Abstract: This invention provides antibodies that specifically bind to and typically neutralize botulinum neurotoxins (e.g., BoNT/A, BoNT/B, BoNT/E, etc.) and the epitopes bound by those antibodies. The antibodies and derivatives thereof and/or other antibodies that specifically bind to the neutralizing epitopes provided herein can be used to neutralize botulinum neurotoxin and are therefore also useful in the treatment of botulism.
Published: with international search report (Art. 21(3))

Date of publication of the international search report: 7 January 2010
### INTERNATIONAL SEARCH REPORT

**A. CLASSIFICATION OF SUBJECT MATTER**
- IPC(8) - A61K 39/40 (2009.01)
- USPC - 424/167.1

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(8): A61K 39/40 (2009.01)
  - USPC: 424/167.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
- USPC: 530/389.5
  - J Mol. Biol., Vol. 346

Electronic database consulted during the international search (name of database and, where practicable, search terms used)
- WEST (PGPBP, USPT, EPAB, JPAB): antibody, botulism, 2A10, VH, VL, CDRs, scFV, IgG, Fab, botulinum esp@orent: botulism, california
- Google Scholar: antibody botulinum 2A10 VH VL, composition kit disposable syringes

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 2004/0175385 A1 (MARKS et al.) 9 September 2004 (09.09.2004), abstract; para [0009], [0101], [0115], [0118], [0021], [0105], [0107], [0164], [0284], [0285], [0286], [0287], [0289], [0290], pg 73.</td>
<td>1, 5-13, 17-26, 29, 30</td>
</tr>
<tr>
<td>A</td>
<td>ARNOLD, JOSEPH W. et al. The Structure of the Neurotoxin-associated Protein HA33/A from Clostridium botulinum Suggests a Reoccurring b-Trefoil Fold in the Progenitor Toxin Complex. 2005 J Mol. Biol., Vol. 346, pp 1083-1093; especially page 1086 (Fig 3a), ISSN 0022-2836.</td>
<td>2-4, 14-16, and 28</td>
</tr>
<tr>
<td>A</td>
<td>US 2006/0251658 A1 (LEDGETTER et al.) 9 November 2006 (09.11.2006), abstract; pg 31.</td>
<td>2-4, 14-16, and 28</td>
</tr>
<tr>
<td>A</td>
<td>WO 03/057857 A2 (CORVALAN et al.) 17 July 2003 (17.07.2003), abstract; pg 47</td>
<td>2-4, 14-16, and 28</td>
</tr>
</tbody>
</table>

- Further documents are listed in the continuation of Box C.

**Date of the actual completion of the international search**
- 13 April 2009

**Date of mailing of the international search report**
- 12 MAY 2009

**Name and mailing address of the ISA/US**
- Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
- P.O. Box 1450, Alexandria, Virginia 22313-1450

**Facsimile No.**
- 571-273-3201

**Authorized officer:**
- Lee W. Young
  - PCT Helpdesk: 571-272-4300
  - PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>
**INTERNATIONAL SEARCH REPORT**

**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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-31 are directed to either a neutralizing antibody for Botulinum neurotoxin (BoNT), a composition thereof, or a method using such, limited to VH and VL CDRs from antibody 2A10 (SEQ ID NOS: 38 and 53).

Group II: Claims 1-31 are directed to either a neutralizing antibody for Botulinum neurotoxin (BoNT), a composition thereof, or a method using such, limited to VH and VL CDRs from antibody 3E1 (SEQ ID NOS: 3 and 54). Applicant may have additional CDR(s) searched for additional search fee(s).

--- Please see continuation on attached 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 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.:
   Claims 1-31, limited to VH and VL CDRs from antibody 2A10

**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.
Continuation of Box (III) - Lack of Unity:

The groups listed above do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

The special technical feature of Group I is antibody 2A10 and its CDR sequences while the special technical feature of Group II is antibody 3E1 and its CDR sequences. The groups do not relate to a single general inventive concept because they are directed to different antibodies with unique CDRs of having sequences that differ in structure and function.

Accordingly, unity of invention is lacking under PCT Rule 13.2 because the groups do not relate to a single general inventive concept.