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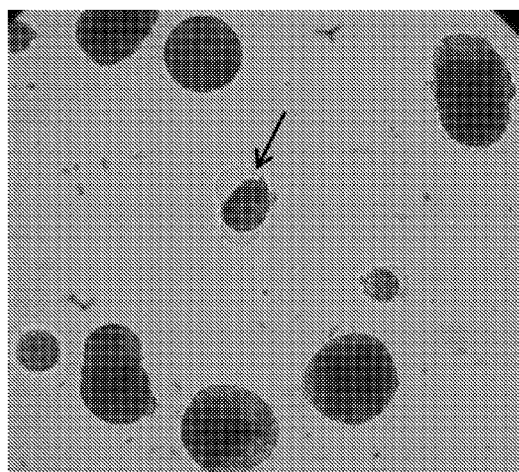
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,

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[Continued on next page]

(54) Title: NOVEL VACCINE COMPOSITIONS FOR PORCINE EPIDEMIC DIARRHEA VIRUS AND PORCINE DELTACORONAVIRUS



PEDV Growth on Vero cells at High Trypsin Concentration, 4ug/ml  
PEDV-infected Vero cells showing a "bubble" effect on cells  
(black arrow).

FIG. 1

(57) Abstract: The present invention is directed to novel immunogenic compositions that protect swine from disease caused by porcine epidemic diarrhea virus (PEDV). The present invention is also directed to novel immunogenic compositions that protect swine from disease caused by porcine deltacoronavirus (PDCoV), alone or as combination vaccine to protect against PEDV. The compositions of the invention provide killed viruses whose effectiveness is enhanced by the selection of preferred adjuvants. Novel culture methods are also employed to increase reproducible yield of cultured viruses. Live vaccines are also provided from the Calaf14 PEDV isolate.





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.

- 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))

**(84) Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

- 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:**  
3 March 2016

**Declarations under Rule 4.17:**

- as to the identity of the inventor (Rule 4.17(i))

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/US2015/039475

**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. A61K39/215 C07K14/165 C12N7/00 A61K39/00  
 ADD.

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)  
 A61K C07K C12N

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)  
 EPO-Internal, WPI Data, EMBASE, BIOSIS, FSTA

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Emily A Collin ET AL: "An inactivated vaccine made from a U.S. field isolate of porcine epidemic disease virus is immunogenic in pigs Running Title: PEDV inactivated vaccine Authors: Present Text Word Count",  1 July 2014 (2014-07-01), XP055222051, Retrieved from the Internet: URL: <a href="http://www.researchgate.net/profile/Faten_Okda/publication/264934006_An_inactivated_vaccine_made_from_a_U.S._field_isolate_of_porcine_epidemic_disease_virus_is_immunogenic_in_pigs/links/53f627060cf22be01c40afd9.pdf?inViewer=true&amp;pdfJsDownload=true&amp;disableCoverPage=true&amp;origin=publication_detail">http://www.researchgate.net/profile/Faten_Okda/publication/264934006_An_inactivated_vaccine_made_from_a_U.S._field_isolate_of_porcine_epidemic_disease_virus_is_immunogenic_in_pigs/links/53f627060cf22be01c40afd9.pdf?inViewer=true&amp;pdfJsDownload=true&amp;disableCoverPage=true&amp;origin=publication_detail</a> [retrieved on 2015-10-19] See lines 24-26, 32, 33 and 158 -/--	1,3,4

Further documents are listed in the continuation of Box C.

See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search <b>20 October 2015</b>	Date of mailing of the international search report <b>21/01/2016</b>
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer <b>Valcárcel, Rafael</b>
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2015/039475

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
  - a.  forming part of the international application as filed:
    - in the form of an Annex C/ST.25 text file.
    - on paper or in the form of an image file.
  - b.  furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
  - c.  furnished subsequent to the international filing date for the purposes of international search only:
    - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
    - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2.  In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2015/039475

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>-----</p> <p>KR 2010 0129247 A (CHOONG ANG VACCINE LAB [KR]) 8 December 2010 (2010-12-08) See abstract, paragraphs [0012], [0016] and [0040]</p>	1,3,4
Y	<p>-----</p> <p>WO 93/19779 A1 (SMITHKLINE BEECHAM CORP [US]; BROWN ALBERT L [US]; DAYALU KRISHNASWAMY) 14 October 1993 (1993-10-14) See claims 6, 18 and 23; page 9, lines 5 and 7; page 11, line 32.</p>	1,3,4
Y,P	<p>-----</p> <p>CN 104 383 528 A (JIANGSU ACAD AGRICULTURAL SCI) 4 March 2015 (2015-03-04) See e.g. the abstract and the embodiment 1</p>	1,3,4
E	<p>-----</p> <p>WO 2015/153425 A1 (BOEHRINGER INGELHEIM VETMED [US]) 8 October 2015 (2015-10-08) See e.g. claims 7-9 and 11; paragraphs [0064], [0068], [0084] and [0087]</p> <p>-----</p>	1,3,4

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2015/039475

## 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:

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 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, 3, 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.

**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, 3, 4

A vaccine composition as defined in claim 1. A method of producing a neutralizing antibody response according to claim 4.

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## 2. claims: 2, 6, 11

A vaccine composition as defined in claim 2. A method as defined in claims 6 and 11.

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## 3. claim: 5

A method as defined in claim 5, i.e. the themof of claim 4 wherein the inactivated virus of the immunogenic composition is a North American, European or Asian isolate, which provides protection against challenge by a North American, European or Asian isolate.

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## 4. claims: 12-15(completely); 7-10(partially)

A vaccine composition according to claims 12-14 (relate to the Calaf14 PEDV strain). The method according to claim 15. The method of claims 7-9 wherein vaccination provides protection against challenge by a PEDV virus that has the percentages of identity to Calaf14 PEDV strain referred to in claims 7-9.

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## 5. claims: 7-10(partially)

The method of claims 7-9 wherein vaccination provides protection against challenge by a PEDV virus that has the percentages of identity to OH581 PEDV strain referred to in claims 7-9.

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## 6. claims: 16-19

A vaccine composition as defined in claims 16-18. A method as defined in claim 19.

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## 7. claims: 20, 21, 23, 24

A vaccine composition as defined in claims 20, 21, 23 and 24.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2015/039475
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Patent document cited in search report	Publication date	Publication date	Patent family member(s)
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