AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claims 1-100 (Cancelled).

Claim 101 (Previously Presented): An isolated or recombinant polypeptide fragment comprising at least 50 consecutive amino acids of any of SEQ ID NOs: 3-18, wherein the fragment comprising at least 50 consecutive amino acids is immunogenic and the immunogenic polypeptide fragment comprises less than 1100 amino acids of the applicable polypeptide of SEQ ID NOs: 3-18.

Claim 102 (**Currently amended**): The ~~isolated or recombinant~~ polypeptide fragment of claim 101 wherein the fragment comprising at least 50 consecutive amino acids includes an amino acid sequence selected from the group consisting of SEQ ID NOs: 219-307 or comprises at least amino acids 595-1008 of SEQ ID NOs: 3-18.

Claims 103-104 (Cancelled).

Claim 105 (Previously Presented): A composition comprising the isolated or recombinant immunogenic polypeptide of claim 101 in admixture with an adjuvant.

Claims 106-108 (Cancelled).

Claim 109 (**Currently amended**): The ~~immunogenic~~ polypeptide fragment of claim 101 comprising a deletion relative to the applicable polypeptide of SEQ ID NOs: 3-18, which increases solubility of the fragment as compared to the applicable full length polypeptide of SEQ ID NOs: 3-18 and wherein the fragment ~~raises a substantially similar immune response in a subject as~~ provides at least 70% of protection in a subject provided by the applicable full length polypeptide of SEQ ID NOs: 3-18.

Claim 110 (**Currently amended**): The ~~immunogenic~~ polypeptide fragment of claim 109, wherein the deletion comprises a putative amino-terminal translocator domain and/or the fragment of at least 50 consecutive amino acids includes the amino acid sequence of SEQ ID NO: 642.

Claim 111 (**Currently amended**): A[[n]] ~~immunogenic~~ composition comprising the polypeptide fragment of claim 109 in admixture with an adjuvant.

Claims 112-113 (Cancelled).

Claim 114 (**New**): A method for raising an immune response in a mammal comprising the step of administering to the mammal an effective amount of the immunogenic composition of claim 105.

Claim 115 (**New**): A method for raising an immune response in a mammal comprising the step of administering to the mammal an effective amount of the immunogenic composition of claim 111.

Office Action Summary	Application No. 13/382,906	Applicant(s) SERINO ET AL.	
	Examiner Patricia A. Duffy	Art Unit 1645	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6-13-2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *101, 102, 105, 109, 110, 111, 114 and 115* is/are pending in the application.

5a) Of the above claim(s) *114 and 115* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *101,102,105 and 109-111* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 6-13-2014 has been entered into the record. Claims 1-100, 103-104, 106-108 and 112-113 have been cancelled. Claims 101, 102, 105, 109, 110, 111, 114 and 115 are pending. Claims 101, 102, 105, 109, 110 and 111 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

Newly submitted claims 114 and 115 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are drawn to a method of use of the product under examination.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 114 and 115 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Rejections Withdrawn

The rejection of claims 109, 110 and 111 under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention is withdrawn based upon the amendment to the claims.

Rejections Maintained

Claims 101, 102, 105, 109, 110 and 111 stand rejected under 35 U.S.C. 101 because the claimed invention is not directed to patent eligible subject matter. Based upon an

analysis with respect to the claim as a whole, claim(s) 101, 102, 105, 109, 110 and 111 are determined to be directed to a law of nature/natural principle.

Applicant's arguments have been considered but are not persuasive. Applicants argue that the polypeptides fragments are not naturally occurring and are markedly different in structure.

Applicant argues that the isolation of the protein fragment confers a marked difference from the naturally existing protein by imparting a significant function on the protein that it would not otherwise exhibit in nature and that by virtue of isolation the claimed protein fragment may function as a vaccine antigen where it previously could not in its full length form. That is the act of isolation of the fragment imparts a new function on the protein as solubility; that is the ability to function as a vaccine. This is not persuasive because in order to be patent eligible, the product or composition must be **both** non-naturally occurring and markedly different from the naturally occurring product. While "isolation" of a protein fragment indicates the hand of man, it is insufficient in this case to confer a marked difference in structure. The structure of a protein fragment is determined by the sequences of amino acids along with any post-translational modifications of the primary amino acid sequence (e.g. prenylation, glycosylation). In the instant case, the method of production or isolation does not on its face provide a difference in the primary amino acid sequence of the fragment as compared to the naturally occurring protein. In contrast to Applicant's assertions, protein fragments do occur in nature as proteins are routinely digested and broken down by proteases. Furthermore, the proteins are built one amino acid at a time and as such every protein at some point exists as a two amino acid fragment, a three amino acid fragment and so forth. The arguments with respect the function of generating a vaccine/immune response that it would not otherwise have in its full length insoluble form, it is noted that an immune response is a property/function of the host and not the protein *per se*. Additionally, denatured and insoluble antigens can generate and immune response and there is no

evidence in the specification that the full-length insoluble fragment is incapable of generating an immune response. The art has long found that insoluble antigens presented in gel fragments or powders are capable of generating an immune response and the art teaches that particulate antigens make excellent immunogens (see Harlow et al, Antibodies A Laboratory Manual, Cold Spring Harbor 1988, Chapter 5, pages 67-71 and page 91). Therefore, the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.") There is no evidence in the specification as filed regarding the lack of an immune response toward the full length antigen. Additionally, the argument is directly contrary to the claims which state that the fragments provide "at least 70% of protection in a subject provided by the applicable full length polypeptide". As such, the full length protein was expected by Applicants to provide for a protective response. If the full length protein is incapable of generating a protective immune response then Applicants argument is not understood as 70% of zero is still zero and the claim limitation would therefore have no meaning. The assertion of vaccines is not relevant to the claims as the claims are not drawn to vaccines. Additionally, the specification does not demonstrate protection from infection as asserted by Applicant's, merely an increased survival from a lethal challenge. No apparent full-length protein was injected or examined as such Applicants assertion of any difference as compared to the full-length protein lacks evidentiary support in the specification as filed. The mere fragmentation of a protein is similar to the 101 guidance for DNA primers, the primers are more soluble and have the function of being able to bind to the nucleic acid and provide for amplification because they are fragments. However, the structure is not markedly different. Similarly, the fragments of the protein likewise do not meet the

statute because they are a fragment of a naturally occurring protein and are not markedly different.

The specification does not describe any manipulation of the actual sequence structure of the protein to produces a marked difference in primary amino acid sequence as compared to the naturally occurring protein product. There is no change to the sequence or structure of the protein fragment *per se*. It does not change the chemical nature of the amino acids in the fragment. As such, the response fails satisfy the markedly different requirement as the protein fragment is derived from a naturally occurring protein found in nature and fails to demonstrate a structural difference from the naturally occurring protein as the fragment does not change its primary structure from that which is found in the full-length protein. The markedly different inquiry focuses on the structural characteristics of the product and not the function of solubility in water. The claims do not state solubility in water and such a comparison cannot apparently be found in the text of the specification. As such, the protein fragment is not markedly different as fragments would be expected to be more soluble in a variety of solvents such as (e.g. urea, acetonitrile, phosphate buffered saline) and the claims merely state any increase and no particular solvent. The specification does not disclose the parameters for solubility of the full-length protein in water as compared to the solubility of the fragments in water as argued. The combination of the fragment with the adjuvant does not change the structure of either the protein fragment or the adjuvant as the mere combination does not change the individual elements from what the individually exists in nature. In this case it is found that the primary amino acid sequence of the structure of the protein fragment *per se* is not changed in a manner and as such, it is not markedly different. The addition of the adjuvant adds a feature that is well-understood, purely conventional and routine in the art in order to use the judicial exception. The combination is a product of two naturally occurring substances that are both naturally occurring or non-naturally occurring and not markedly different in structure with another naturally

occurring adjuvant substance and the mere combination does not provide for a change in structure.

The rejection is maintained.

New Rejections Based on Amendment

Claims 109, 110 and 111 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

The claims now recites "at least 70% protection" but does not state protection from what. As such it unclear what precise condition that 70% protection relates to infection/sepsis/death ?

Claims 109, 110 and 111 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

The claims now recite that the polypeptide fragment "provides at least 70% of protection in a subject provided by the applicable full length polypeptide". The specification at page 65, line 24 indicates that it is protection against lethal challenge. The term protection can also be applicable to protection from infection, protection from disease, protection from sepsis. As such, the contemplation of protection against lethal challenge does not support the genus of protection now claimed.