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Declarations under Rule 4.17:
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(54) Title: FORMULATION FOR ROOM TEMPERATURE STABILIZATION OF A LIVE ATTENUATED BACTERIAL VACCINE

(57) Abstract: This invention provides methods and compositions for stabilizing proteins and vaccines in dried formulations. In particular, a cavitation method and compositions of preparing a dried vaccine are provided that stabilize the viability of live bacteria and live virus vaccines at room temperature.
A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/02 (2011.01)
USPC - 424/234.1

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- 424/234.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 424/130.1; 424/184.1; 424/204.1; 424/243.1; 424/244.1; 424/246.1; 424/248.1; 424/257.1; 424/258.1; 424/260.1

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 2003/0219475 A1 (Truong-Le) 27 November 2003 (27.11.2003) Abstract, para [0002], [0012], [0014], claim 97</td>
<td>1-8, 11, 12, 14-18, 53-54</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>9, 10, 13</td>
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</tbody>
</table>

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

Date of the actual completion of the international search
29 March 2012 (29.03.2012)

Date of mailing of the international search report
01 OCT 2012

Name and mailing address of the ISA/US
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Form PCT/ISA/210 (second sheet) (July 2009)
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.:
   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.

Group I: claims 1-18 and 53-54, drawn to a cavitation-dried composition that comprises a biologically active sample, wherein the composition is prepared from a mixture of the biologically active sample and a formulation, wherein the mixture contains a polyol (20-70% w/v of mixture), and a plasticizer (0.1-10.0% w/w of mixture), at pH 6.0-8.5, wherein to prepare the composition, the mixture is subjected to a vacuum, wherein the mixture temperature, or shelf temperature, is maintained above the freezing point of the mixture, wherein a cavitation-dried structure is produced, and wherein the cavitation-dried structure is a foam or a film.

****************************************************************************************** See Supplemental Sheet to continue ******************************************************************************************

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.: 1-18 and 53-54

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.
In Continuation of Box III. Lack of unity of invention:

Group II: claims 19-52, drawn to a method for preparing a cavitation-dried composition of a biologically active sample, from a mixture of a biologically active sample and a formulation, wherein the formulation comprises a polyl, and a plasticizer or a surfactant, and wherein the mixture is in a container, wherein the method comprises decreasing the chamber pressure in a stepwise manner to reduce the water content of the mixture, wherein the mixture temperature or the shelf temperature, is maintained above the freezing point of the mixture, wherein a foam or film is produced, and wherein the mixture does not freeze and the foam or film does not freeze.

The inventions listed as Groups I-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:

The inventions of Group I do not include the inventive concept of a method for preparing a cavitation-dried composition of a biologically active sample, as required by Group II.

In addition, a cavitation-dried composition of claim 1 does not represent a contribution over prior art as being anticipated by US 2003/0219475 A1 to Truong-Le (hereinafter "Truong") teaches a cavitation-dried composition (para [0002], dried foam matrix) that comprises a biologically active sample (para [0002]), wherein the composition is prepared from a mixture of the biologically active sample and a formulation (para [0012]), wherein the mixture contains a polyl (20-70% w/w of mixture) (para [0012], sucrase), and a plasticizer (0.1-10.0% w/w of mixture) (para[0012], polyethylene and propylene glycol) at pH 6.0-8.5 (para [0012]), wherein to prepare the composition, the mixture is subjected to a vacuum (para[0012]), wherein the mixture temperature, or shelf temperature, is maintained above the freezing point of the mixture (para [0012]), wherein a cavitation-dried structure is produced (para[0012], dried foam), and wherein the cavitation-dried structure is a foam or a film (para [0012]). As said formulation was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.