

(10) International Publication Number
WO 2012/118800 A3(43) International Publication Date
7 September 2012 (07.09.2012)

(51) International Patent Classification:

C12Q 1/04 (2006.01) *G01N* 33/68 (2006.01)
C12Q 1/37 (2006.01)

(21) International Application Number:

PCT/US2012/026935

(22) International Filing Date:

28 February 2012 (28.02.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/447,581 28 February 2011 (28.02.2011) US

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(81) Designated States (unless otherwise indicated, for every
 kind of national protection available): AE, AG, AL, AM,
 AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
 CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
 KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
 MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
 OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD,
 SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR,
 TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
 kind of regional protection available): ARIPO (BW, GH,
 GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
 UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
 DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
 LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
 SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

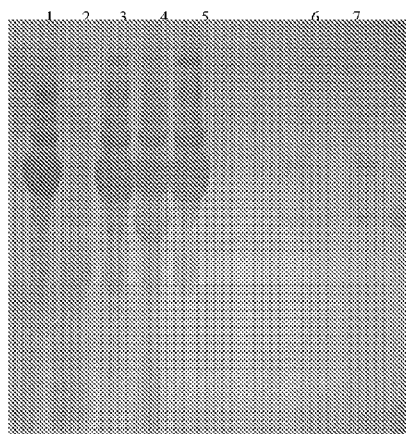
- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

[Continued on next page]

(54) Title: ENHANCING ENDOTOXIN DETECTION

FIGURE 1. Plasma Protein Digestion with EndoPrep™ Treatment.

1. 1:10 Dilution, pH 4.5
2. 1:10 Dilution, pH 1.0
3. 1:10 Dilution, pH 6.0
4. 1:10 Dilution, pH 4.5 (high conc.)
5. 1:10 Dilution, No Treatment
6. 1:100 Dilution, pH 4.5
7. 1:100 Dilution, pH 1.0
8. 1:100 Dilution, pH 6.0
9. 1:100 Dilution, pH 4.5 (high conc.)
10. 1:100 Dilution, No Treatment



(57) Abstract: Provided herein are methods for detecting endotoxin or Gram negative bacteria in a sample. Kits for detecting endotoxin or Gram negative bacteria in a sample are provided.



(88) Date of publication of the international search report:
6 December 2012

A. CLASSIFICATION OF SUBJECT MATTER*C12Q 1/04(2006.01)i, C12Q 1/37(2006.01)i, G01N 33/68(2006.01)i*

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)

C12Q 1/04; C12Q 1/00; C12R 1/01; G01N; C12Q 1/37; G01N 33/16

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: NCBI PubMed, eKOMPASS(KIPO internal) & Keywords: endotoxin detection, acidic protease, pepsin, heating, acidifying, acid, base

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	WO 2010-021872 A2 (BIODTECH, INC.) 25 February 2010 See the whole document, especially Abstract; Claims 1,2,31,33,55,56.	14,15 1-3,5
Y A	US 4495294 A (NAKAHARA, C. et al.) 22 January 1985 See the whole document, especially Abstract; Claims 4-10.	14,15 1-3,5
A	WO 2003-002976 A2 (BIOWHITTAKER, INC.) 09 January 2003 See the whole document, especially Abstract; Claims 21-23.	1-3,5,14,15
A	ZHU, H. et al. 'Bacterial killing in gastric juice-effect of pH and pepsin on Escherichia coli and Helicobacter pylori' Journal of Medical Microbiology, September 2006, Vol. 55, pp. 1265-1270 See the whole document, especially Abstract; Page 1266.	1-3,5,14,15
A	SHAHRIAR, F. et al. 'Identification of lipopolysaccharide-binding proteins in porcine milk' The Canadian Journal of Veterinary Research, October 2006, Vol. 70, pp. 243-250 See the whole document, especially Abstract; Page 245.	1-3,5,14,15



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 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

24 SEPTEMBER 2012 (24.09.2012)

Date of mailing of the international search report

24 SEPTEMBER 2012 (24.09.2012)

Name and mailing address of the ISA/KR

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City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

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INTERNATIONAL SEARCH REPORTInternational application No.
PCT/US2012/026935**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.: 9, 11, 12
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:

The subject matter of claims 9, 11 and 12 is so unclear and indefinite that no meaningful search could be made because these claims are drafted in reference to multiple dependent claims such as claims 8 and 10.
3. ☒ Claims Nos.: 4,6-8,10,13
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:

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 an additional fee, this Authority did not invite payment of any additional fee.
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.:

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

Information on patent family members

International application No.

PCT/US2012/026935

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