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Published:
— with international search report (Art. 21(3))
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:
21 November 2013

(54) Title: IN VITRO POTENCY ASSAY FOR PROTEIN-BASED MENINGOCOCCAL VACCINES

(57) Abstract: The invention uses ELISA or similar assays for analysing a meningococcal vaccine. The assay uses antibodies which bind to meningococcal proteins within the vaccine, and in particular monoclonal antibodies which are bactericidal for meningococcal proteins and which recognise conformational epitopes within the meningococcal proteins. By performing the assay on a series of diluted test vaccines and comparing the results with those obtained using a reference vaccine of known potency, it is possible to determine the relative potency of the test vaccine. This value can be used as a parameter for determining whether a manufactured batch of a vaccine is suitable for release to the public, or whether the vaccine has experienced a production failure and should not be used.
Box No. 1  Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. (means)  
      □ on paper  
      □ in electronic form

   b. (time)  
      □ in the international application as filed  
      □ together with the international application in electronic form  
      □ subsequently to this Authority for the purpose of search

2. □ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:
**INTERNATIONAL SEARCH REPORT**

### 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:

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see additional sheet
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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.:

4. X 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.:

    1 - 17

**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.
INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/05467O

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/569 G01N33/577 C12N15/03

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)
G01N

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 practicable, search terms used)
EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>WO 2009/143168 A2 (NOVARTIS AG [CH]) 26 November 2009 (2009-11-26) claim 1, 4 - 6, 15; page 6, paragraphs 30 &amp; 31; page 27, paragraph 138; page 37, paragraph 173; figure 2</td>
<td>1-17</td>
</tr>
<tr>
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<td>page 24, example 8; page 7, paragraph 41</td>
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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 application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search
8 July 2013

Date of mailing of the international search report
09/10/2013

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Authorized officer
Van Bohemen, Charles
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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-17

A competitive ELISA or inhibition binding assay for in vitro analysis of a meningococcal vaccine sample, comprising steps of (i) permitting a meningococcal protein immunogen within the sample to interact with a monoclonal antibody which either (a) is bactericidal for meningococcus or (b) recognizes a conformational epitope in the meningococcal antigen; then (ii) measuring the interaction between the immunogen and antibody from step (i) and use of the aforementioned method in the analysis of meningococcal test vaccine samples to determine the potency of immunogens in said test samples and a vaccine which has been released for clinical use following the results of any of the aforementioned in vitro assays.

2. claim: 18(partially)

A monoclonal antibody which recognizes meningococcal fHbp and whose variable region comprises SEQ ID NO: 21 and SEQ ID NO: 22.

3. claim: 18(partially)

A monoclonal antibody which recognizes meningococcal fHbp and whose variable region comprises SEQ ID NO: 23 and SEQ ID NO: 24.

4. claim: 18(partially)

A monoclonal antibody which recognizes meningococcal fHbp and whose variable region comprises SEQ ID NO: 25 and SEQ ID NO: 26.

5. claim: 18(partially)

A monoclonal antibody which recognizes meningococcal fHbp and whose variable region comprises SEQ ID NO: 27 and SEQ ID NO: 28.