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- (71) **Applicant:** THE REPUBLICAN GOVERNMENT ENTERPRISE ON THE BASIS OF ECONOMIC CONTROL RIGHTS "RESEARCH INSTITUTE FOR BIOLOGICAL SAFETY PROBLEMS" OF THE SCIENCE COMMITTEE OF THE MINISTRY OF EDUCATION AND SCIENCE OF THE REPUBLIC OF KAZAKHSTAN [KZ/KZ]; Gvardeiskiy, Kordaiskiy region, Zhambylskaya obl., 080409 (KZ).
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- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

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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))

- (88) **Date of publication of the international search report:**
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(54) **Title:** CONSORTIUM OF THE RECOMBINANT INFLUENZA A VIRUSES FLU-NSI-124- L7/L12-H5N1, FLU-NSI-124-OMP16-H5N1, FLU-NSI-124-L7/L12-H1N1 AND FLU-NSI- 124-OMP16-H1N1, FAMILY ORTOMYXOVIRIDAE, GENUS INFLUENZAVIRUS, EXPRESSING BRUCELLA IMMUNODOMINANT PROTEINS DESTINED TO GENERATE A VACCINE AGAINST BRUCELLOSIS

(57) **Abstract:** This invention relates to the fields of biotechnology, veterinary science and public health, and describes a vector vaccine which can be used to prevent brucellosis. The essence of the invention is that reverse genetics methods have been used to construct novel, genetically-stable recombinant influenza viral vectors based on the influenza A viral vectors Flu-NSI-124-L7/L12-H5N1, Flu-NSI-124-Omp16-H5N1, Flu-NSI-124-L7/L12-H1N1 and Flu-NSI-124-Omp16- H1N1 (of the subtypes H5N1 and H1N1) that contain the genetic sequences of the *Brucella* proteins L7/L12 (ribosomal) or Omp16 (outer membrane) inserted into the viral NSI gene, which express these *Brucella* proteins *in vivo* and are safe in cattle. Our studies showed that this vaccine candidate in cattle induced a strong antigen-specific T-cell immune response, and most importantly provided a high level of protectiveness comparable to the commercial *B. abortus* S19 vaccine and superior to the *B. abortus* S19 vaccine in combination with Montanide Gel01 adjuvant. Furthermore it is shown that the developed vaccines can effectively differentiate vaccinated animals from infected animals.



INTERNATIONAL SEARCH REPORT

International application No

PCT/KZ2014/000006

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K39/02

ADD. A61K39/00

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

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, BIOSIS, CHEM ABS Data, EMBASE, SCISEARCH, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE WPI Week 201309 Thomson Scientific, London, GB; AN 2013-A78536 XP002736123, & CN 102 703 505 A (LANZHOU VETERINARY RES INST CHINA AGRIC) 3 October 2012 (2012-10-03) the whole document ----- -/-	1

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

☒ See patent family 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 application or patent 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

18 February 2015

Date of mailing of the international search report

10/03/2015

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/KZ2014/000006

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CABRERA A ET AL: "Vaccination with recombinant Semliki Forest virus particles expressing translation initiation factor 3 of Brucella abortus induces protective immunity in BALB/c mice", IMMUNOBIOLOGY, URBAN UND FISCHER VERLAG, DE, vol. 214, no. 6, 1 June 2009 (2009-06-01), pages 467-474, XP026097400, ISSN: 0171-2985, DOI: 10.1016/J.IMBIO.2008.11.016 [retrieved on 2009-01-17] page 470; table 1 -----	1
Y	D. LUO ET AL: "Protective Immunity Elicited by a Divalent DNA Vaccine Encoding Both the L7/L12 and Omp16 Genes of Brucella abortus in BALB/c Mice", INFECTION AND IMMUNITY, vol. 74, no. 5, 1 May 2006 (2006-05-01), pages 2734-2741, XP055072846, ISSN: 0019-9567, DOI: 10.1128/IAI.74.5.2734-2741.2006 page 2737 - page 2738 table 2 -----	1
Y	SEREINIG S ET AL: "Influenza virus NS vectors expressing the mycobacterium tuberculosis ESAT-6 protein induce CD4+ Th1 immune response and protect animals against tuberculosis challenge", CLINICAL AND VACCINE IMMUNOLOGY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 13, no. 8, 1 August 2006 (2006-08-01), , pages 898-904, XP002604135, ISSN: 1556-6811, DOI: 10.1128/CVI.00056-06 page 901 tables 1,2 -----	1
A	EP 2 535 405 A1 (REPULICAN GOVERNMENTAL ENTPR ON THE RIGHT OF ECONOMIC MAN RES INST FOR) 19 December 2012 (2012-12-19) claim 1 -----	1
A	OLIVEIRA SÉRGIO COSTA ET AL: "Confronting the barriers to develop novel vaccines against brucellosis.", EXPERT REVIEW OF VACCINES SEP 2011, vol. 10, no. 9, September 2011 (2011-09), pages 1291-1305, XP002736124, ISSN: 1744-8395 the whole document ----- -/--	1

INTERNATIONAL SEARCH REPORT

International application No

PCT/KZ2014/000006

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	TABYNOV KAISSAR ET AL: "Novel influenza virus vectors expressing Brucella L7/L12 or Omp16 proteins in cattle induced a strong T-cell immune response, as well as high protectiveness against B. abortus infection", VACCINE, vol. 32, no. 18, 2 March 2014 (2014-03-02) , pages 2034-2041, XP028838503, ISSN: 0264-410X, DOI: 10.1016/J.VACCINE.2014.02.058 the whole document	1
X,P	----- KAISSAR TABYNOV ET AL: "Influenza viral vectors expressing the Brucella OMP16 or L7/L12 proteins as vaccines against B. abortus infection", VIROLOGY JOURNAL, BIOMED CENTRAL, LONDON, GB, vol. 11, no. 1, 10 April 2014 (2014-04-10) , page 69, XP021182141, ISSN: 1743-422X, DOI: 10.1186/1743-422X-11-69 the whole document -----	1

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KZ2014/000006

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 and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. (means)

☒

 on paper
 - ☒

 in electronic form
 - b. (time)

☐

 in the international application as filed
 - ☐

 together with the international application in electronic form
 - ☒

 subsequently to this Authority for the purpose of search
2.

☒

 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.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/KZ2014/000006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 102703505	A	03-10-2012	NONE

EP 2535405	A1	19-12-2012	EP 2535405 A1 19-12-2012
		WO 2011074928 A1	23-06-2011
