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- (71) Applicant: **BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS** [US/US]; 352 Henry Administration Building, 506 S. Wright, Urbana, IL 61801 (US).
- (72) Inventors: **KYEKYOON, Kim**; 1712 Brighton Court, Champaign, IL 61822 (US). **PACK, Daniel, W.**; 3105 Goldmedal Drive, Campagne, IL 61822 (US). **BERKLAND, Cory, J.**; 1001 Country Squire, Urbana, IL 61801 (US).
- (74) Agent: **RAUCH, Paul, E.**; Brinks Hofer Gilson & Lione, P.O. Box 10087, Chicago, 60618 (US).
- (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, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
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(54) Title: METHOD OF FORMING MICROPARTICLES

(57) Abstract: A method of forming particles comprises accelerating a stream comprising a liquid; and vibrating the stream, to form particles. The particles may have a diameter that is smaller than the diameter of the nozzle used to form the stream, allowing for the formation of micro- and nano-sized particle.

## INTERNATIONAL SEARCH REPORT

 Inte      Application No  
 PCT/US 01/25674

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7    A61K9/16      A61K9/50

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, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 265 924 A (KANEGAFUCHI CHEMICAL IND) 4 May 1988 (1988-05-04) page 4, line 40 - line 51 page 5, line 4 - line 14 page 7, line 31 - line 55 page 9, line 13 - line 20; claims 9,26-28; example 9	1-6,9,16
X	DE 27 25 849 A (HOBEG HOCHTEMPERATURREAKTOR) 21 December 1978 (1978-12-21) page 4, paragraph 1 page 5, last paragraph -page 6, paragraph 2 page 8, last paragraph -page 10, paragraph 3; claims 1,6	1-6,13, 16-19,22
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 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
- "I" 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

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 Name and mailing address of the ISA  
 European Patent Office. P.E. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Marttin, E

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/25674

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BITTNER B ET AL: "ULTRASONIC ATOMIZATION FOR SPRAY DRYING: A VERSATILE TECHNIQUE FOR THE PREPARATION OF PROTEIN LOADED BIODEGRADABLE MICROSPHERES"            JOURNAL OF MICROENCAPSULATION, TAYLOR AND FRANCIS INC. LONDON, GB,            vol. 16, no. 3, May 1999 (1999-05), pages 325-341, XP000804804            ISSN: 0265-2048            page 327, paragraph 3 -page 328, paragraph 1; figure 1            page 331, paragraph 1            page 331, paragraph 5            page 332, last paragraph</p>	1-6,13, 16-19,22
X	<p>WO 97 31691 A (SAID SAID ;UNIV KANSAS (US); RAJEWSKI ROGER A (US); STELLA VALENTI) 4 September 1997 (1997-09-04)            page 5, line 29 - line 37            page 6, line 31 -page 8, line 33            page 13, line 1 -page 14, line 22; claims 1,11,13-16; figures 2,3</p>	1-6, 13-19, 22-29
X	<p>WO 99 44735 A (BRANDENBERGER HARRY ;HEINZEN CHRISTOPH (CH); INOTECH AG (CH); WIDM) 10 September 1999 (1999-09-10)            page 3, line 11 -page 5, line 23            page 7, line 4 - line 26; claims 1-6,9-11</p>	1-6,13, 22-24
X	<p>CH 675 370 A (CIBA GEIGY AG)            28 September 1990 (1990-09-28)            column 1, line 64 -column 2, line 7            column 2, line 40 -column 3, line 46;            figure 1            column 6, line 33 - line 55            column 7, line 8 - line 21; claims 1,10</p>	1-8,13, 22
X	<p>SHIGA K ET AL: "Preparation of Poly(D,L-lactide) and copoly(lactide-glycolide) microspheres of uniform size."            JOURNAL OF PHARMACY AND PHARMACOLOGY, vol. 48, no. 9, 1996, pages 891-895, XP008007515            ISSN: 0022-3573            figures 2,4</p>	32-34
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## INTERNATIONAL SEARCH REPORT

Inter al Application No

PCT/US 01/25674

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

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ANONYMOUS: "Microparticle size standards" ALDRICH TECHNICAL BULLETIN AL-203, 'Online! February 1997 (1997-02), pages 1-2, XP002212512 Retrieved from the Internet: <URL:http://www.sigmaaldrich.com/img/assets/3762/al_techbull_al203.pdf> 'retrieved on 2002-09-05! page 2; table 2 ---	32-34
X,P	BERKLAND CORY ET AL: "Fabrication of PLG microspheres with precisely controlled and monodisperse size distributions." JOURNAL OF CONTROLLED RELEASE, vol. 73, no. 1, 18 May 2001 (2001-05-18), pages 59-74, XP002212474 ISSN: 0168-3659 the whole document -----	1-8,10, 13-22, 30-33, 35-40

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/25674

## 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:
  
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.  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.:

1-40

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: 1-40

A method for forming particles comprising accelerating a first stream comprising a first liquid, and vibrating the first stream to form particles and particles prepared by this method; and a method of forming particles comprising accelerating a first stream comprising a first liquid wherein the accelerating comprises applying charge to the first stream, and the particles comprise a core and shell and particles prepared by this method; and particles having an average diameter of 50 to 100  $\mu$ m, wherein 90% of the particles have a diameter that is within 2% of an average diameter of the particles; and particles having an average diameter of 1 to 50  $\mu$ m, wherein 90% of the particles have a diameter that is within 1  $\mu$ m of an average diameter of the particles.

2. Claims: 41-62

An apparatus for forming particles comprising (i) means for forming a first stream of a first liquid, (ii) means for accelerating the first stream, and (iii) means for vibrating the first stream; and an apparatus for forming particles comprising (i) a first nozzle, (ii) a second nozzle and (iii) a charge source; and methods for making particles comprising forming particles with these apparatuses.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/25674

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