

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
17 August 2006 (17.08.2006)

PCT

(10) International Publication Number  
**WO 2006/085908 A3**

(51) International Patent Classification:

A61M 37/00 (2006.01) A61N 1/05 (2006.01)  
A61K 9/00 (2006.01) A61K 49/00 (2006.01)  
A61N 1/30 (2006.01) A61B 5/00 (2006.01)

(21) International Application Number:

PCT/US2005/019021

(22) International Filing Date: 1 June 2005 (01.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/575,946 1 June 2004 (01.06.2004) US  
60/635,780 13 December 2004 (13.12.2004) US  
60/593,832 17 February 2005 (17.02.2005) US  
60/655,785 24 February 2005 (24.02.2005) US

(71) Applicant (for all designated States except US): **MI-CROCHIPS, INC.** [US/US]; 6-B Preston Court, Bedford, Massachusetts 01730 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **HERMAN, Stephen, J.** [US/US]; 50 Sunset Rock Road, Andover, Massachusetts 01810 (US). **KRIEGER, Timothy** [US/US]; 75 Bedford Avenue, Lowell, Massachusetts 01854 (US). **SANTINI, John, T., Jr.** [US/US]; 12 Maynard Circle, North Chelmsford, Massachusetts 01863 (US). **PRESCOTT, James, H.** [US/US]; 85 Trowbridge Street, #3, Cambridge, Massachusetts 02138 (US). **STAPLES, Mark, Andrew** [US/US]; 10 Rogers Street, #906, Cambridge, Massachusetts 02142 (US). **LIPKA, Sara,**

A. [US/US]; 8 Watson Street, Somerville, Massachusetts 02144 (US).

(74) Agents: **KING, Kevin, W.** et al.; SUTHERLAND AS-BILL & BRENNAN LLP, 999 Peachtree Street, NE, Atlanta, Georgia 30309-3996 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, 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, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

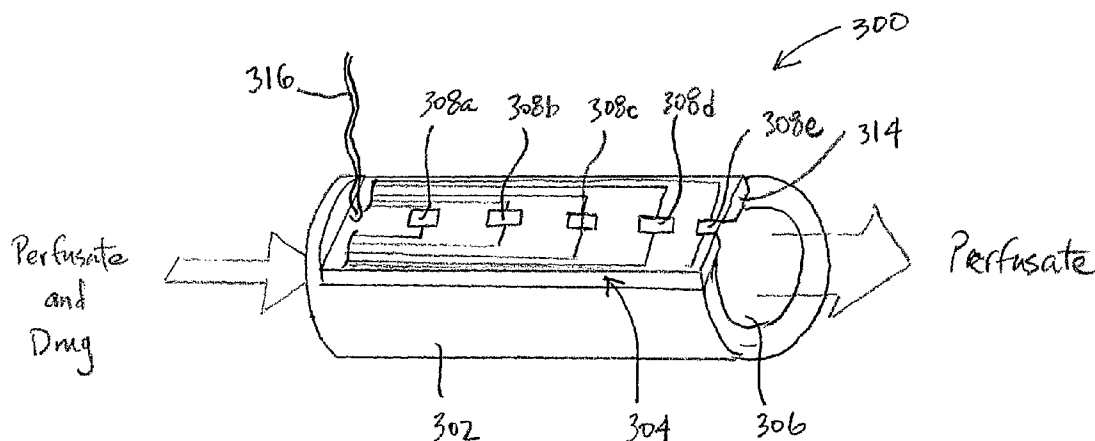
— with international search report

(88) Date of publication of the international search report:  
15 February 2007

(15) Information about Correction:

[Continued on next page]

(54) Title: DEVICES AND METHODS FOR MEASURING AND ENHANCING DRUG OR ANALYTE TRANSPORT TO/FROM MEDICAL IMPLANT



(57) Abstract: Methods and devices are provided for enhancing mass transport through any fibrous tissue capsule that may form around an implanted medical device following implantation. Methods and devices are also provided to enhance vascularization around the implanted device, which also will aid in mass transport to/from the device. The device preferably comprises multiple reservoirs containing (i) a drug formulation for short- or long-term, controlled drug delivery, (ii) sensors for sensing an analyte in the patient, or (iii) a combination thereof.



**Previous Correction:**

see PCT Gazette No. 38/2006 of 21 September 2006

*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

International application No  
PCT/US2005/019021

## A. CLASSIFICATION OF SUBJECT MATTER

INV. A61M37/00 A61K9/00 A61N1/30 A61N1/05 A61K49/00  
A61B5/00

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)

A61K A61M A61N B01L 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, WPI Data, BIOSIS, EMBASE

## 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 93/23012 A (ENDOCON, INC) 25 November 1993 (1993-11-25) page 2, last paragraph - page 3, paragraph 4 page 8, last paragraph - page 9, paragraph 1 page 13, paragraph 3 page 13, paragraph 4 - page 14, paragraph 1; figure 4 page 14, paragraph 2 - page 16, paragraph 3 claims</p> <p style="text-align: center;">----- -/-</p>	<p>1-19, 25, 26, 28-31</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

\*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

3 November 2006

Date of mailing of the international search report

24/11/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5618 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Tiede, Ralph

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/019021

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 2004/026281 A (MICROCHIPS, INC) 1 April 2004 (2004-04-01) cited in the application page 1, line 19 - page 2, line 10 page 5, line 21 - line 33 page 21, line 8 - page 24, line 16 figures 1a,1b,6a,6b claims	1-19,25, 26,28-31
X	WO 94/22423 A (BUKH MEDITEC A/S; BAR-SHALOM, DANIEL) 13 October 1994 (1994-10-13) page 6, line 26 - page 7, line 10 page 18, line 27 - page 19, line 5 claims	1-19,25, 26,28-31
X	WO 00/41740 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; IMEDD) 20 July 2000 (2000-07-20) page 1, line 28 - page 2, line 24 page 3, line 18 - line 24; figure 3 page 13, line 11 - line 26 example G; table 2 claims	1-19,25, 26,28-31
X	WO 2004/022033 A (MICROCHIPS, INC) 18 March 2004 (2004-03-18) page 3, line 26 - line 33 page 4, line 30 - page 5, line 3 page 9, line 26 - page 10, line 25 claims	1-19,25, 26,28-31
A	US 2003/211157 A1 (SIMON DAVID LEW) 13 November 2003 (2003-11-13) paragraph [0020] paragraph [0071] example 16	1-19,25, 26,28-31
P,X	WO 2004/096176 A (MICROCHIPS, INC; PRESCOTT, JAMES, H; UHLAND, SCOTT, A; STAPLES, MARK,) 11 November 2004 (2004-11-11) page 2, line 1 - line 22 page 3, line 13 - line 18 page 13, line 1 - page 15, line 7; table 1 examples claims	1,2,4-9, 25,26,28
	----- -/--	

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2005/019021

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	WO 2005/016558 A (MICROCHIPS, INC; COPPETA, JONATHAN, R; MALONEY, JOHN, M; POLITO, BENJA) 24 February 2005 (2005-02-24) page 1, line 32 - page 2, line 27 page 6, line 10 - page 8, line 32 figure 1 claims	25,26,28
X	----- US 2003/100865 A1 (SANTINI JOHN T [US] ET AL SANTINI JR JOHN T [US] ET AL) 29 May 2003 (2003-05-29) paragraphs [0008], [0009], [0032], [0053]; figures 8,9 paragraphs [0061] - [0064], [0094] - [0097] paragraphs [0065] - [0070] paragraphs [0084] - [0093]	32-34
X	WO 01/64344 A2 (MICROCHIPS INC [US]) 7 September 2001 (2001-09-07)	32,34
Y	page 22, line 30 - page 24, line 30 page 26, lines 16-31	33
Y	----- WISNIEWSKI N, MOUSSY F, REICHERT WM: "Characterization of implantable biosensor membrane biofouling" FRESENIUS J ANAL CHEM, vol. 366, 2000, pages 611-621, XP002404672 page 615	33
A	----- WISNIEWSKI N ET AL: "Characterization of analyte transport over time through implantable biosensor membranes using microdialysis" BMES/EMBS CONFERENCE, 1999. PROCEEDINGS OF THE FIRST JOINT ATLANTA, GA, USA 13-16 OCT. 1999, PISCATAWAY, NJ, USA, IEEE, US, vol. 2, 13 October 1999 (1999-10-13), page 721, XP010357730 ISBN: 0-7803-5674-8 page 721	32-34
P,X	----- WO 2004/071487 A2 (MICROCHIPS INC [US]) 26 August 2004 (2004-08-26) pages 27-30; figures 9,10	32
P,X	----- WO 2005/010240 A2 (MICROCHIPS INC [US]; COPPETA JONATHAN R [US]; UHLAND SCOTT A [US]; POL) 3 February 2005 (2005-02-03) page 27; figures 1-5	32-34

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2005/019021

## Box 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:  
  
Although claims 1-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the 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 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 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.:  
  
1-19, 25, 26, 28-34
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.

☒ 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: 1-19,25 (partially), 26 (part.), 28-31 (part.)

A method of enhancing the transport of drug from an implanted drug delivery device across a tissue capsule, the method comprising:  
controllably releasing a drug formulation from a plurality of discrete reservoirs located in medical device implanted in a patient; and  
controllably releasing an effective amount of a transport enhancer from said medical device implanted in a patient, to facilitate transport of the released drug formulation through a fibrous tissue capsule, if any, which exists around the device at the site of implantation.

---

2. claims: 20-22, 25 (part.), 26 (part.), 28-31 (part.)

A method of enhancing the transport of drug from an implanted drug delivery device and across a tissue capsule, the method comprising:  
controllably releasing a drug formulation, which comprises charged drug molecules, from a plurality of discrete reservoirs of a medical device implanted into a patient, the release of the drug and the release of the enhancing agent being from one or more reservoirs located in the device; and  
utilizing an electromotive method to enhance transport of the charged drug molecules through a tissue capsule, if any, surrounding the implanted medical device.

---

3. claims: 23, 24, 25 (part.), 27, 28-31 (part.)

A method of enhancing the transport of an analyte to a sensor device implanted in a patient, the method comprising:  
controllably releasing an effective amount of a transport enhancer from the implanted sensor device, said device comprising a plurality of discrete reservoirs having sensors located therein.

---

4. claims: 32-34

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An implantable device for testing drug or analyte transport through a tissue capsule, the device comprising:  
a primary body having an outer surface, a perfusate fluid inlet, a perfusate fluid outlet, and a fluid conduit extending between the inlet and the outlet;  
a substrate attached to the primary body;  
at least one reservoir defined in and extending through the substrate, the reservoir having a first opening in the fluid conduit and a second opening which can be open to the outer surface of the device;  
at least one reservoir cap covering the second opening of the reservoir;  
means for selectively disintegrating or removing the reservoir cap.

---



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/019021

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9323012	A	25-11-1993	AU 4378693 A	13-12-1993
WO 2004026281	A	01-04-2004	AU 2003278881 A1	08-04-2004
WO 9422423	A	13-10-1994	AU 6534894 A	24-10-1994
WO 0041740	A	20-07-2000	AU 2494700 A	01-08-2000
			CA 2359474 A1	20-07-2000
			EP 1140024 A2	10-10-2001
			JP 2002534485 T	15-10-2002
WO 2004022033	A	18-03-2004	AU 2003278766 A1	29-03-2004
US 2003211157	A1	13-11-2003	NONE	
WO 2004096176	A	11-11-2004	AU 2004233869 A1	11-11-2004
			CA 2523432 A1	11-11-2004
			EP 1638522 A2	29-03-2006
WO 2005016558	A	24-02-2005	NONE	
US 2003100865	A1	29-05-2003	US 2002173745 A1	21-11-2002
			US 6491666 B1	10-12-2002
WO 0164344	A2	07-09-2001	AU 5289001 A	12-09-2001
			AU 2005204238 A1	15-09-2005
			CA 2399842 A1	07-09-2001
			EP 1261427 A2	04-12-2002
			JP 2003525432 T	26-08-2003
WO 2004071487	A2	26-08-2004	AU 2003303288 A1	06-09-2004
			CA 2495327 A1	26-08-2004
			CN 1681542 A	12-10-2005
			EP 1528940 A2	11-05-2005
			JP 2006515860 T	08-06-2006
WO 2005010240	A2	03-02-2005	NONE	