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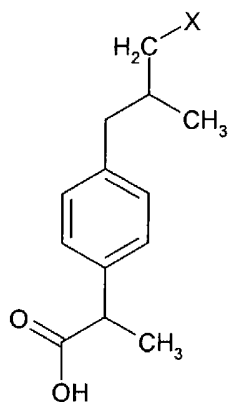
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60/340,855 19 December 2001 (19.12.2001) US
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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[Continued on next page]

(54) Title: ELISA KIT FOR CYP 2C9 METABOLIC PHENOTYPES

(s)-ibuprofen derivatives for CYP2C9
phenotyping by ELISA



Where X=

$(\text{CH}_2)_n\text{COOH}$ $n=1-5$

OR

$(\text{CH}_2)_n\text{NH}_2$ $n=1-5$

OR

$(\text{CH}_2)_n\text{OH}$ $n=2-5$

OR

$(\text{CH}_2)_n\text{NHCOOCH}_2\text{CH}_2\text{COOH}$

$n=1-5$

OR

$(\text{CH}_2)_n\text{OCOCH}_2\text{CH}_2\text{COOH}$ $n=1-5$

OR

$(\text{CH}_2)_n\text{N}=\text{C}=\text{S}$ $N=1-5$

(57) Abstract: The invention relates to an enzyme linked immunosorbent assay (ELISA) method and kit for the rapid determination of metabolic phenotypes for Cytochrome P450 2C9 (CYP 2C9). The kit uses may include but are not limited to, use on a routine basis in a clinical laboratory to determine a Cytochrome P450 2C9 (CYP 2C9) phenotype of an individual; to allow a physician to individualize an individual's treatment with respect to the numerous drugs e.g. ibuprofen, losartan, E-3174 and 2-carboxyibuprofen metabolized by CYP 2C9 based on a phenotypic determination; to predict an individual's susceptibility to carcinogen induced diseases including many cancers, and to screen individuals for a preferred metabolic phenotype in order to determine those individuals with a responsive phenotype for participation in clinical testing.



TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the international search report:
10 March 2005

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

 NR. 4234 — S. 4/5
 International Application no.
 PCT/CA 02/01965

 A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 G01N33/94 C12Q1/26

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 7 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 practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 02/090994 A (UNIV MCGILL ;LEYLAND-JONES BRIAN (US)) 14 November 2002 (2002-11-14) page 67, line 5; claims 1,32	1-14
P, X	WO 02/071060 A (UNIV MCGILL ;LEYLAND-JONES BRIAN (US)) 12 September 2002 (2002-09-12) page 98, line 14 - page 99, line 5	1-14
Y	WO 00/55624 A (LEYLAND JONES BRIAN ;WONG PIERRE (CA)) 21 September 2000 (2000-09-21) page 2, lines 12-17 - page 18, lines 25-29; figure 7 ----- -/-	1-41

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in 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 document 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.

Z document member of the same patent family

Date of the actual completion of the international search

29 September 2003

Date of making of the international search report

25 - 05 - 04

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 02/01965

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GRAEFE K A ET AL: "Development and validation of an indirect enzyme-linked immunosorbent assay (ELISA) for the nonsteroidal anti-inflammatory drug S-ibuprofen." PHARMAZIE, vol. 55, no. 4, April 2000 (2000-04), pages 286-292, XP001155342 ISSN: 0031-7144	1-41
X	see figure in section 2	34-41
A	BJORNSDOTTIR INGA ET AL: "Separation of the enantiomers of ibuprofen and its major phase I metabolites in urine using capillary electrophoresis." ELECTROPHORESIS, vol. 19, no. 3, March 1998 (1998-03), pages 455-460, XP009018093 ISSN: 0173-0835 the whole document	1-14
A	WO 01/11035 A (RUSHMORE THOMAS H ;MEI QIN (US); SHOU MAGANG (US); MERCK & CO INC) 15 February 2001 (2001-02-15) page 2, line 27 - page 3, line 9	1-41
A	TAN S C ET AL: "Stereospecific analysis of the major metabolites of ibuprofen in urine by sequential achiral-chiral high-performance liquid chromatography" JOURNAL OF CHROMATOGRAPHY B: BIOMEDICAL SCIENCES & APPLICATIONS, ELSEVIER SCIENCE PUBLISHERS, NL, vol. 701, no. 1, 7 November 1997 (1997-11-07), pages 53-63, XP004095020 ISSN: 1570-0232 the whole document	1-14
A	EP 1 138 779 A (PFIZER PROD INC) 4 October 2001 (2001-10-04) abstract	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 02/01965

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 1-14, 42-44
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-14, 42-44 are directed to a diagnostic (phenotyping) method practised upon the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 II Observations where unity of invention is lacking (Continuation of item 2 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 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.:
1-41

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-14, 42-44 are directed to a diagnostic (phenotyping) method practised upon the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 1-14,42-44

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 02/01965

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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