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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

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))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
18 October 2012

(54) Title: LYOPHILIZED FORMULATIONS

(57) Abstract: The invention is directed to a method for producing a polypeptide composition comprising: combining a polypeptide with a volatile additive to form a liquid mixture and lyophilizing the liquid mixture to obtain a lyophilized polypeptide composition.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/24452

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 1/02 (2012.01)

USPC - 530/350

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)

USPC- 530/350, 530/324, 530/402

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 practicable, search terms used)

PubWEST(PGPB,USPT,USOC,EPAB,JPAB); Dialog Classic Files -- 654, 652, 349, 348, 340, 35, 65, 155; Google Scholar; Entrez PubMed; Search terms -- polypeptide, lyophilization, tert-butanol, mixture, antibody

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/0017169 A1 (PESTKA) 23 January 2003 (23.01.2003) para [0047], [0067], [0076], [0080], claims 2, 3, 14, 19	1, 2, 4
Y	TEAGARDEN, D.L. et al. Practical aspects of lyophilization using non-aqueous co-solvent systems. European Journal of Pharmaceutical Sciences, 2002, Vol. 15, pages 115-133; pg 115, abstract; pg 117, Table 2; pg 121, col 1, para 2 -- col 2, para 1; pg125, col 1, para 2	1, 2, 4
Y	US 2010/0158814 1 (BUSSAT et al.) 24 June 2010 (24.06.2010) para [0506], [0507], [0543], [0546]	1, 2, 4
Y	SCHWEGMAN, J.J. et al. Practical Formulation and Process Development of Freeze-Dried Products. Pharmaceutical Development and Technology, 2005, Vol. 10, pages 151-173; pg 165, col 2, para 5; pg 166, col 1, pra 3 -- col 2, para 1; pg 169, col 1, para 2	1, 2, 4

☐ Further documents are listed in the continuation of Box C.

* 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 application or patent 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

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26 July 2012 (26.07.2012)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/24452

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.: 20-26 and 28
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:

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-II: claims 1-4, drawn to a method for producing a polypeptide composition comprising: combining a polypeptide with a volatile additive to form a liquid mixture and lyophilizing the liquid mixture to obtain a lyophilized polypeptide composition, wherein the liquid mixture comprises about 2% by volume of volatile additive, and the volatile additive is t-butanol, wherein the polypeptide is an antigen binding polypeptide or the polypeptide comprises at least two GLP-I polypeptides genetically fused to the N-terminus of human serum albumin, respectively.

Group III: claims 5-6, drawn to a dry polypeptide composition produced by the method of claim 1.

SEE CONTINUATION 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 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, 2 and 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 12/24452

Continuation of Box III

Group IV: claims 7-15, drawn to a method for producing a liquid polypeptide composition comprising: obtaining a lyophilized polypeptide produced by the method of claim 1, and reconstituting the lyophilized polypeptide with a sufficient amount of a pharmaceutically acceptable dispersing agent to yield a liquid polypeptide composition.

Group V: claims 16-19, 27, drawn to a composition comprising: a therapeutic polypeptide, a buffer, a surfactant, at least one excipient, and at least one volatile additive.

The inventions listed as Groups I-V 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:

The inventions of Groups I-IV do not include the inventive concept of a composition comprising: a therapeutic polypeptide, a buffer, a surfactant, at least one excipient, and at least one volatile additive, as required by Group V.

The inventions of Groups I-IV share the technical feature of a method of claim 1. However, this shared technical feature does not represent a contribution over prior art as being obvious over US 2010/0158814 A1 to Bussat, et al. (hereinafter "Bussat") that discloses a method for producing a polypeptide composition (Abstract, Fibrin-binding peptides, para [0543], fluffy solid) comprising: combining a polypeptide with a volatile additive to form a liquid mixture and lyophilizing the liquid mixture to obtain a lyophilized polypeptide composition, wherein the liquid mixture comprises t-butanol (para [0542], Preparation of Ac-WQPCPAESWTFCWDPGAGSGK(DPPE-Pro9-Glut-Ttda-Dga)-NH.sub.2cyclic (4.fwdarw.12) peptide; para [0543], "... The crude was redissolved in DCM (1 mL) and Seq005-P3(Ttda-Dga) [Ac-WQPCPAESWTFCWDPGSAGSK(Ttda-Dga)-NH.sub.2] (SEQ ID NO. 145), ... HPLC and MS analysis indicated formation of the desired product. ... The pure product containing fractions were combined and most of the MeOH was removed by rotary evaporation. Tert-Butyl alcohol was added to the mixture and the mixture was frozen and lyophilized to give the product (125 mg, 46.5% yield) as a fluffy solid"). Bussat does not disclose that t-butanol, the volatile additive, was added in the amount of about 2% by volume. However, it would have been obvious to one of ordinary skill in the art how to determine an optimal amount of t-butanol necessary to achieving a dry composition having desired properties. As said method would have been obvious to one of ordinary skill in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Another special technical feature of the inventions listed as Groups I-IV is the specific polipeptide recited therein. As no significant structural similarities can readily be ascertained among the polipeptides, the inventions do not share a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.