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BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM,
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MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG,
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RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY,
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[Continued on next page]

(54) Title: SYSTEMS AND METHODS FOR AUTOMATED, CUSTOMIZABLE SAMPLE PREPARATION TOOL, SOFT-
WARE SCRIPT, AND CALIBRATION ROUTINE FOR DETECTION OF METABOLITES AND LIPIDS

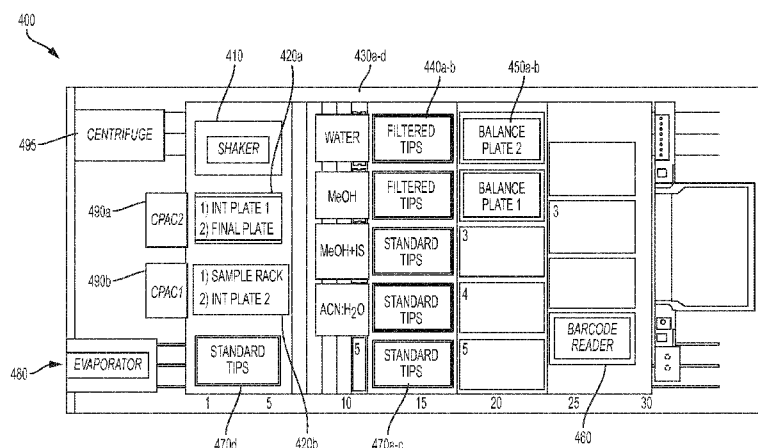


FIG. 4

(57) Abstract: Described herein are automated and customizable sample preparation and analysis systems for detection and quanti-
fication of biomarkers (e.g., metabolites and/or lipids) in biological samples (e.g., blood, serum, or plasma) in a clinical setting. The
automated systems are controlled by scripts that integrate communication between the components of the sample preparation system.
Also described herein are mass spectrometry-based analytical methods featuring efficient system calibration and sample analysis that
provide for accurate quantification of a set of markers in biological samples. The methods are capable of automatic high sample
throughput in a clinical setting for detection and quantification using a mass spectrometry system and high performance liquid chro-
matography column.



GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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, 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))*

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER INV. G01N35/02 G01N35/00 G01N35/04 G01N35/10 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.
Y	US 2015/301002 A1 (DEWITTE ROBERT [CA] ET AL) 22 October 2015 (2015-10-22) paragraphs [0097], [0103], [0108], [0111], [0122], [0126], [0131], [0180], [0207], [0210]; figures 1A, 3A, 3C, 12 -----	1-12
Y A	US 2014/234949 A1 (WASSON JAMES [US] ET AL) 21 August 2014 (2014-08-21) paragraphs [0007], [0029], [0034], [0261], [0265], [0384], [0427], [0483], [0541], [0588], [0698], [0761], [0762]; figures 7, 46 paragraphs [1057], [1103] - [1105], [1112], [1168], [1329], [1404], [1538], [1566], [1658]; figures 26, 35 paragraphs [1758], [1766], [1794], [1865], [1893], [1895], [1922], [1923] ----- -/-	1-7, 9-46 8
☒ 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 16 June 2017		Date of mailing of the international search report 28/06/2017
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 Eidmann, Gunnar

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	paragraphs [0161], [0173]; figures 13,20 -----	1-7,9-12
Y	US 2009/090856 A1 (GRANT RUSSELL PHILIP [US] ET AL) 9 April 2009 (2009-04-09) paragraph [0203] -----	4
Y	US 2015/238617 A1 (KAPLAN DAVID L [US] ET AL) 27 August 2015 (2015-08-27) paragraphs [0100], [0255], [0266] -----	13-46
A	US 2011/256630 A1 (CLINTON CHARLES M [US]) 20 October 2011 (2011-10-20) paragraphs [0002], [0006], [0037], [0038], [0046], [0057], [0073] - [0076], [0100], [0109], [0121], [0123], [0127], [0136]; figures 1,2 -----	13-46
A	US 2007/003965 A1 (RAMSAY STEVEN L [AT] ET AL) 4 January 2007 (2007-01-04) paragraphs [0003], [0013], [0024], [0058], [0074], [0084], [0085], [0095], [0120], [0128]; figure 1 -----	13-46
A	US 2003/199078 A1 (KLEIBER JORG [DE] ET AL) 23 October 2003 (2003-10-23) paragraphs [0004], [0021], [0039], [0051], [0059] - [0062], [0102], [0109], [0112], [0117], [0123] - [0125]; figures 1-5 -----	13-46

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2016/082934

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
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.:
1-9, 11-46(completely); 10(partially)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-4, 8, 11, 12(completely); 5-7, 9, 10(partially)

air displacement pipette

1.1. claim: 4

transportation of a plate

1.2. claim: 11

C18 reverse phase column method

2. claims: 13-46(completely); 5-7, 9(partially)

thawing a biological sample

3. claims: 47-50(completely); 10(partially)

performing two or more analysis methods

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2016/082934

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International application No

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