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- (81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

- (88) **Date of publication of the international search report:**
22 October 2015

(54) **Title:** RAPID ACTION INSULIN FORMULATIONS AND PHARMACEUTICAL DELIVERY SYSTEMS

(57) **Abstract:** The present invention provides rapid-acting insulin and insulin analogue formulations. The invention further provides delivery devices, particularly infusion sets, which allow for the rapid absorption of insulin and insulin analogues, as well as other active agents. Methods of using the insulin and insulin analogue formulations as well as the insulin delivery devices for treating subjects with diabetes mellitus are also provided.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/11202

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/28, 38/00 (2015.01)

CPC - C07K 14/62, 14/622

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)

CPC: C07K 14/62, 14/622

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

CPC: C07K 14/62, 14/622 (text search)

USPC: 514/5.9, 6.2, 6.3; 530/303 (text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Electronic data bases: PatBase; Google Scholar; Google Patents

Search terms: insulin, analog*, monomeric, dimeric, calcium-chelating agent, charge-masking agent, formulation, aqueous, intra-dermal, EGTA, EDTA, alginate, alpha lipoic acid, DMSA or DMPS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,461,031 A (De Felippis) 24 October 1995 (24.10.1995). Especially claim 1, claim 16.	1-4
Y	US 2008/0090753 A1 (POHL et al.) 17 April 2008 (17.04.2008). Especially para [0027], [0035], [0037].	1-4
Y	KRASNER et al. A Review of a Family of Ultra-Rapid-Acting Insulins: Formulation Development. J Diabetes Sci Technol 1 July 2012 Vol 6 No 4 Pages 786-796. Especially entire article (review of field).	1-4

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search 22 June 2015 (22.06.2015)	Date of mailing of the international search report 28 AUG 2015
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/11202

Box No. 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:

- 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.: 5-43 and 48-109
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. 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:
-----go to Extra Sheet for continuation-----

- 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 additional fees, this Authority did not invite payment of additional fees.
- 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.:
1-4

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/11202

----Continuation of Box III (Lack of Unity of Invention)-----

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-4, drawn to a pharmaceutical composition.

Group II: Claims 44-47, drawn to an infusion set.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I has the special technical feature of a monomeric insulin analogue or dimeric insulin analogue and one or more calcium ion-chelating agents or one or more charge-masking agents, not required by Group II.

Group II has the special technical feature of an infusion set comprising a first body, an adhesive surface, a subcutaneous infusion catheter, and one or more of an ultrasound transducer, a tactor, and an electrophoresis electrode, not required by Group I.

Common Technical Feature:

Although the infusion set of Group II could be used to administer the pharmaceutical composition of Group I, Groups I and II do not share any common technical features per se.

Therefore, Groups I and II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature

Note : Claims 5-43 and 48-109 are multiple dependent claims and are not drafted according to the second and third sentences of PCT Rule 6.4(a).