker. In the second method, sialic acid residues and/or N-acetyl-glucosamine residues are de-N-acetylated to give amine groups, and the amine groups are coupled to a carrier protein via a linker. In the third method, linkage is via galactose residues in the capsular saccharide rather than sialic acid residues, which can conveniently be achieved using galactose oxidase.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/48 A61K39/09 A61P37/04

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/011027 A (BAXTER INT [US]; BAXTER HEALTHCARE SA [CH]) 5 February 2004 (2004-02-05) page 2, lines 15-21 page 3, lines 1-18 page 10, lines 23-29 page 14, lines 1-30 page 18, line 1 - page 19, line 2 claims 18-20 figures 4,5	2-5, 7, 8, 10-13
X	WO 94/06467 A (BRIGHAM & WOMENS HOSPITAL [US]; NAT RESEARCH COUNCIL OF CANAND [CA]) 31 March 1994 (1994-03-31) cited in the application page 3, line 32 - page 4, line 10 page 7, line 33 page 15; table 1	2-5, 10-13
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- *&* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/170267 A1 (PAOLETTI LAWRENCE C [US]) 11 September 2003 (2003-09-11) paragraphs [0016], [0022] paragraph [0050]; table 1	2-4, 10-13,25
X	SHEN X ET AL: "Preparation and preclinical evaluation of experimental group B streptococcus type III polysaccharide-cholera toxin B subunit conjugate vaccine for intranasal immunization" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 19, no. 7-8, 22 November 2000 (2000-11-22), pages 850-861, XP004225405 ISSN: 0264-410X abstract page 825, section 2.3	2-4, 10-13,25
X	SHEN X ET AL: "Group B Streptococcus capsular polysaccharide-cholera toxin B subunit conjugate vaccines prepared by different methods for intranasal immunization" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 69, no. 1, January 2001 (2001-01), pages 297-306, XP002447181 ISSN: 0019-9567 abstract page 299; table 1	2-4, 10-13
Y	WO 03/007985 A (CHIRON SPA [IT]; COSTANTINO PAOLO [IT] CHIRON SRL [IT]; COSTANTINO PAO) 30 January 2003 (2003-01-30) page 4, line 32 - page 5, line 10 page 16, line 19 - page 18, line 10 figure 18	1,4-25
Y	WO 03/007985 A (CHIRON SPA [IT]; COSTANTINO PAOLO [IT] CHIRON SRL [IT]; COSTANTINO PAO) 30 January 2003 (2003-01-30) page 4, line 32 - page 5, line 10 page 16, line 19 - page 18, line 10 figure 18	1,4-25
A	US 2004/213804 A1 (MICHON FRANCIS [US] ET AL) 28 October 2004 (2004-10-28) paragraphs [0032], [0046] - [0048], [0052], [0055] figure 1	1-25
X	US 2004/052804 A1 (ARUMUGHAM RASAPPA G [US] ET AL) 18 March 2004 (2004-03-18) paragraph [0041]	27

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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PAOLETTI L C ET AL: "An oligosaccharide-tetanus toxoid conjugate vaccine against type III group B Streptococcus" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BIRMINGHAM, , US, vol. 265, no. 30, 25 October 1990 (1990-10-25), pages 18278-18283, XP002301343 ISSN: 0021-9258 figure 2	27

INTERNATIONAL SEARCH REPORT

International application No.
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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-25, 27

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-25

A process for preparing a conjugate of a Streptococcus agalactiae capsular saccharide and a carrier molecule, comprising the steps as defined in claim 1; a conjugate prepared according to this process.

2. claim: 26

A process for preparing a conjugate of a Streptococcus agalactiae capsular saccharide and a carrier molecule, comprising the steps as defined in claim 26.

3. claim: 27

A process for preparing a conjugate of a Streptococcus agalactiae capsular saccharide and a carrier molecule, comprising the steps as defined in claim 27.

INTERNATIONAL SEARCH REPORT

International application No

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