

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

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| To:                  |
| see form PCT/ISA/220 |

## PCT

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

|                                                    |                                                          |                                              |
|----------------------------------------------------|----------------------------------------------------------|----------------------------------------------|
| International application No.<br>PCT/US2017/017290 | International filing date (day/month/year)<br>10.02.2017 | Priority date (day/month/year)<br>18.02.2016 |
|----------------------------------------------------|----------------------------------------------------------|----------------------------------------------|

International Patent Classification (IPC) or both national classification and IPC  
INV. A61K39/12 C12N7/00

Applicant  
ELI LILLY AND COMPANY

#### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

#### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

|                                                                                                                                                                                                                                       |                                                                       |                                                                                    |                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| <p>Name and mailing address of the ISA:</p>  <p>European Patent Office<br/>D-80298 Munich<br/>Tel. +49 89 2399 - 0<br/>Fax: +49 89 2399 - 4465</p> | <p>Date of completion of this opinion</p> <p>see form PCT/ISA/210</p> | <p>Authorized Officer</p> <p>Heder, Andreas</p> <p>Telephone No. +49 89 2399-0</p> |  |
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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed.
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established 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).
4. ☐ 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.
5. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-19(partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 1-19(partially)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details

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**Box No. IV Lack of unity of invention**

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1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-19(partially)

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement
- |                               |             |                                        |
|-------------------------------|-------------|----------------------------------------|
| Novelty (N)                   | Yes: Claims | <u>3, 9(all partially)</u>             |
|                               | No: Claims  | <u>1, 2, 4-8, 10-19(all partially)</u> |
| Inventive step (IS)           | Yes: Claims |                                        |
|                               | No: Claims  | <u>1-19(partially)</u>                 |
| Industrial applicability (IA) | Yes: Claims | <u>1-19(partially)</u>                 |
|                               | No: Claims  |                                        |
2. Citations and explanations
- see separate sheet**

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**Box No. VIII    Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item IV**

**Lack of unity of invention**

The application relates to several potential inventions:

Invention 1: claims 1-19 (all partially)

Modified PRRSV strain ND99-14 having 90% or more identity with SEQ ID NO: 4, 10, or 11, and uses thereof

Invention 2: claims 1-19 (all partially)

Modified PRRSV strain SD11-21 having 90% or more identity with SEQ ID NO: 9, 12, or 13, and uses thereof

Invention 3: claim 19 (partially)

Vaccine comprising a modified live PRRSV having an unspecified sequence for use in the treatment of a pig

Rule 13.1 PCT stipulates that when an application relates to a group of inventions, said groups of inventions have to be so linked as to form a general inventive concept. Rule 13.2 PCT specifies that the requirement of unity is fulfilled only when the separate inventions involve one or more of the same or corresponding special technical features. "Special technical features" are those technical features that define a contribution which each of the claimed inventions makes over the prior art. The only technical feature linking potential inventions 1-3 is that they all relate to modified live PRRSV strains. The technical problem to be solved, common to all groups of inventions was thus: to provide modified live PRRSV strains. Modified live PRRSV strains are not new (see, e.g., WO2015/140774A1). Therefore, the feature "modified live PRRSV strains" is not a special technical feature in the sense of Rule 13.2 PCT. Note that PRRSV strains having 90% identity to the recited sequences do not credibly provide protection against both homologous and heterologous strains. Furthermore, modified PRRSV strains providing cross-protection against heterologous strains are not novel and inventive (see WO2015/140774A1; see Renukaradhya et al. 2015, Vaccine 33:4069-4080). This means that the groups of inventions identified above are

not united by providing novel and inventive solutions to one common technical problem. Consequently, the present application lacks unity, and the separate groups of potential inventions have been divided as indicated.

The International search report is restricted to invention 1. The present opinion is restricted to invention 1, as well.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1            RENUKARADHYA GOURAPURA J ET AL: "Live porcine reproductive and respiratory syndrome virus vaccines: Current status and future direction", VACCINE, vol. 33, no. 33, 4 July 2015 (2015-07-04), pages 4069-4080, XP029518287, ISSN: 0264-410X, DOI: 10.1016/J.VACCINE.2015.06.092
- D2            WO 2015/140774 A1 (NUTECH VENTURES [US]; VU HIEP LAI XUAN [US]; OSORIO FERNANDO [US]; LAE) 24 September 2015 (2015-09-24)

*Disclosure of the application*

- 1            Live modified PRRSV strains, and their use as vaccine, are disclosed.

*Re: medical use*

- 2            Claims 13-19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment. Patentability, in

particular novelty and inventive step, of said claims has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the substance or composition.

*Re: novelty*

- 3 D2 (claims 1-9, 17, 22-29, examples 4, 5) discloses a live modified PRRSV, named PRRSV-CON (and referred to as SEQ ID NO: 1) which has 95.3% sequence identity to each of present SEQ ID NO: 4, 10, and 11, and confers protection to challenge by heterologous PRRSV. In view of D2, present claims 1, 2, 4-8, and 10-19 lack novelty. Present claims 3 and 9 are novel.

*Re: inventive step*

- 4 Claim 3 does not involve an inventive step. D2 disclosing PRRSV-CON can be taken as closest prior art. The difference is that the claimed PRRSV is 98% identical to SEQ ID NO: 4, 10, and 11, whereas PRRSV-CON is only 95.3% identical to said sequences. The objective technical problem was: the provision of a further live modified PRRSV. Motivation to solve the problem came from the ongoing search for improved PRRSV, e.g. having improved cross-protection (see D1, p. 4077). The skilled man could solve the problem in an obvious manner by passaging PRRSV isolates in cell culture, and testing them in heterologous challenge protocols (see D2, examples 4, 5). The solution according to claim 3 is therefore merely one of several equally obvious alternatives. The degree of cross-protection shown in the application does not amount to an unexpected effect, especially because it is not apparent that the same effect has not been achieved already in D2. For essentially the same reason, claim 9 lacks an inventive step, as well.

**Re Item VIII**

**Certain observations on the international application**

- 5      The term "*ND99-14*" in claims 4, 10, and 12 is an internal designation. It is not clear whether the term would relate only to SEQ ID NO: 4, 10, and 11, or also to variants with 90% sequence identity.