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— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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17 November 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR PRODUCING STORAGE STABLE VIRUSES AND IMMUNOGENIC COMPOSITIONS THEREOF

(57) Abstract: The invention relates to methods for producing storage stable virus compositions. In certain embodiments, the invention relates to one or more formulations and process steps which result in storage stable virus compositions, wherein the composition is storage stable as a lyophilized solid composition or a frozen liquid composition.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/12 A61K39/155

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)
IPC 7 A61K C12N

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, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/086443 A (MEDIMMUNE VACCINES, INC; TRUONG-LE, VU; PHAM, BINH, V; CARPENTER, JOHN) 23 October 2003 (2003-10-23) claims 1-3,8,9,11,12,20-24,46,47,49,59	1-19,57, 60, 63-81, 119,122
X	US 4 273 762 A (MCALEER ET AL) 16 June 1981 (1981-06-16) column 3, paragraph 3 - column 4, paragraph 1 ----- -/--	63-83, 119,122

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 26 August 2005	Date of mailing of the international search report 09. 09. 2005
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center; font-size: 1.2em;">Lonnoy, 0</p>
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/041803

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>MAKOSCHEY B ET AL: "Serum-free produced Bovine Herpesvirus type 1 and Bovine Parainfluenza type 3 virus vaccines are efficacious and safe." CYTOTECHNOLOGY, vol. 39, no. 3, 2002, pages 139-145, XP002333213 ISSN: 0920-9069 table 1</p>	57,60, 119,122
X	<p>TANNOCK G A ET AL: "FREEZE-DRYING OF RESPIRATORY SYNCYTIAL VIRUSES FOR TRANSPORTATION AND STORAGE" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 25, no. 9, 1987, pages 1769-1771, XP008048997 ISSN: 0095-1137 table 2</p>	57,60, 119,122
A	<p>PHILLIPS G O ET AL: "A STUDY OF WATER BINDING IN LYOPHILIZED VIRAL VACCINE SYSTEMS" CRYOBIOLOGY, vol. 18, no. 4, 1981, pages 414-419, XP008049014 ISSN: 0011-2240</p>	
A	<p>WO 02/09749 A (AVENTIS PASTEUR LIMITED; PARRINGTON, MARK; SLOAN, ROBERT, J; SALES, VA) 7 February 2002 (2002-02-07) table 5</p>	
P,X	<p>WO 2004/017990 A (PFIZER PRODUCTS INC; DOMINOWSKI, PAUL, JOSEPH) 4 March 2004 (2004-03-04) page 9, lines 34-36; claim 1</p>	57,60, 119,122
Y	<p>LABCONCO: "FreeZone 1 Liter Benchtop Freeze Dry Systems: User's Manual" 'Online! 2003, XP002342295 Retrieved from the Internet: URL: http://www.labconco.com/manual/freeze/FZ1LManual.pdf > 'retrieved on 2005-08-25! page 24</p>	24-42, 58,61, 86-104, 120,123
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/041803

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JACKSON L A ET AL: "Safety of a trivalent live attenuated intranasal influenza vaccine, FluMist@?, administered in addition to parenteral trivalent inactivated influenza vaccine to seniors with chronic medical conditions" VACCINE, BUTTERWORTH SCIENTIFIC: GUILDFORD, GB, vol. 17, no. 15-16, 9 April 1999 (1999-04-09), pages 1905-1909, XP004165037 ISSN: 0264-410X page 1906, column 2, paragraph 1	121,124
A	WO 02/28422 A (SMITHKLINE BEECHAM BIOLOGICALS S.A; COLAU, BRIGITTE, DESIREE, ALBERTE;) 11 April 2002 (2002-04-11) claims 13-15	43-56, 59,62

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/041803

Box 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 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 fee, this Authority did not invite payment of any additional fee.
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.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- 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: 1-23,57,60,63-85,119 and 122 (all totally)

Process for producing storage stable virus composition comprising a) freezing the virus composition below its glass transition temperature in a time of 60 minutes or less, and b) lyophilizing the virus composition.

1.1. claims: 22,84 (totally) and 1-21,57,60,63-83,119,122 (all partially)

Process for producing storage stable virus composition comprising a) freezing the virus composition below its glass transition temperature in a time of 60 minutes or less, and b) lyophilizing the virus composition, and wherein the temperature in step a) is decreased from 5 degree C to minus 50 degree C at a rate of about minus 1 degree C per minute to about minus 2 degree C per minute, and maintained at minus 50 degree C for 60 minutes.

1.2. claims: 23,85 (totally) and 1-21,57,60,63-83,119,122 (all partially)

Process for producing storage stable virus composition comprising a) freezing the virus composition below its glass transition temperature in a time of 60 minutes or less, and b) lyophilizing the virus composition, and wherein in step a) the vial containing the virus composition is placed on a lyophilization shelf at minus 70 degree C and held at minus 70 degree C for about 60 minutes.

2. claims: 24-42,58,61,86-104,120,123 (all totally)

Process for producing a lyophilization stable bulk volume virus composition comprising a) placing a liquid virus composition having a volume of at least 50 ml in a lyophilization tray, b) freezing the virus composition below its glass transition temperature for at least about 20 minutes in a liquid nitrogen bath and c) lyophilizing the virus composition.

3. claims: 43-56,59,62,105-118,121,124 (all totally)

Process for producing storage stable liquid virus composition comprising steps (a) to (f) of claims 43 or 105.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/041803

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