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Señora

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No 06-101162- -00003-0000

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Tra 11 PATENTEIYII Eje 378 FASENACIONALI
Act 329 CTOINFORMACION Folios 14

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E. S. D.

Referencia: Expediente No. 06.101.162

Solicitud de Patente de Invención titulada: "Atenuación sinérgica de virus de estomatitis vesicular, vectores de éstos y composiciones inmunogénicas de éstos"

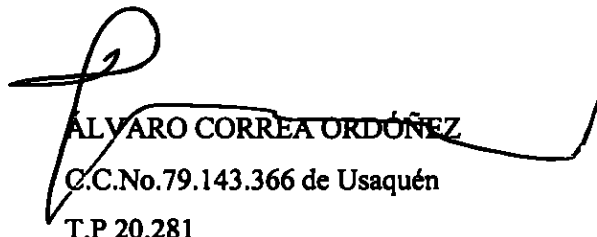
Solicitante Wyeth

MEMORIAL DE ALCANCE

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado según aparece al pie de mi firma, en mi condición de apoderado de la sociedad en referencia, manifiesto lo siguiente.

El día 06 de octubre de 2006, bajo el número de radicación 06 101.162, presenté la solicitud de patente de invención de la referencia, para la cual adjunto informe preliminar internacional sobre patentabilidad, capítulo I del tratado de cooperación en materia de patentes.

Atentamente,



ÁLVARO CORREA ORDÓÑEZ
C.C.No.79.143.366 de Usaquén
T.P 20.281

Anexo: Informe preliminar internacional sobre patentabilidad, capítulo I

NOV.18.2006 11:32AM

PATENT LAW 8456025848

PATENT COOPERATION TREATY

NO.567 P.2/14

PCT/US2005/011499

From the INTERNATIONAL BUREAU

CC: PRINCETON

PCT

NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)
(PCT Rule 44bis.1(c))

To:

OCT 26 2006

BRAZIL, BIL T.
Wyeth
Patent Law Department
Five Glaxo Farms
Madison, NJ 07940
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

19 October 2006 (19.10.2006)

Applicant's or agent's file reference

AM101651

IMPORTANT NOTICE

International application No.

PCT/US2005/011499

International filing date (day/month/year)

05 April 2005 (05.04.2005)

Priority date (day/month/year)

09 April 2004 (09.04.2004)

Applicant

WYETH et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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CAROL E. ROZEK
PATENT LAW DEPARTMENT
PEARL RIVER, NEW YORK

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Authorized officer

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Form PCT/IB/326 (January 2004)

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non-~~+~~

NOV.18.2006 11:32AM

PATENT LAW 8456025848

NO.567-2005P.2/14

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

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NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)
(PCT Rule 44bis.1(c))

To:	OCT 26 2006
BRAZIL, Bill, T. Wyeth Patent Law Department Five Giralda Farms Madison, NJ 07940 ETATS-UNIS D'AMERIQUE	

Date of mailing (day/month/year) 19 October 2006 (19.10.2006)		
Applicant's or agent's file reference AM101651		
IMPORTANT NOTICE		
International application No. PCT/US2005/011499	International filing date (day/month/year) 05 April 2005 (05.04.2005)	Priority date (day/month/year) 09 April 2004 (09.04.2004)
Applicant WYETH et al		

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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NOV 10 2006

CAROL E. ROZEK
PATENT LAW DEPARTMENT
PEARL RIVER, NEW YORK

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Philippe Becamel
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference AM101651	FOR FURTHER ACTION		See item 4 below
International application No PCT/US2005/011499	International filing date (day/month/year) 05 April 2005 (05.04.2005)	Priority date (day/month/year) 09 April 2004 (09.04.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant WYETH			

1	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a)																		
2	This REPORT consists of a total of 12 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead																		
3	This report contains indications relating to the following items <table border="0"> <tr> <td>☒ Box No I</td> <td>Basis of the report</td> </tr> <tr> <td>☐ Box No II</td> <td>Priority</td> </tr> <tr> <td>☒ Box No III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>☐ Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td>☒ Box No V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement</td> </tr> <tr> <td>☒ Box No VI</td> <td>Certain documents cited</td> </tr> <tr> <td>☐ Box No VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td>☒ Box No VIII</td> <td>Certain observations on the international application</td> </tr> </table>			☒ Box No I	Basis of the report	☐ 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 Article 35(2) with regard to novelty, inventive step or 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
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☒ Box No VI	Certain documents cited																		
☐ Box No VII	Certain defects in the international application																		
☒ Box No VIII	Certain observations on the international application																		
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis 2).																		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No +41 22 338 82 70		Date of issuance of this report 11 October 2006 (11.10.2006)
Form PCT/IB/373 (January 2004)		Authorized officer Philippe Becamel e-mail: pt12@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 18 NOV 2005

PCT

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To:

see form PCT/ISA/220

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/220FOR FURTHER ACTION
See paragraph 2 belowInternational application No
PCT/US2005/011499International filing date (day/month/year)
05.04.2005Priority date (day/month/year)
09.04.2004International Patent Classification (IPC) or both national classification and IPC
G12N15/86Applicant
WYETH

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 or 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"). However, 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 56.1bis(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 three 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.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA.



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/US2005/011499**Box No. I Basis of the opinion**

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, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☒ contained in the international application as filed
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/011499

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

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. 110-144

because,

☒ the said international application, or the said claims Nos. 110-144 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ 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.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/011499

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

1 Statement

Novelty (N)	Yes. Claims	9-12, 17-28, 38-41, 50-70, 80-83, 87, 89-109, 117-118, 128-144
	No. Claims	1-8, 13-16, 29-37, 42-49, 71-79, 84-86, 88, 110-116, 119-127
Inventive step (IS)	Yes. Claims	
	No. Claims	9-12, 17-28, 38-41, 50-70, 80-83, 87, 89-109, 117-118, 128-144
Industrial applicability (IA)	Yes. Claims	1-109
	No. Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1 Certain published documents (Rules 43bis.1 and 70.10)

and/or

2 Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain observations on the international application

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

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

Re item I

Basis of the report

- D1: ROSE N F ET AL: "An effective AIDS vaccine based on live attenuated vesicular stomatitis virus recombinants" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 106, no. 5, 7 September 2001 (2001-09-07), pages 539-549, XP002297996 ISSN: 0092-8674
- D2: WO 98/50529 A (THE UAB RESEARCH FOUNDATION) 12 November 1998 (1998-11-12)
- D3: HAGLUND K ET AL: "Expression of Human Immunodeficiency Virus Type 1 Gag Protein Precursor and Envelope Proteins from a Vesicular Stomatitis Virus Recombinant: High-Level Production of Virus-Like Particles Containing HIV Envelope" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 268, no. 1, 1 March 2000 (2000-03-01), pages 112-121, XP004436135 ISSN: 0042-6822
- D4: ROBERTS A ET AL: "Attenuated vesicular stomatitis viruses as vaccine vectors" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 73, no. 5, May 1999 (1999-05), pages 3723-3732, XP002266675 ISSN: 0022-538X
- D5: KAHN J S ET AL: "Replication-competent or attenuated, nonpropagating vesicular stomatitis viruses expressing respiratory syncytial virus (RSV) antigens protect mice against RSV challenge." JOURNAL OF VIROLOGY. NOV 2001, vol. 75, no. 22, November 2001 (2001-11), pages 11079-11087, XP002353198 ISSN: 0022-538X
- D6: FLANAGAN E B ET AL: "Rearrangement of the genes of vesicular stomatitis virus eliminates clinical disease in the natural host: new strategy for vaccine development." JOURNAL OF VIROLOGY. JUL 2001, vol. 75, no. 13, July 2001 (2001-07), pages 6107-6114, XP002353200 ISSN: 0022-538X
- D7: FLANAGAN E BRIAN ET AL: "Vesicular stomatitis viruses with rearranged genomes have altered invasiveness and neuropathogenesis in mice." JOURNAL OF VIROLOGY. MAY 2003, vol. 77, no. 10, May 2003 (2003-05), pages 5740-5748, XP002353201 ISSN: 0022-538X
- D8: US 2003/099671 A1 (FU ZHEN FANG) 29 May 2003 (2003-05-29)
- D9: WO 2004/113517 A (WYETH; PARKS, CHRISTOPHER, L; UDEM, STEPHEN, A; SIDHU, MODINDERJIT, S) 29 December 2004 (2004-12-29)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

D10 FINKE S ET AL: "Replication strategies of rabies virus" VIRUS RESEARCH, AMSTERDAM, NL, vol. 111, no. 2, August 2005 (2005-08), pages 120-131, XP004962561 ISSN: 0168-1702

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. For the assessment of the present claims 110-144 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

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

3. Novelty (Article 33 (2) PCT)

- 3.1 The present application states that the insertion of a foreign nucleic acid sequence (e.g., HIV gag) into the VSV genome 3' to any of the N, P, M, G or L genes effectively results in a "gene shuffling mutation". Thus, in certain embodiments, the two VSV vector mutations are G(stem) mutation and a gene shuffling mutation (see p.8 lines 14-18 and p.20 lines 20-22).

In certain embodiments of the application, a genetically modified VSV comprising at least two different classes of mutations in its genome comprises one or more ts N gene mutation(s) (hereinafter, "N (ts)") a first class of mutation and one or more ts L gene mutation(s) (hereinafter, "L(ts)") as a second class of mutation. By analogy rearrangements of a first and a second gene within the VSV genome are therefore embraced by this definition.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

3.2 WO9850529 describes an infectious cDNA clone of the prototypic vesicular stomatitis virus (VSV). It was manipulated to rearrange the order of four of the five viral genes. Infectious viruses were recovered from each of these rearranged cDNAs and examined for their levels of gene expression, growth potential in cell culture, and virulence in mice. Method of attenuating a virus and making them useful for vaccine are also disclosed (see p.3 to 4 and example 8, Table 3, especially example 22, Fig.1). Two differently rearranged genes are disclosed (see G1N2 or G1N4 in Figure 1).

Haglund et al. describes two genes that can be expressed simultaneously from a single, live-attenuated VSV recombinant. The genes used encode the Pr55<gag> protein precursor of HIV-1 (1.7-kb gene) and an HIV-1 envelope (Env) protein (2.4 kb gene) (see also Fig.1 VSVgagEnvG). This construct rearranges G gene towards a 5' position compared to their wild type position and replaces a second G gene with an Env insert except for a 29 amino acid VSV G cytoplasmic domain. This construct comprises a rearranged VSV G gene and a truncated form of one G gene in which an Env gene has been inserted.

Rose et al. tested the ability of VSV recombinants expressing Env and Gag proteins to immunize rhesus monkeys against the highly pathogenic SHIV 89.6P virus (see p.540 col.1 last paragraph). It used also boosting vectors that are based on the same attenuated VSV recombinant used in the first vaccinations, but have the VSV G protein (G1) replaced with either the G protein of the (GNJ) or (Gch). Since the G proteins include multiple differences at the amino acid sequence level (mutations), the construct used includes a gene shuffling mutation, due to the insertion of Gag and Env genes, and a G gene insertion and/or deletion mutation. No pathogenesis associated with these vectors were observed.

However if further attenuation is required there are also well characterized VSV deletion mutants that are completely or partially attenuated for pathogenesis in young mice (see p.547 col.1 first paragraph).

Roberts et al. describes VSV vectors expressing HA which are completely attenuated for pathogenesis in the mouse model. The first vector has a truncation of the cytoplasmic domain of the VSV G protein and expresses Influenza virus HA

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

(CT1-HA). A second vector with VSV G deleted and expressing HA (DeltaG-HA) is also protective (see abstract, p.3724 col.1 first full paragraph). The construct CT1-HA of Fig.1 comprises a truncated VSV G gene and an insertion of a heterologous gene between the CT1-G and L genes (see Fig.1).

Kahn et al. describes expression of RSV F and G glycoproteins in attenuated, nonpropagating VSVs which lack the VSV G gene (VSVDeltaG) and the incorporation of these RSV proteins into recombinant virions (see abstract). The VSVdeltaG-RSV F G construct of Fig.1 disclose a G deletion mutation and a M and/or L gene shuffling mutation.

In view of the content of these documents claims 1-8,13-16,29-37, 42-49, 71-79, 84-86, 88, 110-116, 119-127 lack novelty.

4. Inventive step (Article 33 (3) PCT)

- 4.1 Document Rose et al. is considered to represent the most relevant state of the art. It discloses VSV recombinants expressing ENV and Gag proteins to immunize rhesus monkeys against the highly pathogenic SHIV 89.6P virus (see also above item 3.2). The difference between the subject-matter of claim 9 and the content of Rose et al. is that it provides a different additional mutation which synergistically attenuate VSV pathogenicity.

The problem to be solved by the present invention may therefore be regarded as to obtain genetically modified, attenuated VSV mutants having significantly reduced (or eliminated) pathogenicity in mammals.

Starting with Rose et al. the skilled person would have known that if further attenuation is required there are also well characterized VSV deletion mutants that are completely or partially attenuated for pathogenesis in young mice (see p.547 col.1 first paragraph). The literature is replete of VSV attenuation methods.

Thus, to solve the problem posed, the skilled person would have combined the teaching of Rose et al. with any of the prior art additional way to attenuate VSV and would have combined said mutations within one construct. The skilled person would have even more been motivated to do so in view of the teaching of US20030099671, which discloses that avirulent rabies virus are constructed by reshuffling rabies virus

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

genes within the rabies virus genome, particularly by moving the G from the fourth position to the first position and reshuffling the P, M and G genes. In addition, the G mutation at arginine 333 is incorporated into each and every reshuffled virus to further attenuate the rabies virus.

Thus, the solution proposed in claim 9 of the present application does not seem to involve an inventive step.

- 4.2 The same conclusion applies to independent claims relating to vectors, immunogenic compositions, method of immunizing a mammalian host and to their dependent claims which introduces modifications which amounts to a selection among different mutations types generally known to the person skilled in the art to be interchangeable. Thus, claims 10-12, 17-28, 38-41, 50-70, 80-83, 87, 89-109, 117-118, 128-144 lack an inventive step.

5. Industrial applicability (Article 34(4)(a)(I) PCT)

- 5.1 Claims 110-144 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2004/1135517	29.12.2004	8.6.2004	9.6.2003

6. WO2004/1135517 discloses rVSVs. Various additional constructs have been generated and recovered using the plasmid T7/electroporation/heat shock method.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/011499

After these rVSV recombinants are rescued, replication rates are examined in vitro, and relative virulence is evaluated in small animal model systems predictive of activity (e. g. , attenuation and immunogenicity) in humans, to determine whether the virus is attenuated sufficiently for use in immunogenic compositions and methods of the invention. Table 8 sets forth various exemplary, attenuated rVSV strains that were rescued according to these methods. Table 9 discloses also other VSV vectors expressing RSV glycoproteins.

Re Item VIII

Certain observations on the international application

7. Clarity (Article 6 PCT)

- 7.1 Claim 1 relates to a product. This product is not characterized by means of its essential features, but only in that it contains two different classes of type of mutations. The claimed product is functionally characterized in that it has to synergistically have an attenuated pathogenicity.
- 7.2 Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. All the constructs satisfying this functional requirement are covered. The technical features necessary for achieving this result must however still be identified in the claim.
- 7.3 It is furthermore unclear in which host the pathogenicity has to be measured and how this pathogenicity has to be experimentally assessed.
- 7.4 It is stressed that claimed products characterized additionally by parameters, which have not been measured in the prior art, while otherwise identical to the prior art products are nevertheless considered to be anticipated by said prior art products, until technical features distinguishing them from the prior art are introduced (see PCT Guidelines Chapter 12 paragraph 12.04).

**WRITTEN OPINION OF THE
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International application No.

PCT/US2005/011499

8 Support (Article 6 PCT)

- 8.1 Claim 1 relates to a VSV construct comprising at least two different classes of mutations in its genome. The mutations was selected from temperature sensitive mutation, gene shuffling mutation, G-stem mutation, non-cytopathic M gene mutation, ambisense RNA mutation, truncation of G gene, a G gene insertion and deletion mutation. The engineered VSV virus shows a synergistically attenuated VSV pathogenicity.

Disregarding the fact that neither the host nor how the attenuated pathogenicity has to be assessed is identified in the claim, the claimed subject-matter is directed to any double mutated VSV wherein the two different mutations leads to synergistically attenuated VSV pathogenicity. There are many examples of mutated VSV in the prior art. However, the present description states that currently available attenuated VSV vectors retain residual virulence when tested in animal models, and as such, are not likely vector candidates for advancement to human clinical trials (see p.16 lines 31-33). Thus, a majority of examples in prior art VSV covered by the claim do not achieve the technical effect underlying the present application.

According to Article 6 PCT the claimed protection should correspond to the technical contribution to the art made by the disclosure of the invention described therein, which excludes protection being extended to subject-matter which, after reading the application, would still not be at the disposal of the skilled person. The available information must therefore enable the skilled person to achieve the envisaged result within the whole ambit of the claim. Hence, this is not the case.

As a consequence, claim 1 lacks support.