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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: 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, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

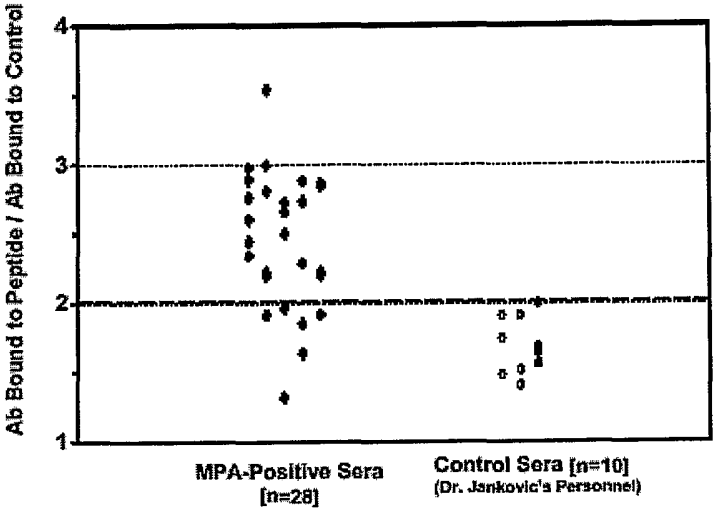
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13 July 2006

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: DETERMINING AND REDUCING IMMUNORESISTANCE TO BOTULINUM TOXIN THERAPY USING BOTULINUM TOXIN A PEPTIDES



(57) Abstract: The present invention provides BoNT/A peptide compositions, tolerogizing compositions, vaccine compositions and antibody compositions, as well as methods of determining immunoresistance to botulinum toxin therapy in an individual, methods of preventing or reducing immunoresistance to botulinum toxin therapy in an individual, methods of vaccinating an individual against botulinum toxin, methods of preparing anti-BoNT/A antibodies, methods of treating botulinum toxicity in an individual and methods of reducing anti-botulinum toxin antibodies in an individual.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/036229

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/33 A61K39/08
ADD. C07K16/12

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 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.
X	ROSENBERG JANA S ET AL: "Localization of the regions on the C-terminal domain of the heavy chain of botulinum toxin A recognized by T lymphocytes and by antibodies after immunization of mice with pentavalent toxoid" IMMUNOLOGICAL INVESTIGATIONS, vol. 26, no. 4, 1997, pages 491-504, XP008046810 ISSN: 0882-0139 abstract page 492, last paragraph - page 493, paragraph 1; figure 1 page 494, paragraph 2 page 495, paragraph 2 - page 498, paragraph 1; table I	1-10, 21-55, 68-89

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[X] Further documents are listed in the continuation of Box C.

[X] 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

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"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

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"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	Date of mailing of the international search report
10 April 2006	27/04/2006

Name and mailing address of the ISA/	Authorized officer
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	Montero Lopez, B

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	OSHIMA MINAKO ET AL: "Immune recognition of botulinum neurotoxin type A: Regions recognized by T cells and antibodies against the protective HC fragment (residues 855-1296) of the toxin" MOLECULAR IMMUNOLOGY, vol. 34, no. 14, October 1997 (1997-10), pages 1031-1040, XP002376352 ISSN: 0161-5890 abstract page 1032, left-hand column, paragraph 2 - page 1039, left-hand column, paragraph 2; table 1	1-10, 21-55, 68-97
X	ATASSI M ZOUHAIR ET AL: "Mapping of the antibody-binding regions on the HN-domain (residues 449-859) of botulinum neurotoxin A with antitoxin antibodies from four host species. Full profile of the continuous antigenic regions of the H-chain of botulinum neurotoxin A." PROTEIN JOURNAL, vol. 23, no. 1, January 2004 (2004-01), pages 39-52, XP002370476 ISSN: 1572-3887 the whole document	1-10
X	OSHIMA MINAKO ET AL: "Antibodies and T cells against synthetic peptides of the C-terminal domain (Hc) of botulinum neurotoxin type A and their cross-reaction with Hc" IMMUNOLOGY LETTERS, vol. 60, no. 1, January 1998 (1998-01), pages 7-12, XP002986041 ISSN: 0165-2478 the whole document	1-10, 21-55, 78-89
P,X	WO 2005/030119 A (ALLERGAN, INC; ATASSI, M., ZOUHAIR) 7 April 2005 (2005-04-07) the whole document	1-108
P,X	US 2004/265935 A1 (ATASSI M. ZOUHAIR) 30 December 2004 (2004-12-30) the whole document	1-108
P,X	ATASSI M ZOUHAIR ET AL: "Submolecular recognition profiles in two mouse strains of non-protective and protective antibodies against botulinum neurotoxin A" MOLECULAR IMMUNOLOGY, vol. 42, no. 12, August 2005 (2005-08), pages 1509-1520, XP002376353 ISSN: 0161-5890 the whole document	1-10, 21-40

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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.
P,X	MARUTA TAKAHIRO ET AL: "Mapping of the synaptosome-binding regions on the heavy chain of botulinum neurotoxin A by synthetic overlapping peptides encompassing the entire chain" PROTEIN JOURNAL, vol. 23, no. 8, November 2004 (2004-11), pages 539-552, XP002370474 ISSN: 1572-3887 the whole document	1-10, 21-40
E	WO 2006/017715 A (ALLERGAN, INC.) 16 February 2006 (2006-02-16) page 8, paragraph 26 - page 9, paragraph 27 page 22, paragraph 60 - page 24, paragraph 62 page 33, paragraph 89 - page 34, paragraph 91 page 43, paragraph 113 - page 44, paragraph 115 page 53, paragraph 143 - page 55, paragraph 146; figure 8	1-10, 41-55
A	NAUMANN M ET AL: "Depletion of neutralising antibodies resensitizes a secondary non-responder to botulinum A neurotoxin" JOURNAL OF NEUROLOGY NEUROSURGERY AND PSYCHIATRY, vol. 65, no. 6, December 1998 (1998-12), pages 924-927, XP000979025 ISSN: 0022-3050 the whole document	98-108
A	US 2002/197278 A1 (ANTHONY ALLISON) 26 December 2002 (2002-12-26) the whole document	11-20, 56-67

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/036229

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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:

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

Continuation of Box II.1

Although claims 41-55 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the composition.

Although claims 56-108 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/036229

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005030119 A	07-04-2005	NONE	
US 2004265935 A1	30-12-2004	NONE	
WO 2006017715 A	16-02-2006	NONE	
US 2002197278 A1	26-12-2002	NONE	