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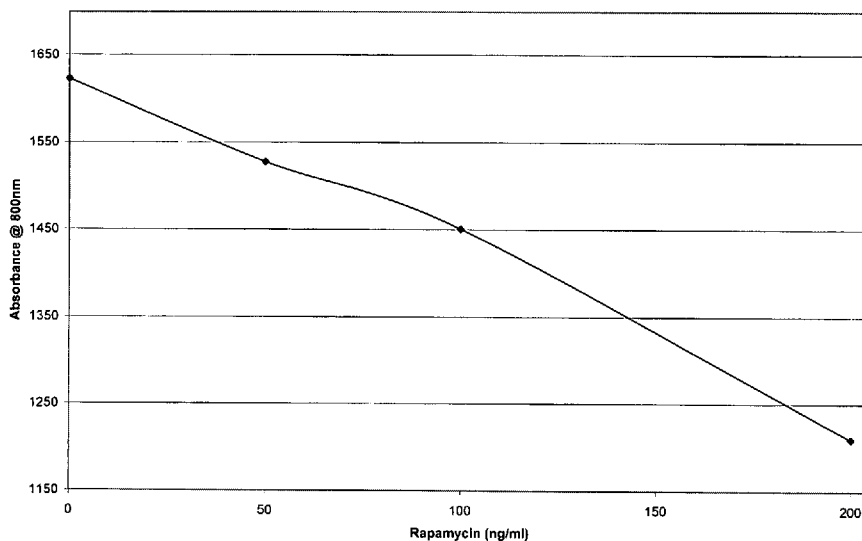
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[Continued on next page]

(54) Title: SINGLE RECEPTOR ASSAYS FOR IMMUNOSUPPRESSIVE DRUGS

FKBP25 Calibration Curve



(57) Abstract: A highly specific homogeneous assay method for an immunosuppressive drug using an immunophilin in a single receptor format is provided. In the simplest format, a single receptor is utilized analogous to a competitive immunoassay whereby an immunophilin is substituted for an antibody, and a competition results between a drug conjugate and the drug analyte for a limited number of immunophilin binding sites. In a microparticle agglutination assay format, an immunophilin is either bound to a particle or in solution. In the case where an immunophilin is bound to a particle, a polyvalent conjugate of the drug analyte is present in solution.

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**Declarations under Rule 4.17:**

- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

**(88) Date of publication of the international search report:**  
10 May 2007

*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.*

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/EP2006/008664

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. G01N33/94 C12Q1/533

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)  
G01N C12Q

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, EMBASE, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 322 772 A (SOLDIN STEVEN J [US]) 21 June 1994 (1994-06-21)	1, 5, 6, 8, 9, 14, 16, 19, 23, 25
Y	page 3, lines 4-23  page 11, line 6 page 11, line 21 - page 12, line 1 page 16, lines 13-24 page 6, lines 6-25 claims 11-14	1-10, 13-20, 23-26

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 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

16 February 2007

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/008664

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LIANG J ET AL: "Structure of the human 25 kDa FK506 binding protein complexed with rapamycin" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 1996 UNITED STATES, vol. 118, no. 5, 1996, pages 1231-1232, XP002405244 ISSN: 0002-7863 cited in the application page 1231, column 1	10,20
Y	EP 1 239 285 A (ROCHE DIAGNOSTICS GMBH [DE]; HOFFMANN LA ROCHE [CH]) 11 September 2002 (2002-09-11) the whole document	2-4,7, 15,17, 18,26
X	EP 0 372 862 A2 (CHILDREN S NATIONAL MEDICAL CE [US]) 13 June 1990 (1990-06-13)	1,5,6,8, 14,16,25
Y	the whole document	2-4,7, 13,17, 18,24
Y	SITTAMPALAM G S ET AL: "HIGH-THROUGHPUT SCREENING: ADVANCES IN ASSAY TECHNOLOGIES" CURRENT OPINION IN CHEMICAL BIOLOGY, CURRENT BIOLOGY LTD, LONDON, GB, vol. 1, 1997, pages 384-391, XP002940175 ISSN: 1367-5931 abstract	13,24
X	WO 91/17439 A (CHILDRENS RES INST [US]) 14 November 1991 (1991-11-14)	1,5,6,8, 11,14, 16,21,25
Y	the whole document	2-4,7, 12,13, 17,18, 22,24
Y	DAVIS ET AL: "An immunophilin-binding assay for sirolimus." CLINICAL THERAPEUTICS. 2000, vol. 22 Suppl B, 2000, pages B62-B70, XP002405243 ISSN: 0149-2918 cited in the application page B66, column 1, lines 11-17 - column 2, lines 1-6; table 2 page B67, column 1, paragraph 2	12,22
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2006/008664

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DECENZO M T ET AL: "FK506-binding protein mutational analysis: defining the active-site residue contributions to catalysis and the stability of ligand complexes."            PROTEIN ENGINEERING. FEB 1996, vol. 9, no. 2, February 1996 (1996-02), pages 173-180, XP002061407            ISSN: 0269-2139            cited in the application            table 2            abstract</p>	12,22
Y	<p>ARMSTRONG V W ET AL: "Drug monitoring of sirolimus and everolimus"            LABORATORIUMSMEDIZIN 2003 GERMANY, vol. 27, no. 5-6, 2003, pages 222-227, XP002420543            ISSN: 0342-3026            page 223, column 1, paragraph 1 - column 2, paragraph 1; figure 1            page 225, column 1, paragraph 3 - page 226, column 2, paragraph 3            abstract</p>	1,5,6,8, 9,13,14, 16,19, 23-25
P, Y	<p>US 2005/208607 A1 (ROBERTS MARK [US] ET AL) 22 September 2005 (2005-09-22)</p> <p>paragraphs [0008], [0009], [0047] - [0089], [0108] - [0149]</p>	1-9,13, 14, 16-19, 23-25

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2006/008664

### 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:
  
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:

see additional sheet

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-7, 13, 14, 16-18, 24, 25 (all fully) and 8 (partially)

method and corresponding kit for determining the presence or amount cyclosporin  
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2. claims: 1-7, 11-14, 16-18, 21, 22, 24, 25 (all fully), 8 (partially)

method and corresponding kit for determining the presence or amount tacrolimus  
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3. claims: 1-7, 10, 13-18, 20, 24, 25, 26 (all fully) and 8, 9, 19, 23 (all partially)

method and corresponding kit for determining the presence or amount rapamycin  
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4. claims: 1-7, 13, 14, 16-18, 24, 25 (all fully) and 8, 9, 19, and 23 (all partially)

method and corresponding kit for determining the presence or amount everolimus  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2006/008664

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