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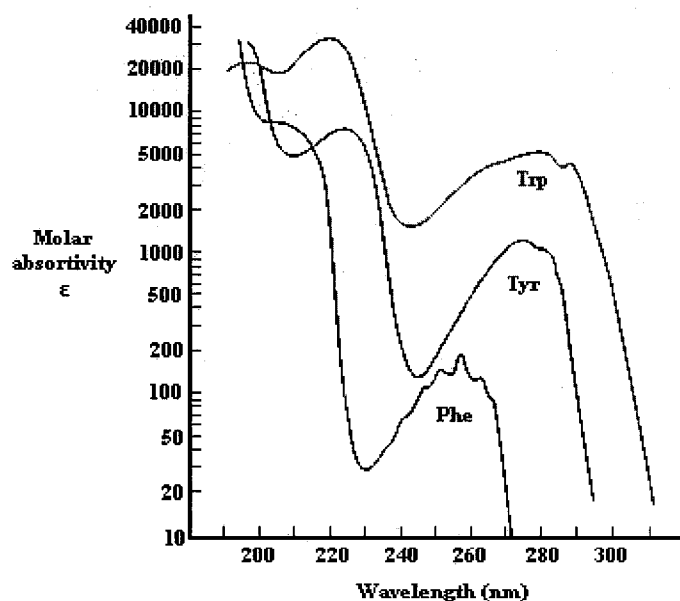
## (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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[Continued on next page]

## (54) Title: ANALYSIS OF MIXTURES INCLUDING PROTEINS

Figure 1



(57) Abstract: The quality control of vaccines is an important step in the release of vaccines to patients. Problems when dealing with vaccines include stability, batch-to-batch consistency and contamination. The invention provides a method of analyzing the composition of a protein-containing sample by electromagnetic spectroscopy, and derivatising the obtained spectrum to obtain a derivative spectrum of the sample. The derivative spectrum may optionally be compared to a reference spectrum, to assess stability, contamination etc. relative to the reference. The derivative analysis technique allows the separation and discrimination between the spectral contributions of different components, thereby allowing differences in the spectra to be assigned to particular groups of the protein, or particular contaminants etc.



(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG).

— *before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
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# INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2008/003678

## A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N21/33 G01N21/64 G01J3/433 G01J3/42 G01J3/44  
A61K39/095

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)

G01J G01N 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, INSPEC, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                     | Relevant to claim No. |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | US 4 921 841 A (OBRIG THOMAS G [US])<br>1 May 1990 (1990-05-01)<br>column 6, line 45 - column 7, line 15<br>-----                                                                                                                                      | 1-3                   |
| X         | TORRES J ET AL: "Spectroscopic studies of bacteriorhodopsin fragments dissolved in organic solution"<br>BIOPHYSICAL JOURNAL USA,<br>vol. 68, no. 5, May 1995 (1995-05), pages 2049-2055, XP002522966<br>ISSN: 0006-3495<br>the whole document<br>----- | 1-6, 15, 16           |
| X         | US 2004/038333 A1 (RANDOLPH THEODORE W. [US] ET AL) 26 February 2004 (2004-02-26)<br>paragraphs [0002], [0076] - [0082], [0172], [0201], [0202], [0211] - [0213]; figures 4, 5, 8, 10<br>-----<br>-/-                                                  | 1-6, 15, 16           |

☒ 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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\*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.

\* & \* document member of the same patent family

Date of the actual completion of the international search

8 April 2009

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09/10/2009

Name and mailing address of the ISA/

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# INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2008/003678

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                       | Relevant to claim No. |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | <p>SABES M ET AL: "Spectrophotometric studies on the tryptophan residues of bacteriorhodopsin during the photocycle" PHOTOBIOCHEMISTRY AND PHOTOBIOPHYSICS NETHERLANDS, vol. 8, no. 2, September 1984 (1984-09), pages 97-101, XP009115110<br/> ISSN: 0165-8646<br/> the whole document</p> <p>-----</p> | 1-6,15                |
| X         | <p>US 6 342 259 B1 (WESLEY IAN JOHN [AU] ET AL) 29 January 2002 (2002-01-29)<br/> column 1, lines 5-12<br/> column 4, line 7 - column 5, line 19<br/> column 8, lines 16-32</p> <p>-----</p>                                                                                                             | 1,15,16               |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2008/003678

### 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 allsearchable 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. ☒ 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.:

1-6, 15, 16

#### 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: 1-6,15,16

UV absorption spectroscopy; Select an order of derivative spectroscopy; Noise reduction

1.1. claims: 1-6

UV absorption spectroscopy

1.2. claims: 1,15

Select an order of derivative spectroscopy

1.3. claims: 1,16

Noise reduction  
---

2. claims: 1-3,7-10

UV fluorescence spectrsocopy  
---

3. claims: 1,11-14

Select a particular protein sample; vaccine  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2008/003678

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date    |
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|                                           |                     | EP 0975961 A1              | 02-02-2000             |
|                                           |                     | JP 2001527646 T            | 25-12-2001             |