(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 14 December 2000 (14.12.2000)

PCT

(10) International Publication Number WO~00/74763~A3

(51) International Patent Classification⁷: A61M 37/00, A61B 10/00

(21) International Application Number: PCT/US00/15312

(22) International Filing Date: 2 June 2000 (02.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/137,621 4 June 1999 (04.06.1999) US 60/146,200 29 July 1999 (29.07.1999) US 09/448,107 23 November 1999 (23.11.1999) US 09/452,979 2 December 1999 (02.12.1999) US 09/453,109 2 December 1999 (02.12.1999) US

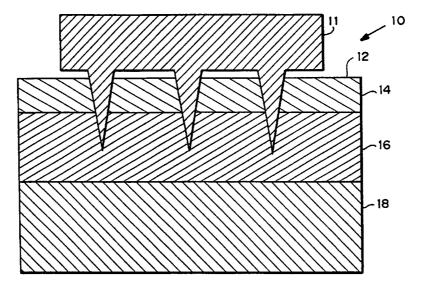
- (71) Applicant: GEORGIA TECH RESEARCH CORPO-RATION [US/US]; 400 Tenth Street, Centennial Research Building, Atlanta, GA 30332-0414 (US).
- (72) Inventors: PRAUSNITZ, Mark, R.; 417 West Howard Avenue, Decatur, GA 30030 (US). ALLEN, Mark, G.;

425 Spalding Drive, Atlanta, GA 30328 (US). HENRY, Sebastien; 1511 Vinings Parkway, Smyrna, GA 30080 (US). MCALLISTER, Devin, V.; 49 Geddes Street, Holley, NY 14470 (US). ACKLEY, Donald, E.; 2033 Cambridge Avenue, Cardiff, CA 92007 (US). GUJRAL, Inder-Jeet; 111-9 Trowbridge Street, Cambridge, MA 02138 (US). JACKSON, Thomas; 7135 Olivetas Avenue, La Jolla, CA 92037 (US).

- (74) Agents: PABST, Patrea, L. et al.; Arnall Golden & Gregory, LLP, 2800 One Atlantic Center, 1201 West Peachtree Street, Atlanta, GA 30309-3450 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, 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, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European

[Continued on next page]

(54) Title: DEVICES AND METHODS FOR ENHANCED MICRONEEDLE PENETRATION OF BIOLOGICAL BARRIERS



(57) Abstract: Microneedle devices are provided for delivery of drugs across biological tissue and for controlled sampling of biological fluids in a minimally-invasive, painless, and convenient manner. The devices permit 1) drug delivery at clinically relevant rates across or into skin or other tissue barriers, and/or 2) in vivo sensing or withdrawal of biological fluids from the body, particularly from or through the skin or other tissue barriers. Drug delivery devices preferably include a plurality of hollow microneedles attached to or integrated into a substrate, and at least one reservoir (containing drug) selectably in communication with the microneedles, wherein the amount of drug to be delivered can be selectively altered. Withdrawal or sensing microneedle devices preferably include microneedles attached to or integrated into a substrate, and at least one collection chamber and/or sensor in communication with the microneedles.



WO 00/74763 A



patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— With international search report.

(88) Date of publication of the international search report: 5 July 2001

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.

nal Application No PCT/US 00/15312

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61M37/00 A61B10/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{array}{ll} \mbox{Minimum documentation searched (classification system followed by classification symbols)} \\ \mbox{IPC 7} & \mbox{A61M} & \mbox{A61B} & \mbox{A61N} \end{array}$

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, PAJ

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	US 3 964 482 A (GERSTEL MARTIN S ET AL) 22 June 1976 (1976-06-22)	1-5, 9-12,22, 23, 29-32,
Α	the whole document	41,50-52 40,55, 60,77, 120
X	EP 0 497 620 A (UNIV CARNEGIE MELLON) 5 August 1992 (1992-08-05)	1-4,13, 23,40,
Α	column 5, line 43 - line 56; figures	41,52 55,60, 77,120
	_/	

χ Further documents are listed in the continuation of box C.	χ Patent family members are listed in annex.
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	Date of mailing of the international search report
22 January 2001	California
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 Kousouretas, I

2

II Anal Application No
PCT/US 00/15312

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 195 25 607 A (BOEHRINGER INGELHEIM KG) 16 January 1997 (1997-01-16) column 3, line 30 -column 5, line 30;	1-7,13, 23,40, 41,55,58 60,62,
	figures 	65,77, 120
X	WO 98 28037 A (ALZA CORP) 2 July 1998 (1998-07-02)	40,120
A	the whole document	1-3,6, 41-66,77
X	WO 98 00193 A (EPPSTEIN JONATHAN A ;SPECTRX INC (US); ALTEA TECHNOLOGIES INC (US)) 8 January 1998 (1998-01-08)	40,77, 78,87, 89,96, 110,118, 119,121
Α	abstract; figures	1,41, 55-66
P,X A	WO 99 64580 A (GEORGIA TECH RES INST) 16 December 1999 (1999-12-16) the whole document	1-36, 40-66 77,120
А	US 5 865 786 A (ROSEN SANFORD ET AL) 2 February 1999 (1999-02-02) column 12, line 53 -column 13, line 10; figures	55-66
X	WO 98 00194 A (SONTRA MEDICAL L P) 8 January 1998 (1998-01-08)	40, 55-66, 77,78, 89,96, 110,121
	page 18, line 11 -page 21, line 24; figures	110,121

International application No. PCT/US 00/15312

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of IIrst sneet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 37–39.67–76 because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT – Method for treatment of the human or animal body by therapy
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. X 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.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. X 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: 1-36,41-54

A device for transport of material across or into a biological barrier comprising a plurality of hollow microneedles, a substrate to which the microneedles are attached, a reservoir in connection with at least one of the microneedles, wherein the volume or amount of material to be transported can selectively be altered.

2. Claim: 40

A kit for delivering a therapeutic fluid comprising a plurality of hollow microneedles, a substrate to which the microneedles are attached a reservoir in communication with the microneedles and a triggering device to activate delivery of the agent from reservoir through the microneedles.

3. Claims: 55-66

A device for sensing an analyte in a biological fluid, comprising a plurality of microneedles, a substrate to which the microneedles are attached and at least a sensor in communication with the microneedles.

4. Claims: 77-121

A device for transport of material across a biological barrier comprising a microneedle, a substrate to which the microneedle is attached and means for improving penetration of the biological barrier by the microneedle.

information on patent family members

I nal Application No
PCT/US 00/15312

		PC1/US 00/15312
Patent document cited in search report	Publication date	Patent family Publication member(s) date
US 3964482	A 22-06-197	76 NONE
EP 0497620	A 05-08-199	US 5312456 A 17-05-1994 AT 169090 T 15-08-1998 DE 69226384 D 03-09-1998 DE 69226384 T 17-12-1998 JP 6323310 A 25-11-1994 US 5569272 A 29-10-1996 US 5676850 A 14-10-1997
DE 19525607	A 16-01-199	AU 722943 B 17-08-2000 AU 6656796 A 18-02-1997 BG 102200 A 31-08-1998 BR 9609796 A 16-03-1999 CA 2226718 A 06-02-1997 CN 1190904 A 19-08-1998 CZ 9800118 A 17-06-1998 WO 9703718 A 06-02-1997 EP 0840634 A 13-05-1998 HU 9802773 A 28-06-1999 JP 11509123 T 17-08-1999 JP 1509123 T 17-08-1999 NO 980147 A 13-03-1998 PL 324530 A 08-06-1998 SK 4998 A 09-09-1998 US 6132755 A 17-10-2000
WO 9828037	A 02-07-199	28 AU 722574 B 10-08-2000 AU 5529498 A 17-07-1998 CN 1233967 A 03-11-1999 EP 0957972 A 24-11-1999
WO 9800193	A 08-01-199	8 AU 3880697 A 21-01-1998 CA 2259437 A 08-01-1998 EP 0921840 A 16-06-1999 JP 2000513971 T 24-10-2000
WO 9964580	A 16-12-199	9 AU 4561699 A 30-12-1999
US 5865786	A 02-02-199	US 5591123 A 07-01-1997 US 5135479 A 04-08-1992 US 4640689 A 03-02-1987 US 4557723 A 11-11-1986 US 4557723 A 10-12-1985 US 5746711 A 05-05-1998 US 5224928 A 06-07-1993 US 5605536 A 25-02-1997 US 5651768 A 29-07-1997 US 5931804 A 03-08-1999 US 4808152 A 28-02-1989 US 5653682 A 05-08-1997 US 5167617 A 01-12-1992 US 5976101 A 02-11-1999 US 4731926 A 22-03-1988 US 5358483 A 25-10-1994 AT 92775 T 15-08-1993 AT 168570 T 15-08-1998 AU 580585 B 19-01-1989 AU 3935285 A 02-05-1986

information on petent family mambers

International Application No PCT/US 00/15312

	· · · · · · · · · · · · · · · · · · ·		Le 1, 02	90/19315
Patent document clied in search report	Publication date	F	³ siont family member(s)	Publication data
US 5865786 A		BR	8504939 A	22-07-1986
		ĈA	1226777 A	15-09-1987
		DE	3587518 A	16-09-1993
		DE	3587518 D	16-09-1993
		DE	3587518 T	02-12-1993
		DE	3588190 D	27-08-1998
		DE	3588190 T	04-02-1999
		ΕP	0178601 A	23-04-1986
		ΕÞ	0197937 A	22-10-1986
		ΕP	0513879 A	19-11-1992
		ΙŢ	1186798 B	16-12-1987
		JP	1828721 C	15-03-1994
		JP	61100264 A	19-05-1986
		KR	9400071 B	05-01-1994
		MX	161423 A	24-09-1990
		WO	8602277 A	24-04-1986
		US	485618B A	15-08-1989
		US	4713050 A	15-12-1987
		AT	45290 T	15-0B-1989
		AU	563137 B	25-06-1987
		AU	3185084 A	21-02-1985
		BR	8404119 A	16-07-1985
		CA	1224993 A	04-08-1987
		DE	3479294 D	14-09-1989
		ΕP	0147524 A	10-07-1985
		JР	1764538 C	28-05-1993
		JP	4056627 B	09-09-1992
		ήÞ	60060860 A	08-04-1985
		KR	9305050 B	15-06-1993
P-P		MX	158181 A	13-01-1989
WD 9800194 A	08-01-1998	EP	0925088 A	30-06-1999