PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference VBLT.P0266WO	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2018/015870	International filing date *(day/month/year)* 30 January 2018	(Earliest) Priority Date *(day/month/year)* 31 January 2017
Applicant VANDERBILT UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 8 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (see Box No. II).

3. ☒ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 1

☐ as suggested by the applicant.

☒ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☒ forming part of the international application as filed:

      ☒ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs: 13-16, 65-68, 123-128, and 201-206 were searched.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

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.: 3-12, 15-24, 27-36, 39-49, 57-59, 67-69, 77, 78, 108-125
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 extra sheet(s).

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.:
1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, and 79-107 to the extent that they read on an antibody of SEQ ID NOs:13, 14, 65, 66, 123, 124, 125, 201, 202, and 203.

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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 35/28; A61K 39/00; A61K 39/395 (2018.01)
CPC - A61K 2039/505; C07K 16/00; C07K 16/1271; C12N 5/0635 (2018.05)

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)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 424/577; 435/326; 435/332; 435/334 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 8,802,375 B2 (SAMPSON et al) 12 August 2014 (12.08.2014) entire document	25, 26 --- 95-99
X -- Y	US 9,238,062 B2 (CHEN et al) 19 January 2016 (19.01.2016) entire document	89-94 --- 95-99, 104
X -- Y	US 2016/0157468 A1 (B CELL DESIGN et al) 09 June 2016 (09.06.2016) entire document	100 --- 101-104
Y	US 8,697,079 B2 (PENICHET et al) 15 April 2014 (15.04.2014) entire document	79-88
Y	US 2014/0315252 A1 (HOFFMANN-LA ROCHE INC.) 23 October 2014 (23.10.2014) entire document	79-88
Y	WO 2016/149137 A1 (EPITOMICS, INC.) 22 September 2016 (22.09.2016) entire document	79-88
Y	FITZSIMMONS et al. "Helminth allergens, parasite-specific IgE, and its protective role in human immunity," 14 February 2014 (14.02.2014), Vol. 5, Article 61, Pgs. 1-12. entire document	85-88, 101-104
A	US 2013/0243750 A1 (GENENTECH, INC.) 19 September 2013 (19.09.2013) entire document	1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, 79-107

☒ 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	Date of mailing of the international search report
15 May 2018	20 JUN 2018
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/0275492 A1 (MUSC FOUNDATION FOR RESEARCH DEVELOPMENT) 18 September 2014 (18.09.2014) entire document	1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, 79-107
A	US 9,127,251 B2 (SPITS et al) 08 September 2015 (08.09.2015) entire document	1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, 79-107
A	ZONE et al. "IgE basement membrane zone antibodies induce eosinophil infiltration and histological blisters in engrafted human skin on SCID mice," J Invest Dermatol, 18 January 2007 (18.01.2007), Vol. 127, Iss. 5, Pgs. 1167-1174. entire document	1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, 79-107

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

Continued from Box No. III Observations where unity of invention is lacking

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 need to be paid.

Group I+: claims 1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, and 79-107 are drawn to test antibodies, and methods and compositions comprising the same.

The first invention of Group I+ is restricted to a test antibody, and methods and compositions comprising the same, the test antibody comprising a heavy chain variable region, wherein in the heavy chain variable region is selected to be SEQ ID NO:65, encoded by SEQ ID NO:13, the heavy chain further comprising heavy chain complementarity determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:123, CDR2 is selected to be SEQ ID NO:124, and CDR3 is selected to be SEQ ID NO:125; and a light chain variable region, wherein the light chain variable region is selected to be SEQ ID NO:66, encoded by SEQ ID NO:14, the light chain further comprising light chain complementarity determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:201, CDR2 is selected to be SEQ ID NO:202, and CDR3 is selected to be SEQ ID NO:203. It is believed that claims 1, 2, 13, 14, 25, 26, 37, 38, 50-56, 60-66, 70-76, and 79-107 read on this first named invention and thus these claims will be searched without fee to the extent that they read on an antibody of SEQ ID NOs:13, 14, 65, 66, 123, 124, 125, 201, 202, and 203.

Applicant is invited to elect additional test antibodies with specified SEQ ID NO for each heavy and light chain CDR1, 2, and 3 to be searched in a specific combination by paying an additional fee for each set of election. An exemplary election would be a test antibody, and methods and compositions comprising the same, the test antibody comprising a heavy chain variable region, wherein in the heavy chain variable region is selected to be SEQ ID NO:67, encoded by SEQ ID NO:15, the heavy chain further comprising heavy chain complementarity determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:126, CDR2 is selected to be SEQ ID NO:127, and CDR3 is selected to be SEQ ID NO:128; and a light chain variable region, wherein the light chain variable region is selected to be SEQ ID NO:68, encoded by SEQ ID NO:16, the light chain further comprising light chain complementarity determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:204, CDR2 is selected to be SEQ ID NO:205, and CDR3 is selected to be SEQ ID NO:206. Additional test antibodies will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on 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.

The inventions listed in Groups I+ 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 Groups I+ formulas do not share a significant structural element responsible for detecting an IgE antibody, requiring the selection of alternatives for the light and heavy chain variable regions of the antibody, where "the test antibody or fragment thereof has clone paired heavy and light chain CDRs from Tables C and D" and "said antibody or antibody fragment is encoded by heavy and light chain variable sequences having 70%, 80%, or 90% identity to clone paired heavy and light chain variable sequences as set forth in Table A" and "said antibody or antibody fragment comprises heavy and light chain variable sequences having 70%, 80% or 90% identity to clone paired heavy and light chain variable sequences as set forth in Table B".

Additionally, even if Groups I+ were considered to share the technical features of a method of detecting a IgE antibody with binding affinity/specificity for a dust mite antigen in a subject comprising: (a) providing a test antibody or fragment thereof having (i) heavy chain CDR1, CDR2, CDR3, and a light chain CDR1, CDR2, and CDR3; (b) contacting the test antibody or fragment thereof with an antibody-containing sample from said subject in the presence of a dust mite antigen; and (c) detecting IgE antibody with binding affinity for dust mite antigen in said sample by measuring the reduction of binding to dust mite antigen by the test antibody or fragment thereof as compared to the binding of the test antibody or fragment thereof in the absence of said sample; a method of detecting a IgE antibody with binding affinity/specificity for a helminth antigen in a subject comprising: (a) providing a test antibody or fragment thereof having clone paired heavy and light chain CDRs; b) contacting the test antibody or fragment thereof with an antibody-containing sample from said subject in the presence of a helminth antigen; and (c) detecting IgE antibody with binding affinity for helminth antigen in said sample by measuring the reduction of binding to helminth antigen by the test antibody or fragment thereof as compared to the binding of the test antibody or fragment thereof in the absence of said sample; a method of detecting an allergen or antigen in a sample comprising: (a) providing a test antibody or fragment thereof having heavy chain CDR1-CDR3 and light chain CDR4-CDR6 from an IgE antibody produced in a subject in response to allergen or antigen stimulation; (b) contacting the test antibody or fragment thereof with a sample suspect of containing an allergen or antigen; and (c) detecting allergen or antigen in said sample by binding of the test antibody or fragment; a method of preventing or treating a dust mite-related allergic reaction in a subject comprising delivering to said subject an IgG antibody or antibody fragment, wherein said antibody or antibody fragment has (i) heavy chain CDR1, CDR2, CDR3, and a light chain CDR1, CDR2, and CDR3; a monoclonal antibody or antibody fragment comprises clone paired heavy and light chain CDRs; a hybridoma or engineered cell encoding an antibody or antibody fragment wherein the antibody or antibody fragment is characterized by clone paired heavy and light chain CDRs; a vaccine formulation comprising one or more IgG antibodies or antibody fragments characterized by clone paired heavy and light chain CDRs; these shared technical features do not represent a contribution over the prior art.

Specifically, US 8,802,375 B2 to Sampson et al. discloses a method of detecting a IgE antibody with binding affinity/specificity for a dust mite antigen in a subject (Methods for performing epitope mapping, and for characterizing the antibody binding affinity and epitope diversity of antibodies in a sample using peptide microarray are provided. In some aspects, methods are provided for the specific characterization of IgE, Abstract; However, some substances are very common allergens, such as, pollen and mold, dust mite droppings, Col. 10, Lns. 46-48; subject) comprising: (a) providing a test antibody or fragment thereof having (i) heavy chain CDR1, CDR2, CDR3, and a light chain CDR1, CDR2, and CDR3 (An intact antibody comprises at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, Col. 14, Lns. 6-7; The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, Col. 14, Lns. 15-21); (b) contacting the test antibody or fragment thereof with an antibody-containing sample from said subject in the presence of a dust mite antigen (obtaining the antibody-containing sample from the subject, Col. 2, Lns. 46-47; incubating the sample with a peptide library corresponding to the allergen immobilized on a solid support, wherein the peptide library includes at least one allergen epitope to form an incubation mixture; incubating a first portion of the incubation mixture with a competitor, wherein the competitor includes at least one epitope of the allergen, and incubating a second portion of the incubation mixture under the same conditions but in the absence of the competitor; detecting antibody binding to the peptide library in the first and second portions of the incubation mixture; and comparing the number of subject antibodies that remain bound to the at least one epitope in the first and second portions of the incubation mixture to determine the affinity of antibody binding to the immobilized allergen epitopes, Col. 3, Lns. 2-15); and (c) detecting IgE antibody with binding affinity for dust mite antigen in said sample by measuring the reduction of binding to dust mite antigen by the test antibody or fragment thereof as compared to the binding of the test antibody or fragment thereof in the absence of said sample (incubating a first portion of the incubation mixture with a competitor, wherein the competitor includes at least one epitope of the allergen, and incubating a second portion of the incubation mixture under the same conditions but in the absence of the competitor, Col. 2, Lns. 50-55; an antibody binds an epitope with high affinity if the strength of antibody binding has a Z score that is greater than 3 and the Z score decreases less than about 50 percent in the first portion as compared to the second portion of the incubation mixture, Col. 4, Lns. 59-63); a method of detecting an allergen or antigen in a sample (Methods for performing epitope mapping, and for characterizing the antibody binding affinity and epitope diversity of antibodies in a sample using peptide microarray are provided. In some aspects, methods are provided for the specific characterization of IgE, Abstract; The methods provide for spotting of microarray slides with a peptide library. In a specific embodiment, the peptide library includes peptides corresponding to amino acid sequences found in milk allergens. However, peptide libraries of other allergens, such as other food allergens, Col. 7, Lns. 31-35) comprising: (a) providing a test antibody or fragment thereof having heavy chain CDR1-CDR3 and light chain CDR4-CDR6 from an IgE antibody produced in a subject in response to allergen or antigen stimulation (An intact antibody comprises at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, Col. 14, Lns. 6-7; The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, Col. 14, Lns. 15-21; obtaining the antibody-containing sample from the subject, Col. 2, Lns. 46-47); (b) contacting the test antibody or fragment thereof with a sample suspect of containing an allergen or antigen; and (c) detecting allergen or antigen in said sample by binding of the test antibody or fragment; (incubating a first portion of the incubation mixture with a competitor, wherein the competitor includes at least one epitope of the allergen, and incubating a second portion of the incubation mixture under the same conditions but in the absence of the competitor, Col. 2, Lns. 50-55; an antibody binds an epitope with high affinity if the strength of antibody binding has a Z score that is greater than 3 and the Z score decreases less than about 50 percent in the first portion as compared to the second portion of the incubation mixture, Col. 4, Lns. 59-63; detecting antibody binding to the peptide library in the first and second portions of the incubation mixture, Col. 3, Lns. 10-11); a monoclonal antibody or antibody fragment comprises clone paired heavy and light chain CDRs (The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, Col. 14, Lns. 15-21; obtaining the antibody-containing sample from the subject, Col. 2, Lns. 46-47; monoclonal biotinylated anti-human IgE, Col. 31, Lns. 65-66); wherein said antibody or antibody fragment has (i) heavy chain CDR1, CDR2, CDR3, and a light chain CDR1, CDR2, and CDR3 (The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, Col. 14, Lns. 15-21; obtaining the antibody-containing sample from the subject, Col. 2, Lns. 46-47; monoclonal biotinylated anti-human IgE, Col. 31, Lns. 65-66); wherein the antibody or antibody fragment is characterized by clone paired heavy and light chain CDRs (The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, Col. 14, Lns. 15-21; obtaining the antibody-containing sample from the subject, Col. 2, Lns. 46-47; monoclonal biotinylated anti-human IgE, Col. 31, Lns. 65-66).

Further, US 9,238,062 B2 to Chen et al. discloses a method of preventing or treating a dust mite-related allergic reaction in a subject (hypoallergenic polypeptides for the treatment of house dust mite allergy, Title; Yet another aspect of the invention is a method of treating and/or preventing an allergic disorder, comprising administering to an individual in need thereof a therapeutically effective amount of the polypeptide or polynucleotide of this invention, Col. 3, Lns. 3-7) comprising delivering to said subject an IgG antibody or antibody fragment, (providing a composition containing IgG antibodies by immunizing a non human mammal ...with the peptide ... measuring whether and/ or to which extent said composition containing IgG antibodies can block the binding of said IgE antibodies to one or more of said allergens Col. 5, Lns. 22-26); a method of de-sensitizing a subject to an allergen comprising: (a) administering to said subject an allergen (hypoallergenic polypeptides for the treatment of house dust mite allergy, Title; Yet another aspect of the invention is a method of treating and/or preventing an allergic disorder, comprising administering to an individual in need thereof a therapeutically effective amount of the polypeptide or polynucleotide of this invention, Col. 3, Lns. 3-7); and (b) administering to said subject an IgG antibody that has a binding specificity to said allergen obtained from an IgE antibody (providing a composition containing IgG antibodies by immunizing a non human mammal ...with the peptide ... measuring whether and/ or to which extent said composition containing IgG antibodies can block the binding of said IgE antibodies to one or more of said allergens Col. 5, Lns. 22-26).

Further still, US 2014/0275492 A1 to MUSC Foundation for Research Development discloses a hybridoma or engineered cell encoding an antibody or antibody fragment (there is provided a method of producing an immortalized human B-cell secreting an antibody specific for a predetermined antigen, Para. [0008]); a vaccine formulation comprising one or more IgG antibodies or antibody fragments characterized by clone paired heavy and light chain CDRs (simultaneous administration of vaccine and antibody may be possible to provide both immediate and long-lasting protection, Para. [0139]; EBV immortalized cells treated with anti-IgM (Fab')2 and IL-6, soluble CD40L alone, or anti-IgM (Fab')2, BAFF and soluble CD40L, preferentially increased IgG secretion, Para. [0191]; the cloning and expression of human immunoglobulin light and heavy chain sequences, Para. [0125]; indicate gaps that have been inserted for CDR alignment purposes, Para. [0076]).

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/015870

"IgE Basement Membrane Zone Antibodies Induce Eosinophil Infiltration and Histological Blisters in Engrafted Human Skin on SCID Mice" to Zone et al. discloses a hydridoma that produces an IgE antibody (A subcutaneous hybridoma secreting IgE antibodies developed, Abstract; we plan to purify large amounts of IgE BMZ antibodies from hybridoma cells, Pg. 1171, right-hand column, third paragraph).

US 2013/0243750 A1 to Genentech Inc. discloses a method of detecting a IgE antibody with binding affinity/specificity for a helminth antigen in a subject (Blood serum samples were assessed for total serum levels of MEMP1972A by quantitative immunoassays, for the presence of anti-therapeutic antibodies (ATA) using a bridge ELISA, and measurement of total and allergen-specific IgE using a standard clinical assay, Para. [0353]; Methods known in the art may be used to detect presence of anti-therapeutic antibodies in a serum sample, Para. [0354]; The term "allergen-specific IgE" refers to IgE that is specific to a particular antigen ...helminths, Para. [0082]) comprising: (a) providing a test antibody or fragment thereof having clone paired heavy and light chain CDRs (The antibodies useful in the present invention can encompass monoclonal antibodies, Para. [0179]; the anti-IgE antibody comprises a heavy chain and a light chain variable region ...HVRs, Para. [0019]; A number of HVR delineations are in use and are encompassed herein. The HVRs that are Kabat complementarity-determining regions (CDRs) are based on sequence variability, Para. [0069]; In an exemplary competition assay, immobilized the M1′ segment of IgE is incubated in a solution comprising a first labeled antibody that binds to the M1′ segment (e.g., antibody 47H4, 47H4 v1, v2, v3, v4, v5 or v6) and a second unlabeled antibody that is being tested for its ability to compete with the first antibody for binding to the M1′ segment., Para. [0057]); b) contacting the test antibody or fragment thereof with an antibody-containing sample from said subject in the presence of a helminth antigen (In an exemplary competition assay, immobilized the M1′ segment of IgE is incubated in a solution comprising a first labeled antibody that binds to the M1′ segment (e.g., antibody 47H4, 47H4 v1, v2, v3, v4, v5 or v6) and a second unlabeled antibody that is being tested for its ability to compete with the first antibody for binding to the M1′ segment, Para. [0057]; The term "allergen-specific IgE" refers to IgE that is specific to a particular antigen ...helminths, Para. [0082]); and (c) detecting IgE antibody with binding affinity for helminth antigen in said sample by measuring the reduction of binding to helminth antigen by the test antibody or fragment thereof as compared to the binding of the test antibody or fragment thereof in the absence of said sample (After incubation under conditions permissive for binding of the first antibody to M1′ segment, excess unbound antibody is removed, and the amount of label associated with immobilized M1′ segment is measured. If the amount of label associated with immobilized M1′ segment is substantially reduced in the test sample relative to the control sample, then that indicates that the second antibody is competing with the first antibody for binding to M1′ segment, Para. [0057]; The term "allergen-specific IgE" refers to IgE that is specific to a particular antigen ...helminths, Para. [0082]).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features