

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
1 December 2011 (01.12.2011)

(10) International Publication Number  
**WO 2011/147762 A3**

(51) International Patent Classification:

*A61K 51/04* (2006.01)      *A61K 47/06* (2006.01)  
*A61K 51/10* (2006.01)      *A61P 35/00* (2006.01)  
*A61K 47/02* (2006.01)      *A61K 101/02* (2006.01)

(21) International Application Number:

PCT/EP2011/058321

(22) International Filing Date:

23 May 2011 (23.05.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/347,961      25 May 2010 (25.05.2010)      US  
10163877.3      26 May 2010 (26.05.2010)      EP

(71) Applicant (for all designated States except US): **BAYER PHARMA AKTIENGESELLSCHAFT** [DE/DE]; Müller Strasse 178, 13353 Berlin (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CYR, John** [US/US]; 553, Dynasty Drive, Fairfield, California 94534 (US). **OLBRICH, Carsten** [DE/DE]; Gneisenaustr. 46, 10961 Berlin (DE). **BORM, Claudia** [DE/DE]; Lessingallee, 14612 Falkensee (DE).

(74) Common Representative: **BAYER PHARMA AKTIENGESELLSCHAFT**; Law and Patents, Patents and Licensing, Müller Strasse 178, 13353 Berlin (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:  
19 January 2012



**WO 2011/147762 A3**

(54) Title: STABILIZED RADIOPHARMACEUTICAL COMPOSITION

(57) Abstract: Stabilized radiopharmaceutical compositions, their use and process for the production thereof are described. Especially described are radioprotectants/ stabilizers for organic molecules, proteins and peptides, which are radiolabeled. More specific described are compositions which comprise a radiolabeled protein and one or more stabilizer.

INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2011/058321

A. CLASSIFICATION OF SUBJECT MATTER  
 INV. A61K51/04 A61K51/10 A61K47/02 A61K47/06 A61P35/00  
 ADD. A61K101/02

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)  
 A61K A61P

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, BIOSIS, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 679 318 A (VANDERHEYDEN JEAN-LUC [US] ET AL) 21 October 1997 (1997-10-21) cited in the application column 3, lines 62-64 column 4, lines 42-51,58 column 5, lines 18-24	1-17, 19-31
A	US 5 384 113 A (DEUTSCH EDWARD A [US] ET AL) 24 January 1995 (1995-01-24) cited in the application column 2, lines 34-53 claims	1-17, 19-31
A	WO 2009/059977 A1 (GE HEALTHCARE BV [NL]; VAN DEN BOS JAN [NL]) 14 May 2009 (2009-05-14) cited in the application page 2, lines 18-30	1-17, 19-31
	----- -/--	

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  22 September 2011	Date of mailing of the international search report  25/11/2011
--	--

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Villard, Anne-Laure
--	---

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2011/058321

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 7 351 398 B2 (CYR JOHN E [US] ET AL) 1 April 2008 (2008-04-01) cited in the application column 1, line 62 - column 2, line 6 column 2, lines 18-26 examples -----	1-17, 19-31
A	US 6 881 396 B2 (CYR JOHN E [US]) 19 April 2005 (2005-04-19) cited in the application column 2, lines 35-39 -----	1-17, 19-31
A	NORONHA O P ET AL: "Factors affecting the preparation of 99mTc-sulfur colloid.", EUROPEAN JOURNAL OF NUCLEAR MEDICINE 1978 LNKD- PUBMED:753622, vol. 3, no. 1, 1978, pages 47-54, XP008143241, ISSN: 0340-6997 page 47, right-hand column, paragraph 3 pages 49-50, paragraph f page 54, left-hand column, lines 6-13 -----	1-17, 19-31
X	WO 2009/073698 A1 (BRACCO IMAGING SPA [IT]; OEHLBERG PETER J [US]; SCHRAMM ERNST [US]) 11 June 2009 (2009-06-11) paragraphs [0002], [0034], [0073], [0081] examples -----	1-6, 8-11, 20-27
X	WO 00/52031 A2 (IDEC PHARMA CORP [US]) 8 September 2000 (2000-09-08) cited in the application page 10, lines 2-8 page 15, lines 1-15 -----	1-6, 8-11, 20-27 7,28
Y	US 2005/074401 A1 (BORSI LAURA [IT] ET AL) 7 April 2005 (2005-04-07) paragraphs [0077], [0078] paragraphs [0097] - [0144] -----	7,28
X	US 5 314 678 A (GRUMMON GLENN D [US] ET AL) 24 May 1994 (1994-05-24)  column 1, lines 5-20 column 2, line 53 - column 3, line 34 -----	1-4, 8-11, 20-25
X	US 3 859 429 A (ELIAS HORST HERMANN) 7 January 1975 (1975-01-07)  column 1, lines 65-67 column 3, lines 19-34 -----	1-5, 8-11, 20-22
	----- -/--	

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2011/058321

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>DATABASE WPI  Week 198517  Thomson Scientific, London, GB;  AN 1985-102741  XP002659670,  &amp; JP 60 048937 A (HITACHI CHEM CO LTD)  16 March 1985 (1985-03-16)  abstract</p> <p style="text-align: center;">-----</p>	<p>1-6,  8-11,  20-22</p>
X	<p>MERTENS J ET AL: "Fast, low-temperature  preparation of carrier-free 17-&lt;123&gt;I-  heptadecanoic acid applied for liver and  heart scintigraphy",  EUROPEAN JOURNAL OF NUCLEAR MEDICINE 1986  DE,  vol. 11, no. 9, 1986, pages 361-362,  XP008143300,  ISSN: 0340-6997  page 362, left-hand column, paragraph 2</p> <p style="text-align: center;">-----</p>	<p>1,2,5,  8-10,  20-22</p>
X	<p>WO 97/14430 A1 (PHARMACIA &amp; UPJOHN AB  [SE]; FRANSSON JONAS [SE]; LUNDIN RONNY  [SE]) 24 April 1997 (1997-04-24)  page 7, line 28  page 8, lines 19-22</p> <p style="text-align: center;">-----</p>	<p>1-6,  8-11,  20-27</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2011/058321

## Box No. 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 No. 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 fees, this Authority did not invite payment of additional fees.
  
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.:

see annex

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- 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: 17, 31(completely); 1-16, 19-30(partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from thiosulfate; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

2. claims: 18, 32(completely); 1-16, 19-30(partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from ascorbate or ascorbic acid; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

3. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from gentisate or gentisic acid; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

4. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from methionine; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

5. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from maltose; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

6. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from inositol; Use as medicament thereof for diagnosis or

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

7. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from benzyl alcohol; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

8. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from trehalose; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

9. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from povidone; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

10. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from niacinamide; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

11. claims: 1, 2, 5-15, 19-29(all partially)

A stabilized composition comprising a radiopharmaceutical and one radioprotectant as stabilizing agent selected from cysteine; Use as medicament thereof for diagnosis or treatment of a disease; A method for the production of said stable ready to use radiopharmaceutical composition.

---

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2011/058321

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5679318	A	21-10-1997	NONE
US 5384113	A	24-01-1995	AT 196428 T 15-10-2000 AU 2462592 A 05-04-1993 CA 2113995 A1 18-03-1993 DE 69231469 D1 26-10-2000 DE 69231469 T2 25-01-2001 DK 0600992 T3 09-10-2000 EP 0600992 A1 15-06-1994 ES 2150916 T3 16-12-2000 GR 3035067 T3 30-03-2001 JP 3853354 B2 06-12-2006 JP H06510539 A 24-11-1994 US 5384113 A 24-01-1995 WO 9304702 A1 18-03-1993
WO 2009059977	A1	14-05-2009	AU 2008324186 A1 14-05-2009 CA 2703518 A1 14-05-2009 CN 101918042 A 15-12-2010 EP 2214722 A1 11-08-2010 JP 2011503239 A 27-01-2011 KR 20100077189 A 07-07-2010 US 2010254902 A1 07-10-2010 WO 2009059977 A1 14-05-2009
US 7351398	B2	01-04-2008	NONE
US 6881396	B2	19-04-2005	NONE
WO 2009073698	A1	11-06-2009	CA 2706111 A1 11-06-2009 US 2010284912 A1 11-11-2010 WO 2009073698 A1 11-06-2009
WO 0052031	A2	08-09-2000	AT 428446 T 15-05-2009 AU 780311 B2 17-03-2005 AU 4004600 A 21-09-2000 BG 65568 B1 30-12-2008 BG 105853 A 28-06-2002 BR 0008635 A 26-12-2001 CA 2362908 A1 08-09-2000 CN 1345249 A 17-04-2002 CZ 20013127 A3 13-02-2002 DE 1156835 T1 23-05-2002 DK 1156835 T3 03-08-2009 EE 200100461 A 15-10-2002 EP 1156835 A2 28-11-2001 EP 2011520 A1 07-01-2009 ES 2165830 T1 01-04-2002 GR 2001300078 T1 31-01-2002 HK 1045656 A1 22-09-2006 HR 20010713 A2 31-12-2002 HU 0105489 A2 29-05-2002 IL 145112 A 15-05-2007 JP 4558947 B2 06-10-2010 JP 2002538164 A 12-11-2002 MX PA01008745 A 24-04-2002 NO 20014239 A 01-11-2001 NZ 513667 A 28-09-2001

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2011/058321

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		PL 350551 A1	16-12-2002
		PT 1156835 E	24-07-2009
		RU 2221807 C2	20-01-2004
		SI 1156835 T1	31-08-2009
		SK 12172001 A3	09-05-2002
		TW I283178 B	01-07-2007
		UA 75036 C2	17-12-2001
		US 6994840 B1	07-02-2006
		US 2006067884 A1	30-03-2006
		US 2007297978 A1	27-12-2007
		WO 0052031 A2	08-09-2000
		ZA 200106945 A	22-11-2002
-----			
US 2005074401	A1	07-04-2005	
		AT 499949 T	15-03-2011
		AU 2004269897 A1	17-03-2005
		AU 2010200271 A1	18-02-2010
		BR PI0414272 A	07-11-2006
		CA 2536256 A1	17-03-2005
		CN 1849144 A	18-10-2006
		CR 8331 A	04-10-2006
		DK 1663320 T3	06-06-2011
		EC SP066499 A	10-10-2006
		EP 1514561 A1	16-03-2005
		EP 1663320 A1	07-06-2006
		EP 2246070 A2	03-11-2010
		ES 2361743 T3	21-06-2011
		HK 1092375 A1	24-12-2009
		JP 2007505065 A	08-03-2007
		KR 20060118430 A	23-11-2006
		NZ 545640 A	31-05-2009
		PT 1663320 E	07-06-2011
		RS P20060176 A	07-08-2008
		SG 162760 A1	29-07-2010
		SI 1663320 T1	30-06-2011
		US 2005074401 A1	07-04-2005
		US 2009214423 A1	27-08-2009
		WO 2005023318 A1	17-03-2005
		ZA 200602014 A	30-05-2007
-----			
US 5314678	A	24-05-1994	
		AU 3480793 A	01-09-1993
		CA 2126848 A1	05-08-1993
		EP 0627937 A1	14-12-1994
		JP H07503468 A	13-04-1995
		US 5314678 A	24-05-1994
		WO 9314788 A1	05-08-1993
-----			
US 3859429	A	07-01-1975	NONE
-----			
JP 60048937	A	16-03-1985	NONE
-----			
WO 9714430	A1	24-04-1997	
		AU 7352096 A	07-05-1997
		WO 9714430 A1	24-04-1997
-----			