

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
5 July 2001 (05.07.2001)

PCT

(10) International Publication Number  
**WO 01/47962 A3**

(51) International Patent Classification<sup>7</sup>: **C07K 14/255**,  
C12N 1/21, C12R 1/42, C12N 15/31, A61K 35/74

(21) International Application Number: PCT/GB00/05002

(22) International Filing Date:  
22 December 2000 (22.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
9930457.8 23 December 1999 (23.12.1999) GB  
9930460.2 23 December 1999 (23.12.1999) GB  
9930455.2 23 December 1999 (23.12.1999) GB  
9930456.0 23 December 1999 (23.12.1999) GB  
9930459.4 23 December 1999 (23.12.1999) GB  
9930458.6 23 December 1999 (23.12.1999) US  
9930461.0 23 December 1999 (23.12.1999) GB

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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:  
10 May 2002

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.

WO 01/47962 A3

(54) Title: ATTENUATED MICROORGANISMS FOR THE TREATMENT OF INFECTION

(57) Abstract: Double mutant *Salmonella* microorganisms help prevent reactivity of the microorganism while maintaining the effectiveness of the microorganism to elicit an immune response. Various specific combinations of mutants are beneficial.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/G. 00/05002

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 C07K14/255 C12N1/21 C12R1/42 C12N15/31 A61K35/74

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 C12R 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SHEA JACQUELINE E ET AL: "Influence of the Salmonella typhimurium pathogenicity island 2 Type III secretion system on bacterial growth in the mouse" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, US, vol. 67, no. 1, January 1999 (1999-01), pages 213-219, XP002151954 ISSN: 0019-9567 abstract; table 1 --- -/--	1,4,9-14

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

1 June 2001

Date of mailing of the international search report

14. 8. 01

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CEDER 0.

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/05002

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>SCHOEDEL F ET AL: "HEPATITIS B VIRUS NUCLEOCAPSID/PRE-S2 FUSION PROTEINS EXPRESSED IN ATTENUATED SALMONELLA FOR ORAL VACCINATION"            JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US,            vol. 145, no. 12,            15 December 1990 (1990-12-15), pages 4317-4321, XP000960317            ISSN: 0022-1767            abstract</p> <p style="text-align: center;">---</p>	1,4,6,7
A	<p>EP 0 400 958 A (LISTER PREVENTIVE MED ;ROYAL SOCIETY (GB); UNIV DUNDEE (GB); WELLC) 5 December 1990 (1990-12-05)            abstract; claims 4,7-9            page 3, line 6 - line 11</p> <p style="text-align: center;">---</p>	1,4,9, 10,13,14
A	<p>HENSEL M ET AL: "FUNCTIONAL ANALYSIS OF SSAJ AND THE SSAK/U OPERON, 13 GENES ENCODING COMPONENTS OF THE TYPE III SECRETION APPARATUS OF SALMONELLA PATHOGENICITY ISLAND 2"            MOLECULAR MICROBIOLOGY, GB, BLACKWELL SCIENTIFIC, OXFORD,            vol. 24, no. 1, 1997, pages 155-167, XP002922652            ISSN: 0950-382X            cited in the application            abstract            page 156, left-hand column</p> <p style="text-align: center;">---</p>	1,4
A	<p>CHATFIELD S N ET AL: "LIVE SALMONELLA AS VACCINES AND CARRIERS OF FOREIGN ANTIGENIC DETERMINANTS"            VACCINE, GB, BUTTERWORTH SCIENTIFIC, GUILDFORD,            vol. 7, no. 6,            1 December 1989 (1989-12-01), pages 495-498, XP000087291            ISSN: 0264-410X</p> <p style="text-align: center;">---</p>	
A	<p>LEVINE M M ET AL: "Attenuated Salmonella as live oral vaccines against typhoid fever and as live vectors"            JOURNAL OF BIOTECHNOLOGY, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM,            vol. 44, no. 1,            26 January 1996 (1996-01-26), pages 193-196, XP004036865            ISSN: 0168-1656            abstract</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 00/05002

## 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:
  
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.:

1,4,6-14 all partially

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

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

1. Claims: 1, 4, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are ssaV and clpP.

2. Claims: 1, 4, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are ssaV and ompR.

3. Claims: 1, 4, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are ssaV and sifA.

4. Claims: 1, 4, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are ssaV and sseC.

5. Claims: 1, 6-14 partially and 5 in totality

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are ssaT and ssaB.

6. Claims: 2, 3, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are aroC and clpP.

7. Claims: 2, 3, 6-14 all partially

A Salmonella microorganism having attenuating mutations in two genes, and its uses in therapy and as a vaccine, wherein the mutated genes are aroC and sifA.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/GB 00/05002
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0400958 A	05-12-1990	AT 127694 T	15-09-1995
		DE 69022290 D	19-10-1995
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		JP 3024982 B	27-03-2000
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