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**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

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(88) Date of publication of the international search report:  
27 October 2005

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: METHODS FOR IMAGING THE LYMPHATIC SYSTEM USING DENDRIMER-BASED CONTRAST AGENTS

(57) Abstract: Methods are disclosed for lymphatic-system imaging using dendrimer conjugates as contrast agents. The disclosed methods are applicable to the imaging of all lymphatic structures, but in particular embodiments are particularly suited for imaging specific parts of the lymphatic system such as lymph nodes or lymphatic vessels. The methods permit the assessment of abnormal conditions within the lymphatic system, such as lymphoma/lymphoproliferative disease, inflammation, and cancer metastasis. The methods also may be used to identify and locate lymph nodes into which lymph fluid flows from a tumor.



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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/001388

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 A61K49/00				
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) IPC 7 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)  EPO-Internal, WPI Data, PAJ, EMBASE, BIOSIS				
<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	KOBAYASHI HISATAKA ET AL: "Comparison of dendrimer-based macromolecular contrast agents for dynamic micro-magnetic resonance lymphangiography." MAGNETIC RESONANCE IN MEDICINE : OFFICIAL JOURNAL OF THE SOCIETY OF MAGNETIC RESONANCE IN MEDICINE / SOCIETY OF MAGNETIC RESONANCE IN MEDICINE. OCT 2003, vol. 50, no. 4, October 2003 (2003-10), pages 758-766, XP002334205 ISSN: 0740-3194 the whole document	1-42		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.</td> <td style="width: 50%; border: none;"><input checked="" type="checkbox"/> Patent family members are listed in annex.</td> </tr> </table>			<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.	<input checked="" type="checkbox"/> Patent family members are listed in annex.			
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;">                     *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                 </td> <td style="width: 50%; border: none;">                     *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.                      *&amp;* document member of the same patent family                 </td> </tr> </table>			*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
*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	Date of mailing of the international search report			
30 June 2005	14/07/2005			
Name and mailing address of the ISA	Authorized officer			
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	ESTANOL, I			

## INTERNATIONAL SEARCH REPORT

 International Application No  
 PCT/US2005/001388

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KOBAYASHI H ET AL: "Novel intravascular macromolecular MRI contrast agent with generation-4 polyamidoamine dendrimer core: Accelerated renal excretion with coinjection of lysine" MAGNETIC RESONANCE IN MEDICINE, ACADEMIC PRESS, DULUTH, MN, US, vol. 46, no. 3, September 2001 (2001-09), pages 457-464, XP002227409 ISSN: 0740-3194 the whole document	1-42
Y	SATO N ET AL: "Pharmacokinetics and enhancement patterns of macromolecular MR contrast agents with various sizes of polyamidoamine dendrimer cores" MAGNETIC RESONANCE IN MEDICINE, ACADEMIC PRESS, DULUTH, MN, US, vol. 46, no. 6, December 2001 (2001-12), pages 1169-1173, XP002227407 ISSN: 0740-3194 the whole document	1-42
Y	KOBAYASHI H ET AL: "Novel liver macromolecular MR contrast agent with a polypropylenimine diaminobutyl dendrimer core: Comparison to the vascular MR contrast agent with the polyamidoamine dendrimer core" MAGNETIC RESONANCE IN MEDICINE, ACADEMIC PRESS, DULUTH, MN, US, vol. 46, no. 4, October 2001 (2001-10), pages 795-802, XP002227408 ISSN: 0740-3194 the whole document	1-42
P,Y	WO 2004/019998 A (THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS; BRECHBIEL, MARTIN;) 11 March 2004 (2004-03-11) claim 3; example 1	1-42
Y	WO 03/001218 A (THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE S) 3 January 2003 (2003-01-03) claim 32	1-42
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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/001388

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BRYANT L H JR ET AL: "Synthesis and relaxometry of high-generation (G = 5, 7, 9, and 10) PAMAM dendrimer-DOTA-gadolinium chelates." JOURNAL OF MAGNETIC RESONANCE IMAGING : JMRI. FEB 1999, vol. 9, no. 2, February 1999 (1999-02), pages 348-352, XP002334206 ISSN: 1053-1807 the whole document	1-42
A	US 5 101 827 A (GOLDENBERG ET AL) 7 April 1992 (1992-04-07) examples 1-8	1-42

# 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 1-42 are directed to a method of treatment and/or to a diagnostic method practised on 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/US2005/001388

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