

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
31 July 2008 (31.07.2008)

PCT

(10) International Publication Number  
**WO 2008/091694 A3**

(51) International Patent Classification:  
**BOIJ 19/00** (2006.01)

(21) International Application Number:

PCT/US2008/001001

(22) International Filing Date: 23 January 2008 (23.01.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/897,002 23 January 2007 (23.01.2007) US

(71) Applicant (for all designated States except US):  
**SIEMENS MEDICAL SOLUTIONS USA, INC.**  
[US/US]; 51 Valley Stream Parkway, Malvern, PA  
19355-1406 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **VANDAM, Robert, Michael** [CA/US]; 1630 Calle Vaquero # 408, Glendale, CA 91206 (US). **ELIZAROV, Arkadij, M.** [RU/US]; 1239-b Chandler Boulevard, Valley Village, CA 91607 (US). **BALL, Carroll, Edward** [US/US]; 12296 Ragweed Street, San Diego, CA 92129 (US). **KOLB, Hartmuth, C.** [DE/US]; 6413 Pacific Avenue, Playa Del Rey, CA 90293 (US).

(74) Agents: **DAVIS, Paul** et al.; Siemens Corporation - Intellectual Property, Department, 170 Wood Avenue South, Iselin, NJ 08830 (US).

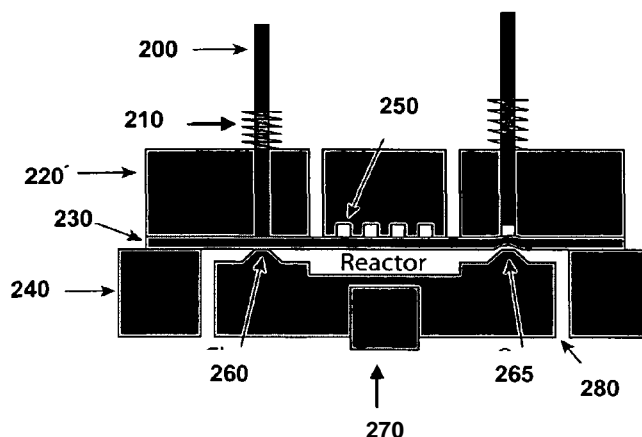
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, 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, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: FULLY-AUTOMATED MICROFLUIDIC SYSTEM FOR THE SYNTHESIS OF RADIOLABELED BIOMARKERS FOR POSITRON EMISSION TOMOGRAPHY

Figure 4. Cross-section of a microfluidic chip illustrating some features in each layer and the architecture of the on-chip diaphragm valves.



(57) Abstract: The present application relates to microfluidic devices and related technologies, and to chemical processes using such devices. More specifically, the application discloses, a fully automated synthesis of radioactive compounds for imaging, such as by positron emission tomography (PET), in a fast, efficient and compact manner. In particular, this application describes an automated, stand-alone, microfluidic instrument for the multi-step chemical synthesis of radiopharmaceuticals, such as probes for PET and method of using such instruments. The systems comprise a microfluidic synthesis chip comprising a reagent source, a controller, a reaction chamber, a membrane, at least one flow channel and at least one valve (260, 265). The systems may additionally comprise radiation shielding and heating or cooling elements (270).

WO 2008/091694 A3



**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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

25 September 2008

# INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/001001

## A. CLASSIFICATION OF SUBJECT MATTER

INV. B01J19/00

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)

BOIJ BOIL

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 , WPI Data, COMPENDEX, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 00/43766 A (CALIPER TECHN CORP [US])  27 July 2000 (2000-07-27)  abstract  page 2, line 25 - page 4, line 13  page 5, line 18 - page 6, line 25  page 9, line 1 - page 10, line 7  page 15,, line 16 - line 30  page 29,, line 19 - page 32, line 17  page 34,, line 15 - page 35, line 8  page 36,, line 5 - page 38, line 15;  claims; figures</p>	<p>1-3, 6-8,  17-30</p>



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 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

<sup>1</sup>T<sup>1</sup> 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.

'S' document member of the same patent family

Date of the actual completion of the international search

10 July 2008

Date of mailing of the international search report

21/07/2008

Name and mailing address of the ISA/

European Patent Office. P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Nazario, Luis

# INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/001001

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document with indication, where appropriate of the relevant passages	Relevant to claim No
X	wo 2006/098817 A (AST MAN INC [WS] ; WEBSTER JAMES RUSSELL; KUO YUAN-FONG; WANG SHAW-TSU;) 21 September 2006 (2006-09-21) abstract page 3, line 19 - page 5, line 19 page 7, line 28 - page 11, line 5 page 11, line 26 - page 14, line 7 claims ; figures -----	1-30
X	wo 03/078358 A (IMAGING RES SOLUTIONS LTD [GB] ; BRADY FRANK [GB] ; LUTHRA SAJINDER KAUR) 25 September 2003 (2003-09-25) abstract page 1, last paragraph - page 2, paragraph 3 page 7, paragraph 2 - page 8, paragraph 2 page 10, paragraph 4 - page 13, paragraph 1 claims; figures; example 1 -----	1-40
X	wo 2006/071470 A (CALIFORNIA INST OF TECHN [US] ; FLUIDIGM CORP [US] ; UNIV CALIFORNIA [US]) 6 July 2006 (2006-07-06) abstract paragraph [0012] - paragraph [0026] paragraph [0066] paragraph [0076] - paragraph [0079] paragraph [0099] - paragraph [0146] paragraph [0156] - paragraph [0162] claims ; figures; examples 1,2,5 -----	1-40
A	wo 2006/116629 A (SIEMENS MEDICAL SOLUTIONS [US] ; KOLB HARTMUTH C [US] ; WALSH JOSEPH C [ ]) 2 November 2006 (2006-11-02) abstract page 5, paragraph 2 - page 14, paragraph 2; claims -----	
P, X, L	wo 2007/041486 A (SIEMENS MEDICAL SOLUTIONS [US] ; ELIZAROV ARKADIJ M [US] ; KOLB HARTMUTH) 12 April 2007 (2007-04-12) abstract page 1, paragraph 1 page 5, paragraph 2 - page 8, paragraph 1 page 11, paragraph 2 - page 16, paragraph 3 page 19, last paragraph - page 23, paragraph 3 page 25, paragraph 1 page 26, paragraph 5; claims ; figures ----- -/--	1-40

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2008/001001

**C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
P,X	<p>WO 2007/092472 A (ELIZAROV ARKADIJ [US]; HEATH JAMES R [US]; KOLB HARTMUTH [US]; VAN DAM) 16 August 2007 (2007-08-16)</p> <p>abstract</p> <p>paragraph [0007] - paragraph [0012]</p> <p>paragraph [0021] - paragraph [0029]</p> <p>paragraph [0037]</p> <p>paragraph [0044] - paragraph [0047]</p> <p>paragraph [0063] - paragraph [0073];</p> <p>claims; figures</p> <p style="text-align: center;">-----</p>	1-40
P <sub>1</sub> X	<p>WO 2007/027928 A (CALIFORNIA INST OF TECHN [US]; ELIZAROV ARKADIJ [US]; HEATH JAMES R [U] 8 March 2007 (2007-03-08)</p> <p>abstract</p> <p>paragraph [0008] - paragraph [0011]</p> <p>paragraph [0019]</p> <p>paragraph [0024]</p> <p>paragraph [0030] - paragraph [0032]</p> <p>paragraph [0053] - paragraph [0061];</p> <p>claims 3-6</p> <p style="text-align: center;">-----</p>	1-40

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/001001

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
wo 0043766	A	27-07-2000	AU	762045 B2	19-06-2003
			AU	2512500 A	07-08-2000
			AU	2003248199 A1	30-10-2003
			CA	2353998 A1	27-07-2000
			EP	1153285 A1	14-11-2001
			US	2002179445 A1	05-12-2002
			US	6416642 B1	09-07-2002
-----					
WO 2006098817	A	21-09-2006	NONE		
-----					
WO 03078358	A	25-09-2003	AU	2003216820 A1	29-09-2003
			EP	1487763 A2	22-12-2004
			JP	2005520827 T	14-07-2005
			US	2005226776 A1	13-10-2005
-----					
WO 2006071470	A	06-07-2006	EP	1838431 A2	03-10-2007
-----					
WO 2006116629	A	02-11-2006	CA	2606094 A1	02-11-2006
			EP	1875240 A2	09-01-2008
			KR	20080000620 A	02-01-2008
-----					
WO 2007041486	A	12-04-2007	CA	2624243 A1	12-04-2007
			EP	1940543 A2	09-07-2008
-----					
WO 2007092472	A	16-08-2007	NONE		
-----					
WO 2007027928	A	08-03-2007	CA	2620629 A1	08-03-2007
			EP	1928603 A1	11-06-2008