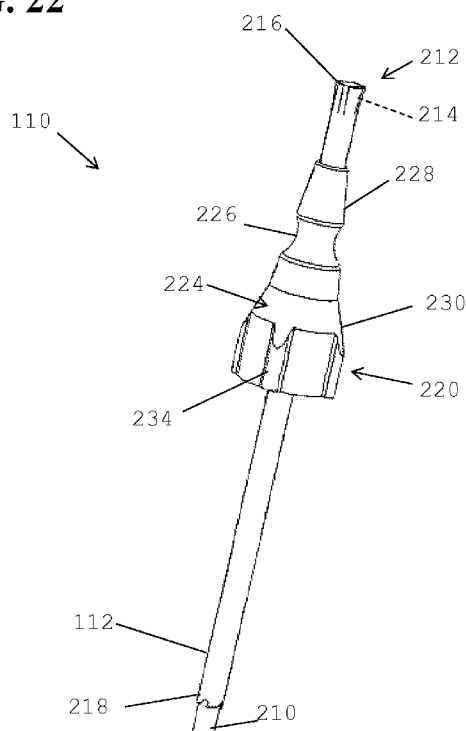




- (51) **International Patent Classification:**
G01N 1/08 (2006.01) *G01N 1/42* (2006.01)
- (21) **International Application Number:** PCT/US2013/051902
- (22) **International Filing Date:** 24 July 2013 (24.07.2013)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/675,016 24 July 2012 (24.07.2012) US
61/784,753 14 March 2013 (14.03.2013) US
- (71) **Applicant:** CRYOEXTRACT INSTRUMENTS, LLC [US/US]; 33 Arch Street, Boston, MA 02110 (US).
- (72) **Inventors:** CHIN, Larry; c/o Cryoextract Instruments, LLC, 33 Arch Street, Boston, MA 02110 (US). BASQUE, Todd; c/o Cryoextract Instruments, LLC, 33 Arch Street, Boston, MA 02110 (US). BETTENCOURT, III, Albert, J.; c/o Cryoextract Instruments, LLC, 33 Arch Street, Boston, MA 02110 (US).
- (74) **Agents:** WALTERS, N., Christopher et al.; Senniger Powers LLP, 100 North Broadway, 17th Floor, St. Louis, MO 63102 (US).
- (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, BN, 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, 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, PA, 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, RU, TJ,

[Continued on next page]

(54) **Title:** APPARATUS AND METHODS FOR ALIQUOTTING FROZEN SAMPLES**FIG. 22**

(57) **Abstract:** A single-use coring probe for collecting a frozen aliquot from a frozen biological sample includes a hollow coring bit and an ejector adapted. The ejector is operable to eject a frozen sample core from the bit as it moves from a retracted position to an extended position. Use of the ejector converts the probe to a disabled configuration to discourage reuse of the coring probe to obtain another sample. The probe may include a locking mechanism adapted to prevent re-use of the single-use coring probe by locking the ejector in the extended position. A hand-held coring device can be used to take frozen sample cores from frozen samples. A tissue container is suitable for holding a frozen tissue sample in frozen storage and also for holding the sample while the sample is sectioned and/or a full-depth frozen sample core is extracted from the frozen tissue.



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, KM, ML, MR, NE, SN, TD, TG).

— *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))*

(88) Date of publication of the international search report:

26 June 2014

Published:

— *with international search report (Art. 21(3))*

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2013/051902

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N1/08 G01N1/42
ADD.

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)

G01N

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/095366 A2 (UNIV JOHNS HOPKINS [US]; BOEKE JEF D [US]; LI MIN [US]; ZHU HENG [US];) 23 August 2007 (2007-08-23) page 9, line 16 - line 21 page 10, line 1 - line 4 page 11, line 6 - line 9 -----	7,9,11
X	DE 200 21 405 U1 (CLINICO VERWALTUNGS GMBH & CO [DE]) 15 February 2001 (2001-02-15) the whole document -----	1-11, 13-50
X	US 2008/227662 A1 (STROMBERG STEVEN ROBERT [US] ET AL) 18 September 2008 (2008-09-18) -----	7,9,11
A	paragraphs [0050], [0069]; figure 3a -----	1
A	US 2005/282246 A1 (POSTOYALKO ANDREW [GB] ET AL) 22 December 2005 (2005-12-22) the whole document -----	1-11, 13-50
	-/--	



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

12 November 2013

Date of mailing of the international search report

25/04/2014

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Hocquet, Alain

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2013/051902

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 999 340 A2 (SOILCORE INC [US]) 10 May 2000 (2000-05-10) paragraph [0032] -----	1-11, 13-50
A	EP 2 249 140 A1 (HOFFMANN LA ROCHE [CH]; ROCHE DIAGNOSTICS GMBH [DE]) 10 November 2010 (2010-11-10) column 11, line 16 - line 28; figure 4 -----	1-11, 13-50
A	WO 2007/084483 A2 (HARVARD COLLEGE [US]; GOULAS NICHOLAS; LARSON DALE [US]; EHRET TREVOR;) 26 July 2007 (2007-07-26) the whole document -----	1-11, 13-50

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/051902

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.: 61
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:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
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 additional sheet

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 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.:

SEE ANNEX

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11, 43-50(completely); 13-42(partially)

single-use coring probe for frozen sample comprising an ejector with a locking mechanism preventing re-use; methods using such a probe

2. claims: 12(completely); 13-42(partially)

single-use coring probe for frozen sample with a coupling mechanism between a coring bit and a coring device

3. claims: 32-42(partially)

single coring probe for frozen sample configured to discourage reuse of the coring probe and comprising a core retaining system

4. claims: 51-60, 62-67(completely); 41, 42(partially)

system with coring probe for frozen sample being hand held and with a motor transmitting rotational movement to the coring probe

5. claims: 68-79

tissue sample container with a coupling to a slide sectioning device

6. claims: 80-94

kit comprising a container and a sacrificial material

7. claims: 95-150

system with a container and a tissue carriage; tissue carriage; methods using a tissue carriage

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 61

claim 61 is defined only by reference to the applicatio: 'a tray as shown and described above'

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2013/051902

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007095366 A2	23-08-2007	US 2010294046 A1 WO 2007095366 A2	25-11-2010 23-08-2007
DE 20021405 U1	15-02-2001	NONE	
US 2008227662 A1	18-09-2008	NONE	
US 2005282246 A1	22-12-2005	AT 527531 T DK 1756545 T3 EP 1756545 A2 EP 2444788 A2 ES 2371081 T3 PL 1756545 T3 PT 1756545 E US 2005282246 A1 WO 2006009733 A2	15-10-2011 19-12-2011 28-02-2007 25-04-2012 27-12-2011 29-02-2012 24-10-2011 22-12-2005 26-01-2006
EP 0999340 A2	10-05-2000	EP 0999340 A2 US 6125948 A	10-05-2000 03-10-2000
EP 2249140 A1	10-11-2010	EP 2249140 A1 US 2011111503 A1	10-11-2010 12-05-2011
WO 2007084483 A2	26-07-2007	CA 2636792 A1 EP 1971810 A2 JP 2009524021 A JP 2013224968 A JP 2013242332 A US 2009019877 A1 US 2013333399 A1 WO 2007084483 A2	26-07-2007 24-09-2008 25-06-2009 31-10-2013 05-12-2013 22-01-2009 19-12-2013 26-07-2007