



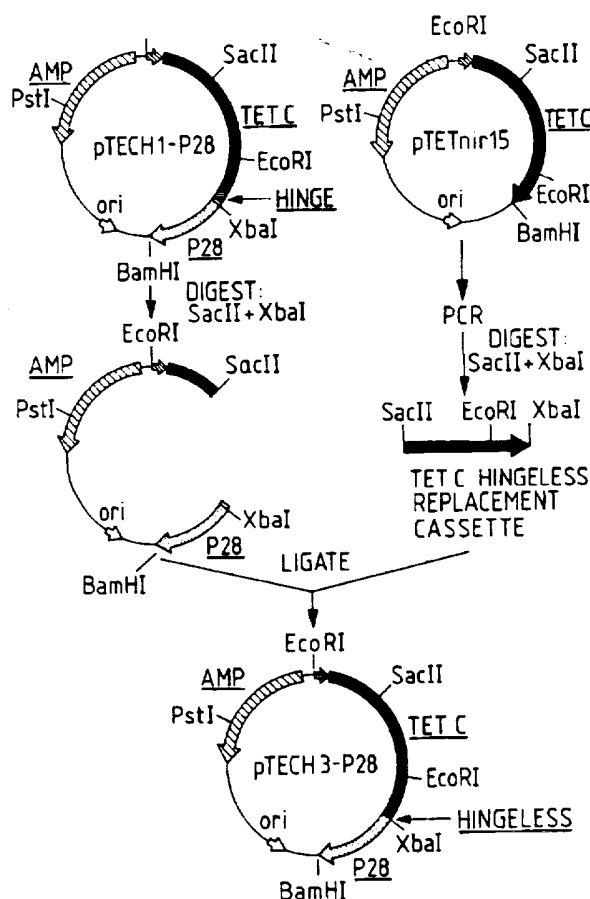
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/GB94/01647		(74) Agents: HUTCHINS, Michael, Richard et al.; Fry Heath & Spence, St. Georges House, 6 Yattendon Road, Horley, Surrey RH6 7BS (GB).	
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(71) Applicant (for all designated States except US): MEDEVA HOLDINGS B.V. [NL/NL]; Churchill-Laan 223, NL-1078 ED Amsterdam (NL).		Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(72) Inventors; and (75) Inventors/Applicants (for US only): KHAN, Mohammed, Anjam [GB/GB]; Cambridge University Dept. of Pathology, Tennis Court Road, Cambridge CB2 1QP (GB). HOR-MAECHE, Carlos, Estenio [GB/GB]; Cambridge University Dept. of Pathology, Tennis Court Road, Cambridge CB2 1QP (GB). CHATFIELD, Steven, Neville [GB/GB]; Medeva Vaccine Research Unit, Dept. of Biochemistry, Imperial College of Science and Technology, London SW7 2AY (GB). DOUGAN, Gordon [GB/GB]; Medeva Vaccine Research Unit, Dept. of Biochemistry, Imperial College of Science and Technology, London SW7 2AY (GB).		(88) Date of publication of the international search report: 16 March 1995 (16.03.95)	

(54) Title: VACCINE COMPOSITIONS CONTAINING RECOMBINANT TETC-FUSION PROTEINS

(57) Abstract

The invention provides a DNA construct comprising a DNA sequence encoding a fusion protein of the formula: TetC-(Z)_a-Het, wherein: TetC is the C fragment of tetanus toxin, or a protein comprising the epitopes thereof; Het is a heterologous protein, Z is an amino acid, and a is zero or a positive integer, provided that (Z)_a does not include the sequence Gly-Pro. The invention also provides replicable expression vectors containing the constructs, bacteria transformed with the constructs, the fusion proteins *per se* and vaccine compositions formed from the fusion proteins or attenuated bacteria expressing the fusion proteins.



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INTERNATIONAL SEARCH REPORT

Intern al Application No

PCT/GB 94/01647

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/62 C12N15/31 C12N15/54 C12N1/21 A61K38/45
 //(C12N1/21, C12R1:42)

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 6 C12N 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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,89 06974 (PRAXIS BIOLOGICS, INC.) 10 August 1989 see page 25, line 12 - page 26, line 9 see page 26, line 25 - page 27, line 14 see page 76, line 1 - page 81, line 4; claims 1-107; tables 12-15 ---	1-14
Y	EP,A,0 432 965 (SMITHKLINE BEECHAM) 19 June 1991 see page 3, line 49 - line 58 see page 5, line 2 - line 4 see page 16, line 24 - line 29 --- -/--	1-14

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

☒ Patent family members are listed in annex.

* Special categories of cited documents:

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search

24 January 1995

Date of mailing of the international search report

15 01 95

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax (+31-70) 340-3016

Authorized officer

Hornig, H

INTERNATIONAL SEARCH REPORT

Intern al Application No

PCT/GB 94/01647

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BIO/TECHNOLOGY, vol.10, no.8, August 1992, NATURE AMERICA, INC., NEW YORK, US; pages 888 - 892 S.N. CHATFIELD ET AL. 'Use of the nirB promoter to direct the stable expression of heterologous antigens in Salmonella oral vaccine strains: Development of a single-dose oral tetanus vaccine' see page 888, right column, line 22 - page 889, left column, line 28 see page 891, left column, line 39 - line 46 ---	1-14
Y	WO,A,92 15689 (THE WELLCOME FOUNDATION LIMITED) 17 September 1992 cited in the application see page 8, line 2 - page 9, line 26; claims 1-12 see page 11, line 20 - line 35 ---	1-14
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A	NUCLEIC ACIDS REASEARCH, vol.19, no.11, 11 June 1991, IRL,OXFORD UNIVERSITY PRESS, UK; pages 2889 - 2892 M.D. OXER ET AL. 'High level heterologous expression in E. coli using the anaerobically-activated nirB promoter' see page 2890, left column, paragraph 4 - page 2892, right column, line 19 ---	1-14
A	WO,A,91 09621 (INSTITUT PASTEUR) 11 July 1991 the whole document ---	1-14
A	WO,A,93 08290 (UNIVERSITY OF SASKATCHEVAN) 29 April 1993 see page 3, line 32 - page 5, line 2 see page 16, line 29 - page 17, line 7 ---	1-14

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INTERNATIONAL SEARCH REPORT

Intern al Application No

PCT/GB 94/01647

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FEMS SYMPOSIUM, NO. 73. BACTERIAL PROTEIN TOXINS; GUSTAV FISCHER VERLAG: STUTTGART, GERMANY; 0 (0). 1994 FREER, J. ET AL (ED.) 6th European Workshop, Stirling, Scotland, UK, June 27- July 2, 1993; the whole document -----	1-14
P,X, L	WO,A,94 03615 (MEDEVA HOLDINGS B.V.) 17 February 1994 cited in the application see claims 1-24 -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB94/01647

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:
Remark: Although claim 14 is directed to a method of treatment of the human body the search has been carried out and based on the alleged effects of the compound/composition.
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 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:

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.:

Remark on Protest

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 94/01647

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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