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(71) Applicant (for all designated States except US): **GLAXO-SMITHKLINE BIOLOGICALS S.A.** [BE/BE]; Rue de l'Institut 89, B-1330 Rixensart (BE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **CASTADO, Cindy** [BE/BE]; GlaxoSmithKline Biologicals s.a., Rue de l'Institut 89, B-1330 Rixensart (BE).

(74) Agents: **LUBIENSKI, Michael, John** et al.; GlaxoSmithKline, Global Patents CN925.1, 980 Great West Road, Brentford Middlesex TW8 9GS (GB).

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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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
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21 March 2013

(54) Title: IMMUNOGENIC COMPOSITION

(57) Abstract: The present invention relates to fusion proteins comprising fragments from toxin A and/or toxin B of *Clostridium difficile*, in particular the invention relates to proteins comprising a first fragment and a second fragment, wherein (v) the first fragment is a toxin A repeating domain fragment; (vi) the second fragment is a toxin B repeating domain fragment; (vii) the first fragment has a first proximal end; (viii) the second fragment has a second proximal end; and wherein the first fragment and the second fragment are adjacent to one another and wherein the polypeptide elicits antibodies that neutralize toxin A or toxin B or both. The invention further relates to compositions comprising fragments or variants of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 or SEQ ID NO:34 or SEQ ID NO:35.



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/059805

A. CLASSIFICATION OF SUBJECT MATTER INV. C12N15/62 C07K14/33 A61K39/08 ADD.		
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) C07K 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 practicable, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data, EMBL		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BELYI IOURI F ET AL: "Construction of a fusion protein carrying antigenic determinants of enteric clostridial toxins", 1 August 2003 (2003-08-01), FEMS MICROBIOLOGY LETTERS, NO LONGER PUBLISHED BY ELSEVIER, PAGE(S) 325 - 329, XP002666608, ISSN: 0378-1097 [retrieved on 2003-08-02]	1-44, 54-67
Y	page 325, right-hand column, lines 2-7, paragraph 1 tables 1, 2 page 328, left-hand column, paragraph 3 - right-hand column, paragraph 1 ----- -/--	56,63
☒ 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 "&" document member of the same patent family		
Date of the actual completion of the international search 21 December 2012		Date of mailing of the international search report 10/01/2013
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 Barnas, Christoph

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/059805

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 00/61762 A1 (TECHLABS INC [US]) 19 October 2000 (2000-10-19) page 2, paragraphs 3, 4 page 4, line 4, paragraph 4 - page 5, line 2 figure 11 claims 11, 12 -----	1-44, 54-67
X	WO 2010/017383 A1 (EMERGENT PRODUCT DEV UK LTD [GB]; EMERGENT BIOSOLUTIONS INC [US]; TELF) 11 February 2010 (2010-02-11) paragraphs [0024], [0025], [0041], [0042], [0047], [0052] claims 17, 34 figure 5 -----	1-44, 54-67
A	YAMAMOTO MITSUYO ET AL: "High level expression of Streptococcus pyogenes erythrogenic toxin A (SPE A) in Escherichia coli and its rapid purification by HPLC", 1995, FEMS MICROBIOLOGY LETTERS, VOL. 132, NR. 3, PAGE(S) 209-213, XP002683420, ISSN: 0378-1097 page 209, left-hand column, paragraph 1 -----	1-44, 54-67
A	CHAUSSEE MICHAEL S ET AL: "Streptococcal erythrogenic toxin B abrogates fibronectin-dependent internalization of Streptococcus pyogenes by cultured mammalian cells", June 2000 (2000-06), INFECTION AND IMMUNITY, VOL. 68, NR. 6, PAGE(S) 3226-3232, XP002683421, ISSN: 0019-9567 page 3226, left-hand column, paragraph 2 -----	1-44, 54-67
X	WO 2011/060431 A2 (UNIV MARYLAND [US]; GALEN JAMES E [US]) 19 May 2011 (2011-05-19) page 12, paragraphs 2, 3 page 14, paragraphs 2, 3 page 22, paragraph 3 claims 1, 2 sequences 15, 19 -----	45-55, 57-62, 64-67 56,63
X,P	-& DATABASE Geneseq [Online] 7 July 2011 (2011-07-07), XP002689643, Database accession no. AZI43725 abstract -----	45-55, 57-62, 64-67 56,63
Y,P		

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/059805

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	-& DATABASE Geneseq [Online]	45-55, 57-62, 64-67
Y,P	7 July 2011 (2011-07-07), XP002689644, Database accession no. AZI43721 abstract -----	56,63

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/059805

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 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. ☐ 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 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: 1-44(completely); 54-67(partially)

A polypeptide comprising a first fragment and a second fragment, wherein(i) the first fragment is a toxin A repeating domain fragment; (ii) the second fragment is a toxin B repeating domain fragment; (iii) the first fragment has a first proximal end; (iv) the second fragment has a second proximal end; and wherein the first fragment and the second fragment are adjacent to one another and wherein the polypeptide elicits antibodies that neutralize toxin A or toxin B or both.

2. claims: 45-53(completely); 54-67(partially)

A polypeptide comprising SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33 or SEQ ID NO:34 or SEQ ID NO:35.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/059805

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0061762	A1	19-10-2000	AU 781175 B2 12-05-2005
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