

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 May 2008 (15.05.2008)

PCT

(10) International Publication Number
WO 2008/056263 A3

(51) International Patent Classification:
A61K 39/39 (2006.01)

(21) International Application Number:
PCT/IB2007/004229

(22) International Filing Date:
6 November 2007 (06.11.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0622282.2 8 November 2006 (08.11.2006) GB

(71) Applicant (for all designated States except US): **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **KLEIN, Norbert** [DE/DE]; Novartis Behring, Emil-von-Behring-Strasse 76, 035041 Marburg (DE).

(74) Agents: **MARSHALL, Cameron, John** et al.; Carpmaels & Ransford, 43-45 Bloomsbury Square, London WC1A 2RA (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, 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, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
31 December 2008

(54) Title: QUALITY CONTROL METHODS FOR OIL-IN-WATER EMULSIONS CONTAINING SQUALENE

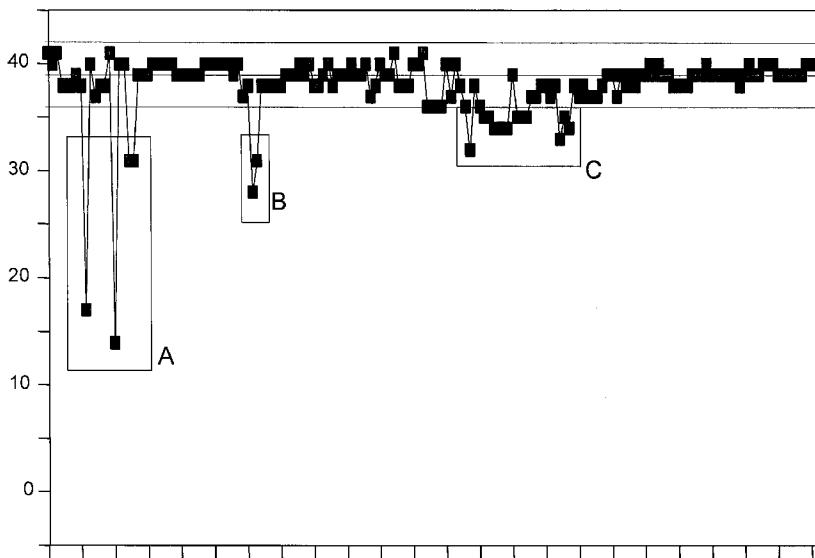


FIGURE 1

(57) Abstract: Measurements of the squalene content in oil-in-water emulsions can be used as a way of checking for problems during production. In particular, it has been found that a drop in squalene content can indicate that filtration problems occurred. Testing the squalene content in the final lots is easier than investigating the characteristics of the filter, and so a squalene assay simplifies the quality control of oil-in-water emulsions.

WO 2008/056263 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2007/004229

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/39

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, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	OTT G. ET AL.: "The Adjuvant MF59: A 10-Year Perspective" METHODS IN MOLECULAR MEDICINE, vol. 42, 15 April 2000 (2000-04-15), pages 211-228, XP002501687 Fig. 1, pages 213, 214-217	1-25
A	SPANGGORD ET AL: "Enhancement of an analytical method for the determination of squalene in anthrax vaccine adsorbed formulations" JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS, NEW YORK, NY, US, vol. 42, no. 4, 11 October 2006 (2006-10-11), pages 494-499, XP005657193 ISSN: 0731-7085 2.2 page 496	1-25

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
- *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.
- *&* document member of the same patent family

Date of the actual completion of the international search

29 October 2008

Date of mailing of the international search report

13/11/2008

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

Kronester-Frei, A

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/004229

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MILES A P ET AL: "MontanideR ISA 720 vaccines: quality control of emulsions, stability of formulated antigens, and comparative immunogenicity of vaccine formulations" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 23, no. 19, 31 March 2005 (2005-03-31), pages 2530-2539, XP004887459 ISSN: 0264-410X 2.2 page 2531 and 3.1 page 2532</p>	1-25
A	<p>EP 0 399 843 A (CHIRON CORP [US]) 28 November 1990 (1990-11-28) cited in the application Examples 1, 5</p>	1-25
A	<p>WO 99/02132 A (CHIRON CORP [US]) 21 January 1999 (1999-01-21) Examples</p>	1-25
A	<p>EP 0 745 387 A (AMERICAN HOME PROD [US]) WYETH CORP [US]) 4 December 1996 (1996-12-04) Example 1, page 4, lines 24ff</p>	1-25
P,A	<p>DEREK T O'HAGAN: "MF59 is a safe and potent vaccine adjuvant that enhances protection against influenza virus infection" EXPERT REV. VACCINES, vol. 6, no. 5, 2007, pages 699-711, XP002501795 Fig. 4, page 703; whole document</p>	1-25
P,A	<p>WACK ET AL: "Combination adjuvants for the induction of potent, long-lasting antibody and T-cell responses to influenza vaccine in mice" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 26, no. 4, 26 December 2007 (2007-12-26), pages 552-561, XP022418985 ISSN: 0264-410X pages 554,558</p>	1-25

INTERNATIONAL SEARCH REPORT

 International application No
 PCT/IB2007/004229

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0399843	A	28-11-1990	AT 108327 T	15-07-1994
			CA 2017507 A1	25-11-1990
			DD 294633 A5	10-10-1991
			DE 69010574 D1	18-08-1994
			DE 69010574 T2	27-10-1994
			DE 399843 T1	02-05-1991
			ES 2033626 T1	01-04-1993
			GR 91300063 T1	15-11-1991
			HK 107695 A	14-07-1995
			HU 61203 A2	28-12-1992
			IE 64766 B1	06-09-1995
			JP 8032638 B	29-03-1996
			JP 5508385 T	25-11-1993
			PT 94168 A	08-01-1991
WO 9902132	A	21-01-1999	AU 8298298 A	08-02-1999
			CA 2295740 A1	21-01-1999
			EP 1006999 A2	14-06-2000
			JP 2002509545 T	26-03-2002
EP 0745387	A	04-12-1996	AT 284710 T	15-01-2005
			AU 712972 B2	18-11-1999
			AU 5457596 A	12-12-1996
			CA 2177668 A1	03-12-1996
			CN 1141810 A	05-02-1997
			DE 69634024 D1	20-01-2005
			DE 69634024 T2	08-12-2005
			DK 745387 T3	21-02-2005
			ES 2233955 T3	16-06-2005
			HU 9601466 A2	28-03-1997
			JP 8325163 A	10-12-1996
			NZ 286699 A	24-10-1997
US 5718904 A	17-02-1998			