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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.

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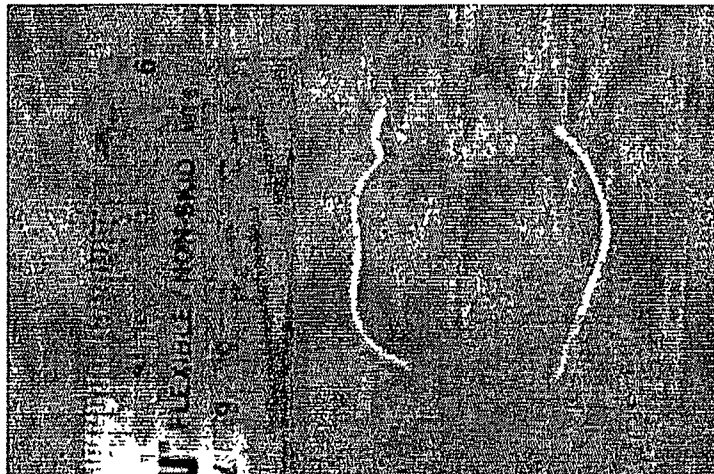
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(54) Title: BIODEGRADABLE DRUG-POLYMER DELIVERY SYSTEM



(57) Abstract: A sustained-release biodegradable polymeric drug-eluting fiber is disclosed. In some embodiments, the therapeutic drug is complexed with cyclodextrin. In certain embodiments, the polymeric component of the fiber comprises cyclodextrin. The fiber may be fabricated to provide a thread and/or suture. The fiber may be used for treatment of ocular diseases or disorders.

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2005/019998

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. A61K47/48		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) A61K		
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		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/022099 A (INSERT THERAPEUTICS INC [US]; CHENG JIANJUN [US]; DAVIS MARK E [US]; K) 18 March 2004 (2004-03-18)  page 57, line 21 - line 28 examples claims  <div style="text-align: center;">----- -/--</div>	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.		
<input checked="" type="checkbox"/> 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  <p style="text-align: center;">2 July 2007</p>	Date of mailing of the international search report  <p style="text-align: center;">20/11/2007</p>	
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  <p style="text-align: center;">Dullaart, Anwyn</p>	

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2005/019998

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X	<p>WO 03/090710 A (UNIV CASE WESTERN RESERVE [US]; BOOTHMAN DAVID [US]; GAO JINMING [US];) 6 November 2003 (2003-11-06)</p> <p>page 41, line 5 - line 12 examples claims</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
X	<p>OOYS T ET AL: "Synthesis and characterization of biodegradable polyrotaxane as a novel supramolecular-structured drug carrier" JOURNAL OF BIOMATERIALS SCIENCE, POLYMER EDITION, vol. 8, no. 6, 1997, pages 437-455, XP002096596 ISSN: 0920-5063 abstract page 439 page 442 page 446 figures page 453, paragraph CONCLUSIONS - page 454</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
X	<p>N. OGATA, K. SANUI, J. WADA: "Novel synthesis of inclusion polyamides" JOURNAL OF POLYMER SCIENCE: POLYMER LETTERS EDITION, vol. 14, no. 8, August 1976 (1976-08), pages 459-462, XP002440017 the whole document</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
X	<p>WO 01/76554 A (MASSACHUSETTS INST TECHNOLOGY [US]) 18 October 2001 (2001-10-18)</p> <p>figures tables claims</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/019998

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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>QUAGLIA F ET AL: "Feeding liquid, non-ionic surfactant and cyclodextrin affect the properties of insulin-loaded poly(lactide-co-glycolide) microspheres prepared by spray-drying"            JOURNAL OF CONTROLLED RELEASE,            vol. 86, no. 2-3,            17 January 2003 (2003-01-17), pages            267-278, XP004401121            ISSN: 0168-3659            abstract            page 272            page 274; figure 3</p>	<p>1-24,            33-48,            68-76,            79-81,            84,87,            89-91,93</p>
X	<p>MURILLO M ET AL: "Modulation of the cellular immune response after oral or subcutaneous immunization with microparticles containing Brucella ovis antigens"            JOURNAL OF CONTROLLED RELEASE,            vol. 85, no. 1-3,            13 December 2002 (2002-12-13), pages            237-246, XP004397782            ISSN: 0168-3659            abstract            page 238, right-hand column, paragraph 2.3            - page 239, right-hand column, paragraph 2.6</p>	<p>1-24,            33-48,            68-76,            79-81,            84,87,            89-91,93</p>
Y	<p>SONG C X ET AL: "Controlled release of U-86983 from double-layer biodegradable matrices: effect of additives on release mechanism and kinetics"            JOURNAL OF CONTROLLED RELEASE,            vol. 45, no. 2,            17 March 1997 (1997-03-17), pages 177-192,            XP004637258            ISSN: 0168-3659            abstract            page 179            figures; table 1</p>	<p>1-24,            33-48,            68-76,            79-81,            84,87,            89-91,93</p>

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/019998

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>TRAPANI GIUSEPPE ET AL: "Encapsulation and release of the hypnotic agent zolpidem from biodegradable polymer microparticles containing hydroxypropyl-beta-cyclodextrin." INTERNATIONAL JOURNAL OF PHARMACEUTICS, vol. 268, no. 1-2, 11 December 2003 (2003-12-11), pages 47-57, XP002440018 ISSN: 0378-5173 abstract page 49 page 54; table 2 page 56, paragraph CONCLUSIONS - page 57; figure 4; table 3</p> <p style="text-align: center;">-----</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
Y	<p>KYLE A SALEM ET AL: "X-Ray Computed Tomography Methods for In Vivo Evaluation of Local Drug Release Systems" IEEE TRANSACTIONS ON MEDICAL IMAGING, vol. 21, no. 10, October 2002 (2002-10), XP011076376 ISSN: 0278-0062 page 1311</p> <p style="text-align: center;">-----</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
Y	<p>QIAN F ET AL: "Quantification of in vivo doxorubicin transport from PLGA millirods in thermoablated rat livers" JOURNAL OF CONTROLLED RELEASE, vol. 91, no. 1-2, 28 August 2003 (2003-08-28), pages 157-166, XP004447901 ISSN: 0168-3659 abstract page 158, right-hand column, paragraph 2.2 page 162 page 164; figure 4 page 165, right-hand column, paragraph CONCLUSION - page 166, left-hand column</p> <p style="text-align: center;">-----</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>
Y	<p>QIAN F ET AL: "Combined modeling and experimental approach for the development of dual-release polymer millirods" JOURNAL OF CONTROLLED RELEASE, vol. 83, no. 3, 30 October 2002 (2002-10-30), pages 427-435, XP004387601 ISSN: 0168-3659 abstract page 430, right-hand column, last paragraph - page 432, right-hand column, line 8 figure 4</p> <p style="text-align: center;">-----</p>	<p>1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93</p>

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/019998

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GAO JINMING ET AL: "In vivo drug distribution dynamics in thermoablated and normal rabbit livers from biodegradable polymers" JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, vol. 62, no. 2, November 2002 (2002-11), pages 308-314, XP002440019 ISSN: 0021-9304 abstract page 309, left-hand column, last paragraph figures page 314	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	----- QIAN FENG ET AL: "Membrane-encased polymer millirods for sustained release of 5-fluorouracil." JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, vol. 61, no. 2, August 2002 (2002-08), pages 203-211, XP002440020 ISSN: 0021-9304 abstract page 204, left-hand column, last paragraph - right-hand column, paragraph 1 figures page 209 - page 210	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	----- QIAN FENG ET AL: "Comparison of doxorubicin concentration profiles in radiofrequency-ablated rat livers from sustained- and dual-release PLGA millirods." PHARMACEUTICAL RESEARCH, vol. 21, no. 3, March 2004 (2004-03), pages 394-399, XP002440021 ISSN: 0724-8741 abstract page 395 page 398 - page 399	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	----- SZYMANSKI-EXNER AGATA ET AL: "Noninvasive monitoring of local drug release using X-ray computed tomography: Optimization and in vitro/in vivo validation." JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 92, no. 2, February 2003 (2003-02), pages 289-296, XP002440022 ISSN: 0022-3549 abstract page 290, right-hand column, last paragraph - page 291, left-hand column, paragraph 1 page 291, right-hand column, last paragraph - page 292, left-hand column, paragraph 2 figures	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/019998

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	QIAN F ET AL: "Fabrication and characterization of controlled release poly(D,L-lactide-co-glycolide) millirods" JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, vol. 55, no. 4, 15 June 2001 (2001-06-15), pages 512-522, XP002440023 ISSN: 0021-9304 abstract page 513, left-hand column, paragraph MATERIALS - page 514, left-hand column, paragraph 1 figures page 519, right-hand column, last paragraph - page 521	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	WO 02/089815 A (ALLERGAN INC [US]) 14 November 2002 (2002-11-14)  example 1	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	WO 99/43359 A (BIOALLIANCE PHARMA S A [FR]; MONZA DA SILVEIRA AIRTON [BR]; PONCHEL GI) 2 September 1999 (1999-09-02)  example 13 table IV claim 1	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	EP 0 780 129 A2 (CAC CORP [JP]) 25 June 1997 (1997-06-25)  claim 1	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93
Y	EP 0 575 976 A (PUETTER MEDICE CHEM PHARM [DE]) 29 December 1993 (1993-12-29)  example 13	1-24, 33-48, 68-76, 79-81, 84,87, 89-91,93

# INTERNATIONAL SEARCH REPORT

International application No.  
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## 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 68-76, 79-81, 84, 87, 89-91 and 93 are directed to a method of treatment of the human/animal body, a 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 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.:
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.:

see annex

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: 1-21, 33-48, 68-76, 79-81, 84, 87, 89-91 and 93 in part, and 22-24

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is a steroid

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2. claims: 1-21, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is a retinoid.

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3. claims: 1-21, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an NSAID.

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4. claims: 1-21, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is a vitamin D3 analog.

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5. claims: 1-21, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is a human carbonic anhydrase inhibitor.

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6. claims: 1-20, 28, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part, 25-27, 31, 32, 85, 86 and 92

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is a nerve growth inducing agent.

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7. claims: 1-20, 28, 33-48, 68-76, 79-81, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an anti-cancer agent.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. claims: 1-20, 28, 33-48, 68-76, 79-81, 84, 87, 89-91 in part, 29, 30, 77, 78, 82, 83 and 88

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an antibiotic agent or antimicrobial agent.

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9. claims: 1-20, 28, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an anti-inflammatory agent.

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10. claims: 1-20, 28, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an immunosuppressant.

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11. claims: 1-20, 28, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an antiviral agent.

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12. claims: 1-20, 28, 33-48, 68-76, 79, 80, 84, 87, 89-91 in part

Fiber comprising one or more polymers, one or more cyclodextrins and one or more therapeutic agents, wherein the therapeutic agent is an anti-proliferative agent.

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13. claims: 49-59

A thread as defined in these claims.

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14. claims: 60-67

A suture as defined in these claims.

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15. claims: 94-108

A process for the preparation as defined in these claims.

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/019998

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