

(51) International Patent Classification:  
A61B 5/08 (2006.01)

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(21) International Application Number:  
PCT/IL2009/000730

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(22) International Filing Date:  
27 July 2009 (27.07.2009)

(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, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
12/219,824 29 July 2008 (29.07.2008) US(71) Applicant (for all designated States except US):  
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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (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, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: BREATH TEST DEVICE AND METHOD

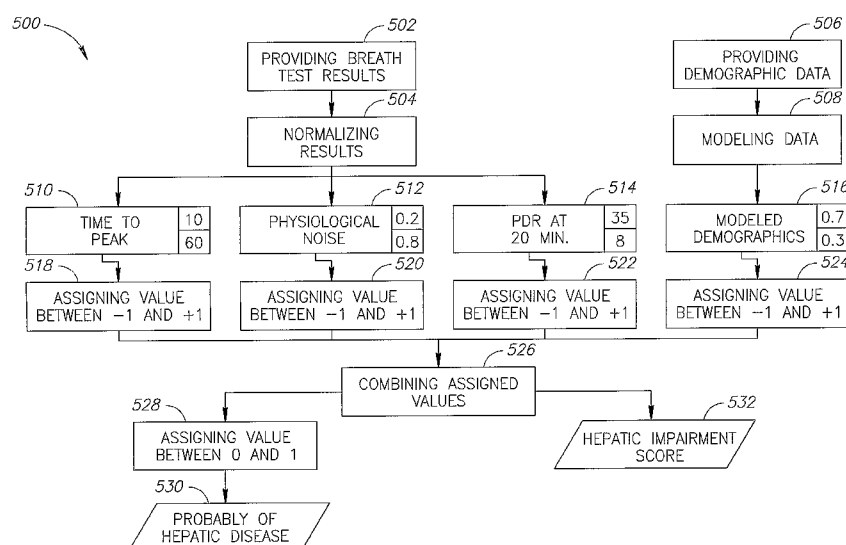


FIG.5

(57) Abstract: There is provided a method of evaluating a liver condition of a subject, the method includes computing a fluctuation parameter from a liver breath test based on at least one of a percentage dose recovery (PDR) curve and a delta over baseline (DOB) curve of an isotope labeled methacetin, or a salt or a derivative thereof, and evaluating at least one liver condition of the subject, based at least on the fluctuation parameter. There is provided herein a method of evaluating a liver condition of a subject, the method includes computing a hepatic impairment score based at least on a breath test related parameter and on a demographic parameter.

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

25 March 2010

- *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))*

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 09/00730

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/08 (2009.01)

USPC - 600/532

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)

IPC(8): A61B 5/08 (2009.01)

USPC: 600/532

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

USPC: 600/532, 600/529

IPC(8): A61B 5/08 (2009.01)

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

Electronic Databases Searched: Google Scholar; USPTO PubWest (US Patents full-text, US PGPubs full-text, EPO Abstracts, JPO Abstracts) Search Terms Used: liver, disease, breath, test, hepatic, impairment, methacetin, significance, based, medical, signif\$, noise, smooth, value, above, below, contrib?, depend\$, averag\$, paramet\$, based, display

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	WO 2007/054940 A2 (BEN-OREN, et al.) 18 May 2007 (18.05.2007), entire document, especially, Fig. 1, abstract, para [0012], [0041], [0042], [0045], [0050], [0062], [0065], [00105], [00107], [00113], [00139]	1, 2, 6-12, 16-22, 27, 34-36, 41, 48  3-5, 13-15, 23-26, 28-33, 37-40, 42-47
Y	US 2003/0216660 B1 (BEN-OREN, et al.) 20 November 2003 (20.11.2003), Figs. 9B, 19B, 23C, 23D, 24, para [0035], [0037], [0039], [0104], [0153], [0164], [0304], [0377]	3-5, 13-15, 23, 28, 29, 37, 42, 43
Y	US 2004/0253637 A1 (BUECHLER, et al.) 16 December 2004 (16.12.2004), para [0102]	24, 38
Y	US 2008/0167533 A1 (LEYENDECKER, et al.) 10 July 2008 (10.07.2008), para [0079]	25, 39
Y	US 2004/0122790 A1 (WALKER, et al.) 24 June 2004 (24.06.2004), para [0068], [0073]	26, 40
Y	US 2007/0135725 A1 (HATLESTAD) 14 June 2007 (14.06.2007), para [0065]	30-33, 44-47

☐

Further documents are listed in the continuation of Box C.

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\* 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

"&amp;"

document member of the same patent family

Date of the actual completion of the international search

14 December 2009 (14.12.2009)

Date of mailing of the international search report

11 JAN 2010

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

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PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 09/00730

## 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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-48 are directed to a method of evaluating a liver condition of a subject, the method comprising computing a fluctuation parameter from a liver breath test based on at least one of a percentage dose recovery (PDR) curve and a delta over baseline (DOB) curve of an isotope labeled methacetin, or a salt or a derivative thereof; and evaluating at least one liver condition of the subject, based at least on the fluctuation parameter.

Group II: Claims 49-95 are directed to a storage stable methacetin composition for use in a breath test, the composition comprising methacetin, or a salt or derivative thereof substantially dissolved in water, wherein the composition is substantially free of anisidine.

-----see continuation 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 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.:  
1-48

### 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/IL 09/00730

Box No. III Continued:

Group III: Claim 96 is directed to a method of assessing insulin resistance in a subject, the method comprising monitoring a metabolic product of octanoic acid, a salt or a derivative of octanoic acid, in a subject's breath after administering to the subject isotope labeled octanoic acid, a salt or a derivative thereof, assessing insulin resistance in a subject based at least on the rate/amount of metabolism of the labeled octanoic acid, a salt or a derivative thereof.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is a method of evaluating a liver condition of a subject, the method comprising computing a fluctuation parameter from a liver breath test based on at least one of a percentage dose recovery (PDR) curve and a delta over baseline (DOB) curve of an isotope labeled methacetin, or a salt or a derivative thereof; and evaluating at least one liver condition of the subject, based at least on the fluctuation parameter, which is not present in Group II that has a special technical feature of a storage stable methacetin composition for use in a breath test, the composition comprising methacetin, or a salt or derivative thereof substantially dissolved in water, wherein the composition is substantially free of anisidine, which is not present in Group III that has a special technical feature of a method of assessing insulin resistance in a subject, the method comprising monitoring a metabolic product of octanoic acid, a salt or a derivative of octanoic acid, in a subject's breath after administering to the subject isotope labeled octanoic acid, a salt or a derivative thereof, assessing insulin resistance in a subject based at least on the rate/amount of metabolism of the labeled octanoic acid, a salt or a derivative thereof.

Groups I and II share the technical feature of methacetin for use in a breath test. However, this shared technical feature fails to make a contribution over the prior art of US 2007/0026480 A1 to Modak, et al. (para[0054]). Accordingly, unity of invention is lacking under PCT Rule 13.1.