Abstract: The present invention relates to the characterization and production of omalizumab.

Omalizumab HC sequence (SEP ID NO:l):

EVQLVESGGGLVQPSGGSLRLSCAVSGYSITSGYSWWNIRQAPKGPLEKVASITYDGSTNYNPSV
KGRILITRSRDSKNTFLYQMSLSRAEDTAVYCAEGHSHYFGHWHFAVWGQGITVTVSSASTKGPS
VFPLAPSSTSGTGAALGCLVKDYFPEPVTWSWNGALTSGVHTFPALQSSGLYSLSSVVT
PSSSLGTQTYICNVMHPNKTVDKKEPSDKCDHIHTCPCCPAPLLGLPSVFLFPFPPKDTLM
ISRTPEVIVCVVHVDHPEVKNHIVDFGVEVHINAKTRKPEEQYINSTYRVSNTTQLTVHPOQLNG
KEYRCVSNHAPPIEKTIKAKQGQPREDQVYTLPSREEMTKNQVSLTCLVGYFSDIAVE
WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQGTGVFVSCSMHEALNHYITQKSLSL
PGK

Abstract:

Omalizumab HC sequence (SEP ID NO:l):

EVQLVESGGGLVQPSGGSLRLSCAVSGYSITSGYSWWNIRQAPKGPLEKVASITYDGSTNYNPSV
KGRILITRSRDSKNTFLYQMSLSRAEDTAVYCAEGHSHYFGHWHFAVWGQGITVTVSSASTKGPS
VFPLAPSSTSGTGAALGCLVKDYFPEPVTWSWNGALTSGVHTFPALQSSGLYSLSSVVT
PSSSLGTQTYICNVMHPNKTVDKKEPSDKCDHIHTCPCCPAPLLGLPSVFLFPFPPKDTLM
ISRTPEVIVCVVHVDHPEVKNHIVDFGVEVHINAKTRKPEEQYINSTYRVSNTTQLTVHPOQLNG
KEYRCVSNHAPPIEKTIKAKQGQPREDQVYTLPSREEMTKNQVSLTCLVGYFSDIAVE
WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQGTGVFVSCSMHEALNHYITQKSLSL
PGK

Abstract:

Omalizumab HC sequence (SEP ID NO:l):
### A. CLASSIFICATION OF SUBJECT MATTER

**IPC(8) -** A61K 39/00, 39/395 (2013.01)

**USPC -** 424/133.1, 130.1

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 39/00, 39/395 (2013.01)

**USPC -** 424/133.1, 130.1

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)


### 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>Y</td>
<td>US 2002/0054878 A1 (LOWMAN, HB et al.) May 9, 2002; figure 12; paragraphs [0010], [0016], [0048], [0049], [0221], [0223], [0224], [0342]-[0346], [0383], [0385]; Claims 5, 22, 23; Table A; SEQ ID NOs: 13, 14</td>
<td>1-7, 8/6, 8/7, 9, 10, 11/6/6, 11/6/7, 12/10, 12/1 1/8/6, 12/1 1/8/7, 13-18, 22/1, 22/2, 22/4, 22/9, 22/13-22/1 5, 22/17, 24/1, 24/2, 24/4, 24/9, 24/13-24/15, 24/17, 25/1, 25/2, 25/4, 25/9, 25/13-25/1 5, 25/17, 26/1, 26/2, 26/4, 26/9, 26/1-26/15, 26/17, 27/1, 27/2, 27/4, 27/9, 27/3-27/15, 27/17, 28/1, 28/2, 28/4, 28/9, 28/13-28/15, 28/17</td>
</tr>
</tbody>
</table>

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

* 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 claims

"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: 04 January 2014 (04.01.2014)

Date of mailing of the international search report: 16 JAN 2014

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: Shane Thomas
PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774
<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>Y</td>
<td>US 2010/01 13294 A1 (VENKATARAMAN, G et al.) May 6, 2010; figures 2, 3; paragraphs [0024], [0066], [0074], [0106], [0107], [0130], [0131], [0135], [0138], [0248], [0306], [0417M0420], [0451], [0452]; Claims 1, 8; Tables 1, 3</td>
<td>1-7, 8/6, 8/7, 9, 10, 11/6/8, 11/8/7, 12/10, 12/1/8/6, 12/1/8/7, 12/1/8/8, 13-18, 22/1, 22/2, 22/4, 22/9, 22/13-22/15, 22/17, 24/1, 24/2, 24/9, 24/13-24/15, 24/17, 25/1, 25/2, 25/4, 25/9, 25/13-25/15, 25/17, 26/1, 26/2, 26/4, 26/9, 26/1-26/15, 26/17, 27/1, 27/2, 27/4, 27/9, 27/13-27/15, 27/17, 27/17, 28/1, 28/2, 28/4, 28/9, 28/13-28/15, 28/17</td>
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<td>A</td>
<td>WO 2011/127322 A1 (COLLINS, BE et al.) October 13, 2011; figure V, paragraph [0002]</td>
<td>1, 4, 6, 7, 8, 11/8/6, 11/8/7, 12/10, 12/1/8/6, 12/1/8/7, 22/1, 22/4, 24/1, 24/4, 25/1, 25/4, 26/1, 26/4, 27/1, 27/4, 28/1, 28/4</td>
</tr>
</tbody>
</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. E [Claims Nos.: 19-21, 23]
   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:

-""""Continued on Next Supplemental Page""""

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. X 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.:

   **Group I: Claims 1-18, 22, 24-28. restricted to omalizumab reference parameters 1 and 2 and SEQ ID NOS: 1 and 2**

**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.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)
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.

Groups I-: Claims 1-18, 22, 24-28, omalizumab reference parameters 1, 2 and SEQ ID NO:s 1 and 2 (recombinant antibody amino acids) are directed toward a method of manufacturing an omalizumab drug product, comprising: providing or obtaining a test glycoprotein preparation; acquiring at least one value for an omalizumab parameter listed in Table 1 for the test glycoprotein preparation; and processing at least a portion of the test glycoprotein preparation as omalizumab drug product if the at least one value for the test glycoprotein preparation meets a reference criterion shown in Table 1 for the parameter, thereby manufacturing an omalizumab drug product; a method of manufacturing an omalizumab drug product, comprising: providing a host cell that is genetically engineered to express a first amino acid sequence having a sequence with at least about 85% identity to SEQ ID NO: 1 (e.g., 90, 95, 98, or 100% identity to SEQ ID NO: 2 (e.g., 90, 95, 98, or 100% identity to SEQ ID NO: 2), wherein the expressed amino acid sequences form a recombinant antibody composition, culturing the host cell under conditions whereby the cell expresses the first and second amino acid sequences, wherein the expressed first and second amino acid sequences form recombinant antibodies, harvesting the recombinant antibodies from the host cell culture to produce an antibody preparation, acquiring a value for each parameter listed in Table 1 for the antibody preparation; and processing at least a portion of the antibody preparation into omalizumab drug product if the value for each parameter listed in Table 1 for the antibody preparation meets the reference criterion shown in Table 1, thereby manufacturing an omalizumab drug product; and a method of manufacturing an omalizumab drug product, comprising: providing a host cell that is genetically engineered to express a first amino acid sequence having the sequence of SEQ ID NO: 1 and a second amino acid sequence having the sequence of SEQ ID NO: 2, wherein the expressed amino acid sequences form a recombinant antibody composition, culturing the host cell under conditions whereby the cell expresses the first and second amino acid sequences, wherein the expressed first and second amino acid sequences form recombinant antibodies, harvesting the recombinant antibodies from the host cell culture to produce an antibody preparation, acquiring at least one value for an omalizumab parameter listed in Table 1 for the antibody preparation; and processing or directing the processing of at least a portion of the antibody preparation as omalizumab drug product if the at least one value for the antibody preparation meets a reference criterion shown in Table 1, thereby manufacturing an omalizumab drug product.

The method of manufacturing an omalizumab drug product of Groups I- will be searched to the extent that they encompass omalizumab reference parameter numbers 1 and 2. It is believed that Claims 1-18, 22 and 24-28 encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass omalizumab reference parameter numbers 1 and 2. Applicants must indicate, if applicable, the claims which encompass the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the, "*" group(s) will result in only the first claimed invention to be searched/examined. Additional omalizumab reference parameters can be searched upon they payment of additional fees. An Exemplary Election would be: omalizumab reference parameter number 3.

Groups I+ share the technical features including a method of manufacturing an omalizumab drug product, comprising: providing or obtaining a test glycoprotein preparation; acquiring at least one value for an omalizumab parameter listed in Table 1 for the test glycoprotein preparation; and processing at least a portion of the test glycoprotein preparation as omalizumab drug product if the at least one value for the test glycoprotein preparation meets a reference criterion shown in Table 1 for the parameter, thereby manufacturing an omalizumab drug product; and a method of manufacturing an omalizumab drug product, comprising: providing a host cell that is genetically engineered to express a first amino acid sequence having a sequence with at least about 85% identity to SEQ ID NO: 1 (e.g., 90, 95, 98, or 100% identity to SEQ ID NO: 2 (e.g., 90, 95, 98, or 100% identity to SEQ ID NO: 2), wherein the expressed amino acid sequences form a recombinant antibody composition, culturing the host cell under conditions whereby the cell expresses the first and second amino acid sequences, wherein the expressed first and second amino acid sequences form recombinant antibodies, harvesting the recombinant antibodies from the host cell culture to produce an antibody preparation, acquiring at least one value for an omalizumab parameter listed in Table 1 for the antibody preparation; and processing or directing the processing of at least a portion of the antibody preparation as omalizumab drug product if the at least one value for the antibody preparation meets a reference criterion shown in Table 1, thereby manufacturing an omalizumab drug product.
However, these shared technical features are previously disclosed by US 2010/01 13294 A 1 to Venkataraman, et al. (hereinafter ‘Venkataraman’). Venkataraman discloses a method of manufacturing (method for the production (manufacture); paragraphs [0007], [0138]) omalizumab (omalizumab; Table I) drug product (drug product; paragraph [0138]), comprising; providing or obtaining a test glycoprotein preparation (a glycoprotein product (a test glycoprotein preparation); paragraph [0137]); acquiring at least one value for a parameter for the test glycoprotein preparation (acquiring at least one value for a parameter for the test glycoprotein preparation; paragraph [0137]); and processing at least a portion of the test glycoprotein preparation (processing at least a portion of the test glycoprotein preparation; paragraphs [0137], [0138]) as an omalizumab (omalizumab; Table I) drug product (drug product; paragraph [0138]) if the at least one value for the test glycoprotein preparation meets a reference criterion for the parameter (if the at least one value for the test glycoprotein preparation meets a reference criterion for the parameter; paragraph [0138]), thereby manufacturing (manufacturing; paragraphs [0007], [0138]) an omalizumab (omalizumab; Table I) drug product (drug product; paragraph [0138]), and comprising; providing a host cell (providing a genetically engineered cell that produces the glycoprotein (a host cell); paragraph [0254]) that is genetically engineered to express a first amino acid sequence (genetically engineered to produce a first protein (amino acid sequence); paragraph [0254]), wherein the expressed amino acid sequence forms a recombinant (recombinant; paragraph [0280]) antibody composition (antibody; paragraph [0219]; Table I), culturing the host cell under conditions whereby the cell expresses the amino acid sequence (culturing the host cell under conditions whereby the cell expresses the amino acid sequence; paragraph [0283]), wherein the expressed amino acid sequences (expressed glycoproteins (amino acid sequences); paragraph [0254]) form recombinant (recombinant; paragraph [0280]) antibodies (antibodies; paragraphs [0219], Table I), harvesting the recombinant antibodies from the host cell culture (purifying (harvesting); paragraphs [0417], [0418]) the recombinant (recombinant; paragraph [0280]) antibodies (antibodies; paragraphs [0219], Table I) from the host cell culture (from the host cell culture; paragraphs [0283], [0418]) to produce (produce; paragraph [0138]) an antibody preparation (antibodies; paragraphs [0219], Table I), acquiring at least one value (acquiring at least one value; paragraph [0137]) for an omalizumab (omalizumab; Table I) parameter for the preparation (parameter for the test preparation; paragraph [0137]); and processing at least a portion of the preparation (processing at least a portion of the preparation; paragraphs [0137], [0138]) as an omalizumab (omalizumab; Table I) drug product (drug product; paragraph [0138]) if the at least one value for the preparation meets a reference criterion for the parameter (if the at least one value for the preparation meets a reference criterion for the parameter; paragraph [0138]), thereby manufacturing (manufacturing; paragraphs [0007], [0138]) an omalizumab (omalizumab; Table I) drug product (drug product; paragraph [0138]).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Venkataraman reference, unity of invention is lacking.