

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
5 February 2004 (05.02.2004)

PCT

(10) International Publication Number
WO 2004/011054 A3

(51) International Patent Classification⁷: **A61K 9/00**, 47/34

(21) International Application Number:

PCT/US2003/023439

(22) International Filing Date: 28 July 2003 (28.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/399,832 31 July 2002 (31.07.2002) 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, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

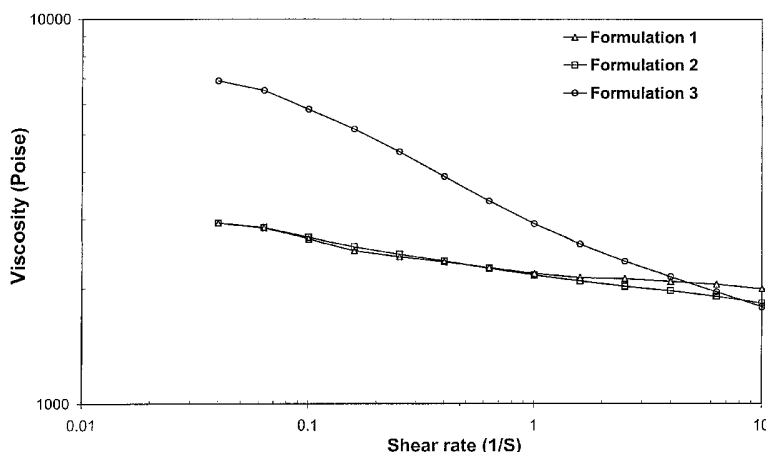
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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

1 April 2004

[Continued on next page]

(54) Title: INJECTABLE MULTIMODAL POLYMER DEPOT COMPOSITIONS AND USES THEREOF



(57) Abstract: Injectable depot compositions are provided that include a polymer matrix having a plurality of bioerodible, bio-compatible polymers wherein each polymer of the plurality of polymers has a specified weight average molecular weight; and the polymer matrix has a broad molecular weight distribution of the plurality of polymers; a solvent having a miscibility in water of less than or equal to 7 wt.% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith; and a beneficial agent. The compositions are have substantially improved the shear thinning behavior and reduced injection force, rendering the compositions readily implanted beneath a patient's body surface by injection. The most preferred polymer matrix is made of poly (lactide-co-glycolide) copolymers, commonly referred to as PLGA. The most preferred solvents are derivatives of benzoic acid, such as benzylbenzoate.

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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/US 03/23439

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/00 A61K47/34

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 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, WPI Data, PAJ, EMBASE, MEDLINE, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAVIVARAPU H B ET AL: "Polymer and microsphere blending to alter the release of a peptide from PLGA microspheres" EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 50, no. 2, September 2000 (2000-09), pages 263-270, XP004257200 ISSN: 0939-6411 *Formulations C, D and E* * p. 263, col. 2, 2nd full sentence- p. 264, col. 1, 1st sentence*figures 2-6; table 1	1,2,4, 7-17
Y	----- -/--	56-84

☒ 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
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- *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.
- *G* document member of the same patent family

Date of the actual completion of the international search

2 February 2004

Date of mailing of the international search report

09/02/2004

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/23439

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JAIN R A: "The manufacturing techniques of various drug loaded biodegradable poly(lactide-co-glycolide) (PLGA) devices" BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, vol. 21, no. 23, 1 December 2000 (2000-12-01), pages 2475-2490, XP004216917 ISSN: 0142-9612 * p. 2482, 3.4 In situ formed devices- p. 2484*figures 1,2	1,2,4, 7-17
Y	-----	56-84
X	WO 02/45689 A (SEO MIN HYU ; KIM JAE HONG (KR); LEE SANG JUN (KR); SAMYANG CORP (KR);) 13 June 2002 (2002-06-13) claims 1-14; table 1	1,2,7-11
A	----- LAMBERT W J ET AL: "DEVELOPMENT OF AN IN SITU FORMING BIODEGRADABLE POLY-LACTIDE-CO- GLYCOLIDE SYSTEM FOR THE CONTROLLED RELEASE OF PROTEINS" JOURNAL OF CONTROLLED RELEASE, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 33, no. 1, 1995, pages 189-195, XP000482915 ISSN: 0168-3659 *p. 189, 2.1 Materials - p. 190*figures 1,2	
P,X	----- WO 03/041684 A (ALZA CORP) 22 May 2003 (2003-05-22) paragraphs '0085!, ' 100! - '0102!; table 1	1,2,4, 7-22
P,X	----- WO 03/041757 A (ALZA CORP) 22 May 2003 (2003-05-22) paragraphs '0098!, ' 112! - ' 114!; table 1	1,2,4, 7-22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/23439

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.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 56-83 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:

Present claims 1-84 relate to an extremely large number of possible compositions. A meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims relating to the lactic acid based polymers .
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:

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.:

Remark on Protest

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/23439

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0245689	A	13-06-2002	AU 2273302 A	18-06-2002
			CA 2430481 A1	13-06-2002
			EP 1339389 A1	03-09-2003
			WO 0245689 A1	13-06-2002
			KR 2002045569 A	19-06-2002
WO 03041684	A	22-05-2003	NO 20033177 A	04-09-2003
			NO 20033178 A	04-09-2003
			WO 03041684 A2	22-05-2003
			WO 03041757 A2	22-05-2003
			US 2003170289 A1	11-09-2003
			US 2003180364 A1	25-09-2003
WO 03041757	A	22-05-2003	NO 20033177 A	04-09-2003
			NO 20033178 A	04-09-2003
			WO 03041684 A2	22-05-2003
			WO 03041757 A2	22-05-2003
			US 2003170289 A1	11-09-2003
			US 2003180364 A1	25-09-2003