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(54) Title: ADJUVANT COMPOSITION COMPRISING ALUMINIUM PHOSPHATE AND 3D-MPL

(57) Abstract: An immunogenic composition comprising: (i) an antigen; (ii) an aluminum phosphate adjuvant; and (iii) a 3-O-deacylated monophosphoryl lipid A adjuvant. Components (ii) and (iii) can also be used as a separate adjuvant system. Various features of the compositions are disclosed, including that at least 50 % of the 3-O-deacylated monophosphoryl lipid A adjuvant should be adsorbed to the aluminum phosphate adjuvant. The adjuvant mixture is particularly useful with hepatitis B virus surface antigen.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/39 A61P31/00

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)
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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, EMBASE, 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.
X	WO 00/23574 A2 (SMITHKLINE BEECHAM BIOLOG [BE]; HONDT ERIK D [BE]) 27 April 2000 (2000-04-27) the whole document pages 12-13	1-26
X	US 2001/053365 A1 (FRIEDE MARTIN [US] ET AL) 20 December 2001 (2001-12-20) the whole document	1-26
X	WO 01/17551 A2 (SMITHKLINE BEECHAM BIOLOG [BE]; WETTENDORFF MARTINE ANNE CECIL [BE]) 15 March 2001 (2001-03-15) the whole document	1-26
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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	WO 00/23105 A2 (SMITHKLINE BEECHAM BIOLOG [BE]; GARCON NATHALIE [BE]) 27 April 2000 (2000-04-27) the whole document	1-26
A	----- BOLAND G ET AL: "Safety and immunogenicity profile of an experimental hepatitis B vaccine adjuvanted with AS04" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 23, no. 3, 2 December 2004 (2004-12-02), pages 316-320, XP004629160 ISSN: 0264-410X abstract	1-26
A	----- ANNE WALSH: "GlaxoSmithKline receives European approval for Fendrix , an adjuvanted vaccine to prevent infection from hepatitis B for specific high-risk patients" GSK-PRESS RELEASE OF 11 FEBRUARY 2005, [Online] XP002407537 Retrieved from the Internet: URL:HTTP://WWW.GSK-BIO.COM> abstract	1-26
A	----- OGUNNIYI A D ET AL: "Protection against Streptococcus pneumoniae elicited by immunization with pneumolysin and CbpA." INFECTION AND IMMUNITY. OCT 2001, vol. 69, no. 10, October 2001 (2001-10), pages 5997-6003, XP002407391 ISSN: 0019-9567 the whole document	1-26
A	----- WO 96/26741 A (SMITHKLINE BEECHAM BIOLOG S A [BE]; HAUSER PIERRE [BE]; GARCON NATHAL) 6 September 1996 (1996-09-06) the whole document	1-26
A	----- THOELEN S ET AL: "Safety and immunogenicity of a hepatitis B vaccine formulated with a novel adjuvant system." VACCINE. APR 1998, vol. 16, no. 7, April 1998 (1998-04), pages 708-714, XP002407392 ISSN: 0264-410X the whole document	1-26
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2006/000557

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>VERNACCHIO L ET AL: "Effect of monophosphoryl lipid A (MPL<(>R)) on T-helper cells when administered as an adjuvant with pneumococcal-CRM197 conjugate vaccine in healthy toddlers" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 20, no. 31-32, 1 November 2002 (2002-11-01), pages 3658-3667, XP004388607 ISSN: 0264-410X abstract</p>	1-26
A	<p>-----</p> <p>THOELEN S ET AL: "A prophylactic hepatitis B vaccine with a novel adjuvant system" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 19, no. 17-19, 21 March 2001 (2001-03-21), pages 2400-2403, XP004231056 ISSN: 0264-410X abstract</p>	1-26
A	<p>-----</p> <p>STANBERRY L R ET AL: "Glycoprotein-D-adjuvant vaccine to prevent genital herpes" NEW ENGLAND JOURNAL OF MEDICINE 21 NOV 2002 UNITED STATES, vol. 347, no. 21, 21 November 2002 (2002-11-21), pages 1652-1661, XP002407393 ISSN: 0028-4793 abstract</p> <p>-----</p>	1-26

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2006/000557

Patent document cited in search report	Publication date	Patent family member(s)	Publication date		
WO 0023574	A2	27-04-2000	CA 2347084 A1 27-04-2000		
			EP 1121420 A2 08-08-2001		
			JP 2002527105 T 27-08-2002		
			US 6991929 B1 31-01-2006		
			US 2005112144 A1 26-05-2005		

US 2001053365	A1	20-12-2001	NONE		
WO 0117551	A2	15-03-2001	AT 321569 T 15-04-2006		
			AT 312624 T 15-12-2005		
			AU 766494 B2 16-10-2003		
			AU 7775100 A 10-04-2001		
			BR 0014171 A 21-05-2002		
			CA 2384064 A1 15-03-2001		
			CN 1387443 A 25-12-2002		
			CN 1618465 A 25-05-2005		
			CZ 20020843 A3 14-08-2002		
			DE 60024893 T2 06-07-2006		
			DE 60027029 T2 19-10-2006		
			DK 1210113 T3 03-07-2006		
			EP 1210113 A2 05-06-2002		
			ES 2253636 T3 01-06-2006		
			GC 0000201 A 29-03-2006		
			HU 0202804 A2 28-12-2002		
			JP 2003508495 T 04-03-2003		
			JP 2004067696 A 04-03-2004		
			MX PA02002484 A 28-08-2002		
			NO 20021116 A 30-04-2002		
			NO 20033715 A 30-04-2002		
			NZ 517621 A 26-09-2003		
			NZ 527560 A 24-12-2004		
			PL 354039 A1 15-12-2003		
			PT 1210113 T 31-07-2006		
			SG 110072 A1 28-04-2005		
			SI 1410805 T1 30-04-2006		
			TR 200200607 T2 21-06-2002		
			US 6936255 B1 30-08-2005		
			ZA 200201810 A 31-03-2004		
			ZA 200306402 A 02-08-2004		

			WO 0023105	A2	27-04-2000
AU 1151800 A 08-05-2000					
BR 9915545 A 14-08-2001					
CA 2347099 A1 27-04-2000					
CN 1330553 A 09-01-2002					
CN 1572324 A 02-02-2005					
CZ 20011341 A3 12-09-2001					
EP 1126876 A2 29-08-2001					
HU 0203091 A2 28-12-2002					
JP 2003519084 T 17-06-2003					
NO 20011801 A 30-05-2001					
NZ 511113 A 27-09-2002					
PL 348121 A1 06-05-2002					
TR 200101055 T2 21-09-2001					
TW 586936 B 11-05-2004					

WO 9626741	A	06-09-1996			
			AR 002279 A1 11-03-1998		

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2006/000557

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9626741	A	AT 209045 T	15-12-2001
		AU 695921 B2	27-08-1998
		AU 4878096 A	18-09-1996
		BG 101851 A	30-04-1998
		BR 9607458 A	30-06-1998
		CA 2212552 A1	06-09-1996
		CN 1176604 A	18-03-1998
		CZ 9702674 A3	18-02-1998
		DE 69617211 D1	03-01-2002
		DK 810877 T3	25-02-2002
		EP 0810877 A1	10-12-1997
		ES 2166879 T3	01-05-2002
		FI 973457 A	22-08-1997
		HK 1004117 A1	20-09-2002
		HU 9801242 A2	28-08-1998
		IL 117249 A	21-11-2000
		JP 11501018 T	26-01-1999
		MA 23814 A1	01-10-1996
		NO 973873 A	22-08-1997
		NZ 302674 A	28-01-1999
		OA 10612 A	29-08-2002
		PL 321966 A1	05-01-1998
		PT 810877 T	29-04-2002
		SK 115097 A3	04-02-1998
		TR 9700849 T1	21-01-1998
		TW 467745 B	11-12-2001
		US 5972346 A	26-10-1999
		ZA 9601460 A	29-08-1996