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SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER
			1656	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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sughrue@sughrue.com
USPTO@sughrue.com

Office Action Summary

Application No.
14/650,767

Applicant(s)
MIZUMURA ET AL.

Examiner
DAVID J. STEADMAN

Art Unit
1656

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 03/16/2017.
☐ 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) 43,47-54,57-61 and 63-78 is/are pending in the application.
5a) Of the above claim(s) 51-53,58-61 and 64 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 43,47-50,54,57,63 and 65-78 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:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ 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: ____.

DETAILED ACTION

Status of the Application

1. The present application is being examined under the pre-AIA first to invent provisions.
2. Claims 43, 47-54, 57-61, and 63-78 are pending in the application.
3. Applicant's amendment to the claims, filed on 3/16/2017, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
4. Applicant's amendment to the specification, filed on 3/16/2017, is acknowledged.
5. Applicant's remarks filed on 3/16/2017 in response to the non-final rejection mailed on 9/16/2016 have been fully considered.
6. Rejections previously applied to claims 44-46, 55, 56, and 62 are withdrawn solely in view of the instant amendment to cancel these claims.
7. The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

8. Claims 51-53, 58-61, and 64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 8/24/2016.

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9. Claims 43-50, 54-57, 62, and 63 are being examined on the merits with claim 49 being examined only to the extent the claim reads on the elected subject matter of the species of SEQ ID NO: 2.

Information Disclosure Statement

10. The information disclosure statement (IDS) submitted on 10/26/2016 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification/Informalities

11. The objection to the disclosure because it contains an embedded hyperlink and/or other form of browser-executable code is maintained for the reasons of record and the reasons set forth below. Applicant's amendment to the specification to remove "http://" is acknowledged, however, the disclosure of "www.pssj.jp..." is still considered to be browser executable code. In the interest of compact prosecution, applicant may consider amending the "www.pssj.jp..." to "available on the world wide web at pssj.jp..."

Claim Objection

12. Claim 54 is objected to in the recitation of "Chinese hamster cell" and in the interest of improving claim form, it is suggested that the noted phrase be amended to recite, *e.g.*, "Chinese hamster ovary cell".

Claim Rejections - 35 USC § 112, Fourth Paragraph

The following is a quotation of pre-AIA 35 U.S.C. 112, fourth paragraph:

Subject to the following paragraph [i.e., the fifth paragraph of pre-AIA 35 U.S.C. 112], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

13. Claims 49 and 77 are rejected under 35 U.S.C. 112(d) or pre-AIA 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends. This rejection is necessitated by applicant's amendment to claims 43 and 54 to recite "wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*".

As amended, the horseshoe crab Factor C of claims 43 and 54 is limited to a *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, or *Tachypleus gigas* Factor C. In view of the recitation of "but which includes substitution, deletion, insertion, or addition of one or several amino acid residues", the amino acid sequences encompassed by claims 49 and 77 are unlimited and thus do not further limit claims 43 and 54, respectively. Applicant may cancel the claim(s), amend the claim(s) to place the claim(s) in proper dependent form, rewrite the claim(s) in independent form, or present a sufficient showing that the dependent claim(s) complies with the statutory requirements. Applicant may consider amending claims 49 and 77 to delete parts (B) and (D).

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Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 49 and 77 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. This rejection is necessitated by applicant's amendment to claims 43 and 54 to recite "wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*".

As amended, the horseshoe crab Factor C of claims 43 and 54 is limited to a *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, or *Tachypleus gigas* Factor C. However, in view of the recitation of "but which includes substitution, deletion, insertion, or addition of one or several amino acid residues" in claims 49 and 77, the amino acid sequences encompassed by claims 49 and 77 (which depend from claims 43 and 54, respectively) are unlimited and thus it is unclear as to the scope of Factor C polypeptides that are intended as being encompassed by claims 49 and 77. It is suggested that applicant clarify claims 49 and 77. In the interest of compact prosecution, applicant may consider amending claims 49 and 77 to delete parts (B) and (D).

Claim Rejections - 35 USC § 112, First Paragraph

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15. The written description and scope of enablement rejections of claims 43, 47-50, 54, 57, and 63 under 35 U.S.C. 112 (pre-AIA), first paragraph, are withdrawn in view of applicant's amendment to claims 43 and 54 to recite "A horseshoe crab Factor C...wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*". Recombinant expression of Factor C polypeptides of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas* were well-known at the time of the invention. Also, it was well-known in the prior art at the time of the invention that different cell types add a sialic acid to an expressed polypeptide using only a particular linkage, *e.g.*, Chinese Hamster Ovary (CHO) cells are only able to add sialic acid using an α -2,3 linkage (see, *e.g.*, paragraph 8 of Cottingham et al., US 2014/0249082, which has priority to 2010, cited on the IDS filed on 10/26/2016). As such, one of skill in the art would recognize that the specification in view of the state of the art at the time of the invention adequately describes and enables the full scope of the claimed horseshoe crab Factor C polypeptides.

Claim Rejections - 35 USC § 102

16. The rejection of claims 43, 49, 50, and 57 under pre-AIA 35 U.S.C. 102(b) as being anticipated by Mizumura et al. (WO 2012/118226 A1; cited on the IDS filed on 6/9/2015; hereafter "Mizumura") is withdrawn in view of applicant's amendment to claim 43 to recite "which contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C

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expressed using Sf9 as a host cell". According to the specification, a *Tachypleus tridentatus* Factor C polypeptide recombinantly produced using insect Sf9 cells as an expression host does not react with a (α -2,3)-linked terminal sialic acid-specific lectin (specification at paragraph 153), indicating that (α -2,3)-linked terminal sialic acid is not present on the Sf9 cell-produced *T. tridentatus* Factor C polypeptide. Further according to the specification, a native *Tachypleus tridentatus* Factor C polypeptide reacts with a (α -2,3)-linked terminal sialic acid-specific lectin (specification at paragraph 153), indicating that (α -2,3)-linked terminal sialic acid is present on the native *T. tridentatus* Factor C polypeptide. As such, Mizumura's Sf9 cell-produced *T. tridentatus* Factor C polypeptide *does not* contain (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell, and thus does not satisfy all claim limitations.

17. The rejection of claims 54, 62, and 63 under pre-AIA 35 U.S.C. 102(b) as being anticipated by Koshiba et al. (*J. Biol. Chem.* 282:3962-3967, 2007; cited on Form PTO-892; hereafter "Koshiba") is withdrawn in view of the amendment to claim 54 to recite "having activity of Factor C". According to the specification, "the activity of Factor C refers to such an activity that the Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B" (specification at p. 36, paragraph 28), which as noted by applicant, is considered to be the "protease activity" of Factor C, and does not refer to the ability to bind to LPS (remarks at p. 14, footnote). Koshiba does not teach a

horseshoe crab Factor C having "Factor C activity" as defined according to the specification.

Claim Rejections - 35 USC § 102/103

18. The rejection of claims 43, 48-50, and 57 under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Nakamura et al. (*J. Biochem.* 99:847-857, 1986; cited on the IDS filed on 6/9/2015; hereafter "Nakamura") as evidenced by Mizumura (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection has been modified to address applicant's amendment to the claims.

Claims 43, 48-50, 57, and 65 are rejected under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Nakamura (*supra*) as evidenced by Mizumura (*supra*).

Claims 43, 48-50, and 65 are drawn to a horseshoe crab Factor C having activity of Factor C, which contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell, wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*.

Claim 57 is drawn to an endotoxin assay kit comprising an endotoxin assay agent containing the Factor C according to claim 43 and one or more elements.

Regarding claim 43, Nakamura teaches an activated Factor C polypeptide purified from the hemocyte lysate of *Tachyplesus tridentatus* (p. 848, sentence bridging columns 1 and 2). Nakamura teaches activation of factor B by the activated Factor C (p. 851, column 2), and thus Nakamura's purified Factor C has "activity of Factor C".

Nakamura does not teach the activated factor C polypeptide purified from the hemocyte lysate of *T. tridentatus* contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell. However, according to the specification, Factor C polypeptide derived from *T. tridentatus* has (α -2,3)-linked terminal sialic acid (paragraph 153), while *T. tridentatus* factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid (paragraph 154). As such, since factor C polypeptide derived from *T. tridentatus* has (α -2,3)-linked terminal sialic acid and since *T. tridentatus* factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid, it follows that Nakamura's activated Factor C polypeptide purified from *T. tridentatus* necessarily has a greater amount of (α -2,3)-linked terminal sialic acid than *T. tridentatus* factor C polypeptide expressed in Sf9 as a host cell.

Regarding claims 48 and 65, Nakamura does not teach the activated factor C polypeptide purified from the hemocyte lysate of *T. tridentatus* has a molecular weight as recited in the claims. However, the specification teaches that factor C polypeptide derived from *T. tridentatus* has a molecular weight of 124 kDa by SDS-PAGE under non-reducing conditions (paragraph 144 and Table 1). As such, since Nakamura's

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activated factor C polypeptide is derived from *T. tridentatus*, it follows that Nakamura's activated factor C polypeptide necessarily has a molecular weight of 124 kDa by SDS-PAGE under non-reducing conditions.

Regarding claim 49, Nakamura does not teach the amino acid sequence of the activated factor C polypeptide purified from the hemocyte lysate of *T. tridentatus* has the amino acid sequence of SEQ ID NO: 2. However, evidentiary reference of Mizumura is cited to show that the amino acid sequence of *Tachypleus tridentatus* factor C is identical to SEQ ID NO: 2 herein (see Appendix A at pp. 30 and 31 of the Office action mailed on 9/16/2016).

Regarding claim 50, Nakamura teaches the Factor C has catalytic activity in an aqueous buffer (p. 852, Figure 6) and thus Nakamura's Factor C is considered to be water-soluble.

Regarding claim 57, Nakamura teaches reconstitution of the LPS-mediated clotting system, including the activated factor C polypeptide purified from the hemocyte lysate of *T. tridentatus*, which is considered to be an endotoxin assay kit as encompassed by claim 57.

19. RESPONSE TO REMARKS: Beginning at p. 14 of the remarks, applicant argues that Nakamura discloses native *T. tridentatus* Factor C and does not disclose a recombinantly expressed Factor C of *T. tridentatus* using a mammalian cell as a host cell. Applicant argues that the specification at paragraph 153 discloses that a recombinantly expressed Factor C of *T. tridentatus* using a mammalian cell as a host

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cell contains (α -2,3)-linked terminal sialic acid in a greater amount as compared with native *T. tridentatus* Factor C, which native *T. tridentatus* Factor C is the same as Nakamura's Factor C and thus the Factor C of claim 43 is different from Nakamura's Factor C.

Applicant's argument is not found persuasive. First, claims 43, 48-50, 57, and 65 do not require a recombinantly expressed Factor C of *T. tridentatus* using a mammalian cell as a host cell. Second, claim 43 recites the alternative of containing (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell. As noted above, according to the specification, Factor C polypeptide derived from *T. tridentatus* has (α -2,3)-linked terminal sialic acid (paragraph 153), while *T. tridentatus* factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid (paragraph 154). Thus, Factor C polypeptide derived from *T. tridentatus* contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell. For these reasons, Nakamura's native *T. tridentatus* Factor C anticipates the claims.

20. The rejection of claims 43, 47-50, 54, 57, and 63 under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Ding et al. (US 5,716,834; cited on Form PTO-892 mailed on 9/16/2016; hereafter "Ding") as evidenced by Mizumura (*supra*) is maintained for the reasons of record and

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the reasons set forth below. The rejection has been modified to address applicant's amendment to the claims.

Claims 43, 47-50, 54, 57, 63, and 65-78 are rejected under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Ding (*supra*) as evidenced by Mizumura (*supra*). See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103 and see MPEP 2131.01 regarding a multiple reference 35 U.S.C. 102 rejection.

Claims 43, 47-50, and 65-69 are drawn to a horseshoe crab Factor C having activity of Factor C, which contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell, wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*.

Claims 54 and 70-78 are drawn to a horseshoe crab Factor C having activity of Factor C producible by a method for producing a horseshoe crab Factor C, the method comprising expressing the horseshoe crab Factor C using a mammalian cell as a host cell,

wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*,

wherein the mammalian cell is selected from the group consisting of a Chinese hamster cell and a human cell.

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Claims 57 and 63 are drawn to an endotoxin assay kit comprising an endotoxin assay agent containing the Factor C according to claim 43 or 54, respectively, and one or more elements.

Regarding claims 43 and 54, the reference of Ding teaches a mammalian host cell transformed with a recombinant vector for expressing a horseshoe crab Factor C (column 2, lines 46-55). Ding teaches a method for producing the horseshoe crab Factor C by culturing the host cell and recovering the horseshoe crab Factor C protein (column 2, lines 58-63). Ding teaches the mammalian host cell includes a Chinese Hamster Ovary cell (column 19, lines 39-43). Ding teaches four species of horseshoe crab, including *T. tridentatus* and *C. rotundicauda* (column 1, lines 18-20) and polynucleotides encoding each of the *T. tridentatus* and *C. rotundicauda* Factor C polypeptides (Figure 11). Ding teaches activation of the horseshoe crab Factor C by endotoxin (column 2, lines 7-9).

Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells has (α -2,3) linked terminal sialic acid in a greater amount as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell. However, the specification teaches that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells has (α -2,3) linked terminal sialic acid (paragraph 154), while a native horseshoe crab Factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid (paragraph 154). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells has (α -2,3)-linked terminal sialic acid and a native horseshoe

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crab Factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily has a greater amount of (α -2,3)-linked terminal sialic acid than horseshoe crab Factor C polypeptide expressed in Sf9 as a host cell.

Regarding claims 47 and 70, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 10% sodium citrate with a dilution factor of 8, which, according to the specification is about 21 mM sodium citrate (p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate.

Regarding claims 48, 65, 75, and 76, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells has a molecular weight as recited in the claims. However, the specification teaches that *T. tridentatus* factor C polypeptide recombinantly expressed and recovered

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from CHO cells has a molecular weight of 128 kDa by SDS-PAGE under non-reducing conditions (paragraph 144 and Table 1). As such, since Ding's activated *T. tridentatus* factor C polypeptide is recombinantly expressed and recovered from CHO cells, it follows that Ding's activated factor C polypeptide necessarily has a molecular weight of 128 kDa by SDS-PAGE under non-reducing conditions.

Regarding claims 49 and 77, Ding does not teach the amino acid sequence of *T. tridentatus* factor C has the amino acid sequence of SEQ ID NO: 2. However, evidentiary reference of Mizumura is cited to show that the amino acid sequence of *T. tridentatus* factor C is identical to SEQ ID NO: 2 herein (see Appendix A at pp. 30 and 31 of the Office action mailed on 9/16/2016).

Regarding claims 50 and 78, Ding teaches the horseshoe crab factor C can be secreted into the culture medium (column 3, lines 47-48) and thus the horseshoe crab factor C is considered to be water-soluble.

Regarding claims 57 and 63, Ding teaches the recombinant horseshoe crab Factor C may be employed in a chromogenic assay, wherein upon activation by endotoxin, the horseshoe crab Factor C converts the substrate to a colored product, thereby detecting and quantifying endotoxin (column 2, lines 7-11), which is considered to be an endotoxin assay kit as encompassed by claims 57 and 63.

Regarding claims 66 and 71, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogencarbonate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide

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recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of about 7% sodium citrate with a dilution factor of 8, which, according to the specification is about 52 mM sodium hydrogencarbonate (specification at p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogencarbonate, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogenate.

Regarding claims 67 and 72, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of about 10% sodium citrate with a dilution factor of 4, which, according to the specification is about 214 mM sodium chloride (specification at p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride.

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Regarding claims 68 and 73, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of about 0.5 M magnesium sulfate with a dilution factor of 16, which, according to the specification is about 16 mM magnesium sulfate (specification at p. 88). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate.

Regarding claims 69 and 74, Ding does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 35% or higher in the presence of 2.5 mM calcium chloride. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 35% or higher in the presence of 0.5 M calcium chloride with a dilution factor of 100, which, according to the specification is about 2.5 mM calcium chloride (specification at p. 88). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a

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residual activity of 35% or higher in the presence of 2.5 mM calcium chloride, it follows that Ding's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 35% or higher in the presence of 2.5 mM calcium chloride.

21. RESPONSE TO REMARKS: Beginning at p. 16 of the remarks, applicant argues that Ding does not teach or suggest a Factor C having Factor C activity as claimed. According to applicant, Ding "does not practically prepare a recombinant cell having ability for expressing Factor C having activity of Factor C" and "does not show any scientific evidence for presuming that Factor C in Ding has activity of Factor C", rather than just endotoxin binding activity. As evidence, applicant points to Example 12 of Ding, which evaluated endotoxin binding but according to applicant, did not evaluate Factor C activity.

Applicant's argument is not found persuasive. Ding discloses polynucleotides encoding each of the *T. tridentatus* and *C. rotundicauda* Factor C polypeptides (Figure 11), experimental methods for making a recombinant cell that expresses and produces a horseshoe crab Factor C polypeptide (e.g., column 9, line 55 to column 21, line 35), a method for purifying the Factor C proenzyme (abstract; column 21, line 36 to column 24, line 16), and a method for activating Factor C by LPS endotoxin to activated Factor C that converts a fluorometric substrate (column 25, lines 25-27). Ding discloses that the recombinant horseshoe crab Factor C has "the same *enzymatic activity* as Factor C protein in assays for Gram negative bacterial endotoxin" (emphasis added; column 2,

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lines 16-18) and notes that in the assay, when the Factor C is activated by endotoxin, it converts the substrate to a colored product (column 2, lines 7-11). At the time of the invention, the activation of Factor C to an enzymatically active form by endotoxin was well known in the prior art. For example, the reference of Iwanaga, S. (*Curr. Opin. Immun.* 5:74-82, 1993; cited on the IDS filed on 6/9/2015) teaches "In the presence of LPS, an LPS-sensitive serine protease zymogen, factor C, is autocatalytically activated. The active factor C then activates zymogen factor B" (p. 74, column 1). As such, given Ding's teachings that Factor C is activated to a substrate-cleaving form by endotoxin and that the recombinant horseshoe crab Factor C has the same *enzymatic activity* as Factor C protein in assays for Gram negative bacterial endotoxin, one would recognize that the activated recombinant horseshoe crab Factor C of Ding has "activity of Factor C" as defined in the specification, *i.e.*, Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B (specification at p. 36, paragraph 28) or as defined by applicant, *i.e.*, "protease activity" of Factor C (applicant's remarks at p. 14, footnote).

It should be noted that Ding's horseshoe crab Factor C and the horseshoe crab Factor C of the claims are made by identical or substantially identical processes and according to MPEP 2112.01.I, "[w]here the claimed and prior art products are...produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established". Moreover, it is known in the prior art that CHO cells are only able to add sialic acid using the α -2,3 linkage (see, *e.g.*, paragraph 8 of Cottingham et al., US 2014/0249082, which has priority to 2010, cited on

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the IDS filed on 10/26/2016). Since the Office does not have the facilities for examining and comparing applicant's recombinant Factor C with the Factor C of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Although applicant cites to Example 12 of Ding as allegedly disclosing only the evaluation of endotoxin (LPS) binding and not Factor C activity, Ding discloses that when Factor C was complexed to LPS strips and incubated with its fluorometric substrate, the Factor C activity remained detectable (column 25, lines 25-27). Thus, in view of Ding's teaching that Factor C is activated by endotoxin to have the activity of converting a substrate to a colored product (column 2, lines 7-11), one would recognize that the horseshoe crab Factor C of Ding's Example 12 has "activity of Factor C" as defined in the specification, i.e., Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B (specification at p. 36, paragraph 28) or as defined by applicant, i.e., "protease activity" of Factor C (applicant's remarks at p. 14, footnote).

In this case, it appears that applicant has discovered a new property of a prior art composition, e.g., a *T. tridentatus* recombinantly expressed by a CHO cell has increased (α -2,3)-linked terminal sialic acid as compared with native *T. tridentatus* Factor C and a horseshoe crab Factor C expressed using Sf9 as a host cell. However,

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the discovery of a previously unappreciated property of a prior art composition does not render the old composition patentably new to the discoverer (MPEP 2112.I).

22. The rejection of claims 43, 47-50, 54, 57, and 63 under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Ding et al. (US 5,858,706; cited on the IDS filed on 6/9/2015; hereafter "Ding2") as evidenced by Mizumura (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection has been modified to address applicant's amendment to the claims.

Claims 43, 47-50, 54, 57, 63, and 65-78 are rejected under pre-AIA 35 U.S.C. 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Ding2 (*supra*) as evidenced by Mizumura (*supra*). See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103. See MPEP 2131.01 regarding a multiple reference 35 U.S.C. 102 rejection.

Claims 43, 47-50, and 65-69 are drawn to a horseshoe crab Factor C having activity of Factor C, which contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell, wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*.

Claims 54 and 70-78 are drawn to a horseshoe crab Factor C having activity of Factor C producible by a method for producing a horseshoe crab Factor C, the method

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comprising expressing the horseshoe crab Factor C using a mammalian cell as a host cell,

wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*,

wherein the mammalian cell is selected from the group consisting of a Chinese hamster cell and a human cell.

Claims 57 and 63 are drawn to an endotoxin assay kit comprising an endotoxin assay agent containing the Factor C according to claim 43 or 54, respectively, and one or more elements.

Regarding claims 43 and 54, the reference of Ding2 teaches a mammalian host cell, including a CHO cell, transformed with a recombinant vector for expressing a cDNA encoding a Factor C (column 9, Example 1). Ding2 teaches cDNAs for expressing any horseshoe crab Factor C polypeptide, including the representative examples of *T. tridentatus* and *C. rotundicauda* Factor C polypeptides (column 3, lines 14-20). Ding2 teaches a method for producing the Factor C by culturing the host cell and recovering the Factor C protein (column 9, Example 1). Ding2 teaches mammalian host cells include Chinese Hamster Ovary cells (column 9, Example 1). Ding2 teaches activation of the Factor C by endotoxin (column 1, lines 44-47).

Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells has (α -2,3) linked terminal sialic acid in a greater amount as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell. However, the specification teaches that horseshoe crab Factor C

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polypeptide recombinantly expressed and recovered from CHO cells has (α -2,3) linked terminal sialic acid (paragraph 154), while a native horseshoe crab Factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid (paragraph 154). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells has (α -2,3)-linked terminal sialic acid and a native horseshoe crab Factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily has a greater amount of (α -2,3)-linked terminal sialic acid than horseshoe crab Factor C polypeptide expressed in Sf9 as a host cell.

Regarding claims 47 and 70, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 10% sodium citrate with a dilution factor of 8, which, according to the specification is about 21 mM sodium citrate (p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from

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CHO cells necessarily exhibits a residual activity of 10% or higher in the presence of 21 mM sodium citrate.

Regarding claims 48, 65, 75, and 76, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells has a molecular weight as recited in the claims. However, the specification teaches that *T. tridentatus* factor C polypeptide recombinantly expressed and recovered from CHO cells has a molecular weight of 128 kDa by SDS-PAGE under non-reducing conditions (paragraph 144 and Table 1). As such, since Ding2's activated *T. tridentatus* factor C polypeptide is recombinantly expressed and recovered from CHO cells, it follows that Ding's activated factor C polypeptide necessarily has a molecular weight of 128 kDa by SDS-PAGE under non-reducing conditions.

Regarding claims 49 and 77, Ding2 does not teach the amino acid sequence of *T. tridentatus* factor C has the amino acid sequence of SEQ ID NO: 2. However, evidentiary reference of Mizumura is cited to show that the amino acid sequence of *T. tridentatus* factor C is identical to SEQ ID NO: 2 herein (see Appendix A at pp. 30 and 31 of the Office action mailed on 9/16/2016).

Regarding claims 50 and 78, Ding2 teaches solubilization of the factor C (column 7, lines 456-53) and thus the factor C is considered to be water-soluble.

Regarding claims 57 and 63, Ding2 teaches the recombinant Factor C for use in an assay for endotoxin detection and teaches elements for conducting such an assay (column 8, lines 50-60), which is considered to be an endotoxin assay kit as encompassed by claims 57 and 63 respectively.

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Regarding claims 66 and 71, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogencarbonate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of about 7% sodium citrate with a dilution factor of 8, which, according to the specification is about 52 mM sodium hydrogencarbonate (specification at p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogencarbonate, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 25% or higher in the presence of 52 mM sodium hydrogenate.

Regarding claims 67 and 72, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of about 10% sodium citrate with a dilution factor of 4, which, according to the specification is about 214 mM sodium chloride (specification at p. 87). As such, since horseshoe crab Factor C recombinantly expressed and recovered

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from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 25% or higher in the presence of 214 mM sodium chloride.

Regarding claims 68 and 73, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate. However, Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of about 0.5 M magnesium sulfate with a dilution factor of 16, which, according to the specification is about 16 mM magnesium sulfate (specification at p. 88). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 15% or higher in the presence of 16 mM magnesium sulfate.

Regarding claims 69 and 74, Ding2 does not teach the activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 35% or higher in the presence of 2.5 mM calcium chloride. However,

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Figure 7 of this application shows that horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells exhibits a residual activity of 35% or higher in the presence of 0.5 M calcium chloride with a dilution factor of 100, which, according to the specification is about 2.5 mM calcium chloride (specification at p. 88). As such, since horseshoe crab Factor C recombinantly expressed and recovered from CHO cells recombinantly expressed and recovered from CHO cells exhibits a residual activity of 35% or higher in the presence of 2.5 mM calcium chloride, it follows that Ding2's activated horseshoe crab Factor C polypeptide recombinantly expressed and recovered from CHO cells necessarily exhibits a residual activity of 35% or higher in the presence of 2.5 mM calcium chloride.

23. RESPONSE TO REMARKS: Beginning at p. 17 of the remarks, applicant argues that Ding2 teaches a recombinant Factor C having endotoxin binding activity and does not teach or suggest a Factor C "having activity of Factor C" as claimed. Applicant argues that although Ding2 discloses cloning a cDNA encoding a horseshoe Factor C into a mammalian expression vector, the production of a recombinant Factor C was conducted using a yeast cell, and not a mammalian cell. Applicant argues that the subject of Ding2 is to offer a recombinant Factor C having endotoxin-binding activity, but not "having activity of Factor C" and Ding2 does not disclose uses other than endotoxin binding for the recombinant Factor C. Applicant argues that since activated Factor C cannot be used for endotoxin detection based on protease activity, one of skill in the art

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would recognize that Ding2's recombinant Factor C has endotoxin binding activity, but not activity of Factor C.

Applicant's argument is not found persuasive. As noted above, the reference of Ding2 discloses cDNAs for expressing any horseshoe crab Factor C polypeptide, including the representative examples of *T. tridentatus* and *C. rotundicauda* Factor C polypeptides (column 3, lines 14-20); teaches a mammalian host cell, including a CHO cell, transformed with a recombinant vector for expressing the cDNA encoding a Factor C (column 9, Example 1); and teaches a method for producing the Factor C by culturing the host cell and recovering the Factor C protein (column 9, Example 1). Thus, contrary to applicant's position, the disclosure of Ding2 is not limited to producing a recombinant Factor C by a yeast cell.

The reference of Ding2 further discloses that upon binding to endotoxin, the serine protease activity of Factor C becomes activated (column 1, lines 44-47) and teaches assessing its endotoxin-triggered enzymatic activity by a method of removing detergent from a solubilized Factor C and assaying the endotoxin-activated serine protease activity of the recombinant Factor C by fluorometric or calorimetric methods (column 8, line 64 to column 9, line 11). As such, contrary to applicant's position, one of skill in the art would recognize the recombinant Factor C of Ding2 as having activity of Factor C.

Applicant further argues that in a subsequent publication of Ding (US Patent 6,645,724) discloses that the endotoxin LPS could not activate the enzymatic activity of yeast recombinant Factor C. According to applicant, this is an admission by Ding

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himself that yeast recombinant Factor C does not have activity of Factor C, and cannot be used for endotoxin detection based on enzymatic activity.

Applicant's argument is not found persuasive. The rejection is not directed to the recombinant Factor C produced by a yeast cell. Rather, the rejection is directed to Ding2's teachings of producing a recombinant Factor C using a CHO cell and subsequently activating the recombinant Factor C, which, as noted above, activated Factor C is disclosed by Ding2 as having serine protease activity.

It should be noted that Ding2's CHO cell-expressed horseshoe crab Factor C and the horseshoe crab Factor C of the claims are made by identical or substantially identical processes and according to MPEP 2112.01.I, "[w]here the claimed and prior art products are...produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established". Moreover, it is known in the prior art that CHO cells are only able to add sialic acid using the α -2,3 linkage (see, *e.g.*, paragraph 8 of Cottingham et al., US 2014/0249082, which has priority to 2010, cited on the IDS filed on 10/26/2016). Since the Office does not have the facilities for examining and comparing applicant's recombinant Factor C with the Factor C of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the CHO cell-expressed horseshoe crab Factor C of the prior art does not possess the same material structural and functional characteristics of the claimed Factor C). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

In this case, it appears that applicant has discovered a new property of a prior art composition, *e.g.*, a *T. tridentatus* recombinantly expressed by a CHO cell has increased (α -2,3)-linked terminal sialic acid as compared with native *T. tridentatus* Factor C and a horseshoe crab Factor C expressed using Sf9 as a host cell. However, the discovery of a previously unappreciated property of a prior art composition does not render the old composition patentably new to the discoverer (MPEP 2112.I).

Claim Rejections - 35 USC § 101

24. The rejection of claims 43, 48-50, and 57 under 35 U.S.C. 101 because the claimed invention is directed to a judicial exception (i.e., a law of nature, a natural phenomenon, or an abstract idea) without significantly more is maintained for the reasons of record and the reasons set forth below. The rejection has been modified to address applicant's amendment to the claims.

Claims 43, 48-50, 57, and 65 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a judicial exception (i.e., a law of nature, a natural phenomenon, or an abstract idea) without significantly more.

Claims 43, 48-50, and 65 are drawn to a horseshoe crab Factor C having activity of Factor C, which contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C and/or a horseshoe crab Factor C expressed using Sf9 as a host cell, wherein the horseshoe crab is selected from the group consisting of *Tachypleus tridentatus*, *Limulus polyphemus*, *Carcinoscorpius rotundicauda*, and *Tachypleus gigas*. Given a broadest reasonable interpretation, the

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horseshoe crab Factor C of claims 43 and 48-50 encompasses a naturally occurring horseshoe crab Factor C, *e.g.*, activated factor C polypeptide present in the hemocytes of *T. tridentatus*. According to the specification, a native Factor C polypeptide derived from *T. tridentatus*, which has a molecular weight of 123 kDa, reacts with a (α -2,3)-linked terminal sialic acid-specific lectin, but Factor C recombinantly produced in Sf9 cells does not react (paragraphs 126 and 153).

Claim 57 is drawn to an endotoxin assay kit comprising an endotoxin assay agent containing the Factor C according to claim 43 and one or more elements. Given a broadest reasonable interpretation, the endotoxin assay kit of claim 57 is considered to encompass naturally occurring horseshoe crab hemocytes, which comprise an activated Factor C.

Thus, the claims are considered to encompass naturally occurring products. Because there is no difference in characteristics (structural, functional, or otherwise) between the claimed and naturally occurring products, the claimed products do not have markedly different characteristics from what exists in nature, and thus are a “product of nature” exception. Accordingly, the claims are directed to judicial exceptions. Because the claims do not include any additional features that could add significantly more to the exception, the claims do not qualify as eligible subject matter.

25. RESPONSE TO REMARKS: Beginning at p. 20 of the remarks, applicant argues the claims do not encompass a naturally occurring product because the amended claim

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43 recites that the Factor C contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a native horseshoe crab Factor C.

Applicant's argument is not found persuasive because claim 43 recites the alternative of containing (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell.

According to the specification, Factor C polypeptide derived from *T. tridentatus*, which has a molecular weight of 123 kDa, has (α -2,3)-linked terminal sialic acid (paragraph 153), while *T. tridentatus* factor C polypeptide expressed in Sf9 as a host cell does not have any (α -2,3) linked terminal sialic acid (paragraphs 126 and 154). Thus, Factor C polypeptide derived from *T. tridentatus*, which is a natural product, contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell. As such, contrary to applicant's position, the claims encompass naturally occurring products.

Conclusion

26. Status of the claims:

Claims 43, 47-54, 57-61, and 63-78 are pending.

Claims 51-53, 58-61, and 64 are withdrawn from consideration.

Claims 43, 47-50, 54, 57, 63, and 65-78 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656