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8 January 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NOVEL VACCINE COMPOSITIONS AND METHODS OF VACCINE PREPARATION FOR VETERINARY AND HUMAN DISEASES

(57) Abstract: The anti-pathogen vaccine of the present invention is produced in recombinant bacteria and/or transgenic plants and then administered through standard vaccine introduction method or through standard vaccine introduction method or through the oral administration. A DNA sequence encoding for the expression of an antigen of a pathogen is isolated and ligated to a promoter which can regulate the production of the surface antigen in a bacterial or transgenic plant. Preferably, a foreign gene is expressed in a portion of the plant or bacteria, and all or part of the antigen expressing plant or bacteria used for vaccine administration. In a preferred procedure, the vaccine is administered through the consumption of the edible plant as food, or the bacteria administered orally.



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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K39/187 A61K39/215 A61K39/12 C12N15/82 C07K14/165
 C07K14/18 C07K14/03 C07K14/08

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)
 IPC 7 C12N A61K C07K

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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KIM HYUNSOON ET AL: "Expression of hog cholera virus in transgenic potato plants." PLANT BIOLOGY (ROCKVILLE), vol. 2001, 2001, page 142, XP001161300 Joint Annual Meetings of the American Society of Plant Biologists and the Canadian Society of Plant Physiologists; Providence, Rhode Island, USA; July 21-25, 2001	1-3,5,8, 9,12,13, 16,17, 19,20, 23-27
Y	the whole document ----- -/--	4,14

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° 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 document 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

Date of the actual completion of the international search

4 August 2003

Date of mailing of the international search report

10. 11. 2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/25126

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>VAN GENNIP A H G P ET AL: "Chimeric classical swine fever viruses containing envelope protein E or E2 of bovine viral diarrhoea virus protect pigs against challenge with CSFV and induce a distinguishable antibody response" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 19, no. 4-5, 15 October 2000 (2000-10-15), pages 447-459, XP004218115 ISSN: 0264-410X the whole document</p>	4,14
A	<p>WO 99 08706 A (HAMMOND JEFFREY MICHAEL ;JOHNSON MICHAEL ANTHONY (AU); COMMW SCIEN) 25 February 1999 (1999-02-25) page 17 - page 18</p>	
A	<p>HULST M M ET AL: "Glycoprotein E1 of hog cholera virus expressed in insect cells protects swine from hog cholera" JOURNAL OF VIROLOGY, NEW YORK, US, US, vol. 67, no. 9, 1 September 1993 (1993-09-01), pages 5435-5442, XP002080070 ISSN: 0022-538X the whole document</p>	
A	<p>VAN RIJN P A ET AL: "An experimental marker vaccine and accompanying serological diagnostic test both based on envelope glycoprotein E2 of classical swine fever virus (CSFV)" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 17, no. 5, February 1999 (1999-02), pages 433-440, XP004153825 ISSN: 0264-410X the whole document</p>	
A	<p>WIGDOROVITZ A ET AL: "Induction of a Protective Antibody Response to Foot and Mouth Disease Virus in Mice Following Oral or Parenteral Immunization with Alfalfa Transgenic Plants Expressing the Viral Structural Protein VP1" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 255, no. 2, 15 March 1999 (1999-03-15), pages 347-353, XP004440022 ISSN: 0042-6822 the whole document</p>	
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/25126

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>STREATFIELD S J ET AL: "Plant-based vaccines: unique advantages" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 19, no. 17-19, 21 March 2001 (2001-03-21), pages 2742-2748, XP004231106 ISSN: 0264-410X page 2745, right-hand column</p>	
A	<p>TUBOLY T ET AL: "Immunogenicity of porcine transmissible gastroenteritis virus spike protein expressed in plants" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 18, no. 19, April 2000 (2000-04), pages 2023-2028, XP004202498 ISSN: 0264-410X the whole document</p>	
A	<p>PLANA DURAN ET AL: "Baculovirus expression of proteins of Reproductive and Respiratory Syndrome Virus strain Olot/91. Involvement of ORF3 and ORF5 proteins in protection" VIRUS GENES, KLUWER ACADEMIC PUBLISHERS, BOSTON, US, vol. 14, no. 1, 1997, pages 19-29, XP002103647 ISSN: 0920-8569</p>	
A	<p>LAFAYETTE PETER R ET AL: "Engineering soybeans for the production of edible vaccines for poultry." PLANT BIOLOGY (ROCKVILLE), vol. 2000, 2000, page 138, XP002250043 Annual Meeting of the American Society of Plant Physiologists; San Diego, California, USA; July 15-19, 2000 the whole document</p>	
A	<p>WO 94 20135 A (EDIBLE VACCINES INC ; LAM DOMINIC MAN KIT (US); ARNTZEN CHARLES JOE) 15 September 1994 (1994-09-15) the whole document</p>	
A	<p>DANIELL H ET AL: "MEDICAL MOLECULAR FARMING: PRODUCTION OF ANTIBODIES, BIOPHARMACEUTICALS AND EDIBLE VACCINES IN PLANTS" TRENDS IN PLANT SCIENCE, ELSEVIER SCIENCE, OXFORD, GB, vol. 6, no. 5, May 2001 (2001-05), pages 219-226, XP001037864 ISSN: 1360-1385</p>	

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	CHAN CAROL W M ET AL: "Expression of Hog Cholera Virus E2 in transgenic Arabidopsis." PLANT BIOLOGY (ROCKVILLE), vol. 2002, 2002, page 57, XP002250044 Annual Meeting of the American Society of Plant Biologists on Plant Biology; Denver, CO, USA; August 03-07, 2002, 2002 the whole document	12,13, 15, 17-20, 24-26
P,X	----- EP 1 293 573 A (MALTAGEN FORSCHUNG GMBH) 19 March 2003 (2003-03-19) the whole document -----	1-3,5,8, 9,12,13, 16,17, 19,20, 24-27

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:
Claim 19 is identical to claim 17. Moreover, claim 22 is referring to the hog cholera virus; said claim should rather refer to the IBDV virus and was searched accordingly. Claim 26 was searched with respect to "Agrobacterium"-mediated transformation and not Arabidopsis-mediated
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 II Observations where unity of invention is lacking (Continuation of item 2 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 fee, this Authority did not invite payment of any additional fee.
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.:

see FURTHER INFORMATIN sheet, invention 1.

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: -

Claim 19 is identical to claim 17. Moreover, claim 22 is referring to the hog cholera virus; said claim should rather refer to the IBDV virus and was searched accordingly. Claim 26 was searched with respect to "Agrobacterium"-mediated transformation and not Arabidopsis-mediated transformation.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4,8,12,13,14,15,16-19,23-28 partially, 5,9,20, completely

Orally acceptable immunogenic composition comprising recombinant HCV expressed in a plant wherein said immunogen is highly expressed to confer oral immunisation by interaction with the mucosal membrane; a vaccine comprising said immunogen, a plant composition comprising said viral immunogen, a transgenic expressing said immunogen, a vaccine composition comprising said immunogen, a food comprising said transgenic plant material, a method for constructing a transgenic plant cell by constructing a vector comprising said immunogen specific DNA sequence and transforming said plant cell with said vector, a method for producing a pharmaceutical vaccine composition comprising the steps of constructing a DNA vector, transforming a plant with said vector and recovering said vaccine composition from said plant.

2. claims: 1-4,8,12,13,14,15,16-19,23-28 partially, 7,11,22 completely

Orally acceptable immunogenic composition comprising recombinant IBV expressed in a plant wherein said immunogen is highly expressed to confer oral immunisation by interaction with the mucosal membrane; a vaccine comprising said immunogen, a plant composition comprising said viral immunogen, a transgenic expressing said immunogen, a vaccine composition comprising said immunogen, a food comprising said transgenic plant material, a method for constructing a transgenic plant cell by constructing a vector comprising said immunogen specific DNA sequence and transforming said plant cell with said vector, a method for producing a pharmaceutical vaccine composition comprising the steps of constructing a DNA vector, transforming a plant with said vector and recovering said vaccine composition from said plant.

3. claims: 1-4,12 partially,

Orally acceptable immunogenic composition comprising recombinant IBV expressed in a plant wherein said immunogen is highly expressed to confer oral immunisation by interaction with the mucosal membrane; a plant composition comprising said viral immunogen.

4. claims: 1-4,12 partially,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Orally acceptable immunogenic composition comprising recombinant ILTV expressed in a plant wherein said immunogen is highly expressed to confer oral immunisation by interaction with the mucosal membrane; a plant composition comprising said viral immunogen.

5. claims: 1-4,8,12,13,14,15,16-19,23-28 partially, 6,10,21 completely

Orally acceptable immunogenic composition comprising recombinant PRRSV expressed in a plant wherein said immunogen is highly expressed to confer oral immunisation by interaction with the mucosal membrane; a vaccine comprising said immunogen, a plant composition comprising said viral immunogen, a transgenic expressing said immunogen, a vaccine composition comprising said immunogen, a food comprising said transgenic plant material, a method for constructing a transgenic plant cell by constructing a vector comprising said immunogen specific DNA sequence and transforming said plant cell with said vector, a method for producing a pharmaceutical vaccine composition comprising the steps of constructing a DNA vector, transforming a plant with said vector and recovering said vaccine composition from said plant.

6. claims: 29-34,35,39-41 partially , 36 completely

Immunogenic composition comprising recombinant HCV immunogen expressed in bacteria, a vaccine comprising an immunogen of HCV expressed in bacteria, a method for producing an immunogenic response to an immunogen comprising the steps of expressing the recombinant immunogen in bacteria at a level such that upon administration to an animal, an immunogenic response is observed.

7. claims: 29-34,35,39-41 partially , 38 completely

Immunogenic composition comprising recombinant IBDV immunogen expressed in bacteria, a vaccine comprising an immunogen of HCV expressed in bacteria, a method for producing an immunogenic response to an immunogen comprising the steps of expressing the recombinant immunogen in bacteria at a level such that upon administration to an animal, an immunogenic response is observed.

8. claims: 29-34,39-41 partially , completely

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Immunogenic composition comprising recombinant IBV immunogen expressed in bacteria, a method for producing an immunogenic response to an immunogen comprising the steps of expressing the recombinant immunogen in bacteria at a level such that upon administration to an animal, an immunogenic response is observed.

9. claims: 29-34,39-41 partially , completely

Immunogenic composition comprising recombinant ILTV immunogen expressed in bacteria, a method for producing an immunogenic response to an immunogen comprising the steps of expressing the recombinant immunogen in bacteria at a level such that upon administration to an animal, an immunogenic response is observed.

10. claims: 29-34,35,39-41 partially , 37completely

Immunogenic composition comprising recombinant PRRSV immunogen expressed in bacteria, a vaccine comprising an immunogen of HCV expressed in bacteria, a method for producing an immunogenic response to an immunogen comprising the steps of expressing the recombinant immunogen in bacteria at a level such that upon administration to an animal, an immunogenic response is observed.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/25126

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