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**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv))

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21 December 2006

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: CONTROLLED PRODUCTION AND DELIVERY OF BIOLOGICALLY ACTIVE AGENTS BY GUT BACTERIA

(57) Abstract: The invention provides gut commensal bacteria that have been modified to express one or more biologically active polypeptides or protiens, the bacteria includes a promoter, such as a xylanase promoter, which is induced in response to the presence of xylan in the diet and which regulates the expression of the biologically active polypeptide or protien.



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# INTERNATIONAL SEARCH REPORT

International application No  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b>				
INV. C12N15/74	C12N1/21	A61K38/17 A61K35/74		
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b>				
Minimum documentation searched (classification system followed by classification symbols) A61K C12N				
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, BIOSIS, EMBASE, SCISEARCH				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	EP 0 965 641 A (SOCIETE DES PRODUITS NESTLE S.A) 22 December 1999 (1999-12-22) claims	1,2,4-10		
X	<p style="text-align: center;">-----</p> WHITEHEAD T R ET AL: "HETEROLOGOUS EXPRESSION OF THE BACTEROIDES-RUMINICOLA XYLANASE GENE IN BACTEROIDES-FRAGILIS AND BACTEROIDES-UNIFORMIS" FEMS MICROBIOLOGY LETTERS, vol. 66, no. 1-3, 1990, pages 61-66, XP009071498 ISSN: 0378-1097 the whole document <p style="text-align: center;">-----</p> <p style="text-align: center;">-/--</p>	1-8		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <span style="margin-left: 200px;"><input checked="" type="checkbox"/> See patent family annex.</span>				
* Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </td> <td style="width: 50%; border: none; vertical-align: top;"> <p>"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</p> <p>"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</p> <p>"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.</p> <p>"&amp;" document member of the same patent family</p> </td> </tr> </table>			<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&amp;" document member of the same patent family</p>
<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&amp;" document member of the same patent family</p>			
Date of the actual completion of the international search		Date of mailing of the international search report		
25 August 2006		19/09/2006		
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  Chakravarty, A		

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2006/000222

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>STEIDLER L ET AL: "Biological containment of genetically modified Lactococcus lactis for intestinal delivery of human interleukin 10" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 21, no. 7, July 2003 (2003-07), pages 785-789, XP002276104 ISSN: 1087-0156 the whole document</p>	1-21
A	<p>STEIDLER L ET AL: "Treatment of murine colitis by Lactococcus lactis secreting interleukin-10" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 289, no. 5483, 25 August 2000 (2000-08-25), pages 1352-1355, XP002208404 ISSN: 0036-8075 cited in the application</p>	
A	<p>SELINGER L B ET AL: "The rumen: a unique source of enzymes for enhancing livestock production." ANAEROBE. OCT 1996, vol. 2, no. 5, October 1996 (1996-10), pages 263-284, XP002396325 ISSN: 1075-9964 page 271, column 2, paragraph 2 - page 274, column 2, paragraph 2</p>	
P,X	<p>FARRAR M D ET AL: "Engineering of the gut commensal bacterium Bacteroides ovatus to produce and secrete biologically active murine interleukin-2 in response to xylan." JOURNAL OF APPLIED MICROBIOLOGY. 2005, vol. 98, no. 5, May 2005 (2005-05), pages 1191-1197, XP002396180 ISSN: 1364-5072 the whole document</p>	1-21

# INTERNATIONAL SEARCH REPORT

International application No.  
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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 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:  

Although claims 16-2 are directed to a method of treatment of the human/animal 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 III Observations where unity of invention is lacking (Continuation of item 3 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/GB2006/000222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0965641	A	EP 0564965 A2	13-10-1993