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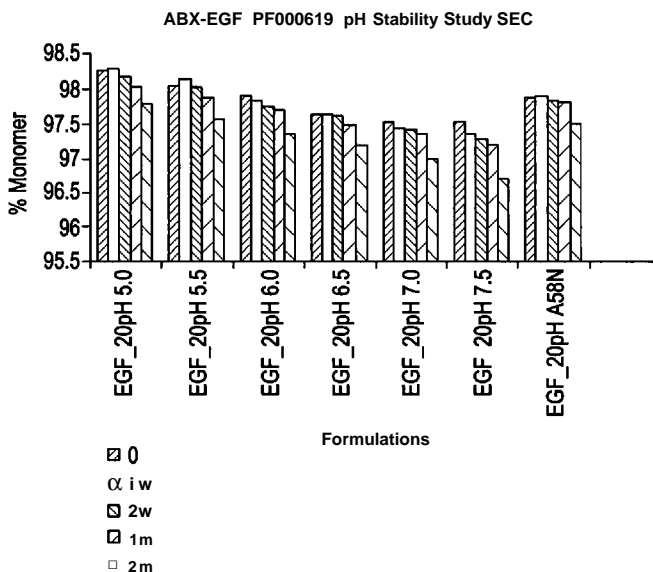
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[Continued on next page]

(54) **Title:** STABLE POLYPEPTIDE FORMULATIONS



(57) **Abstract:** The invention provides a formulation including a buffer having a pH less than 6.0, a divalent cation between about 5-200 mM, an excipient comprising a sugar or polyol and an effective amount of a therapeutic polypeptide. Also provided is a method of stabilizing a polypeptide. The method includes contacting a therapeutic polypeptide with a concentration of divalent cation between about 5-150 mM in a buffer having a pH less than 6.0 and an excipient comprising a sugar or polyol.

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A. CLASSIFICATION OF SUBJECT MATTER

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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)
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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, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2004/039826 A (CENTOCOR INC [US]) 13 May 2004 (2004-05-13) page 47, lines 12-24 page 48, line 18 page 50, lines 3-19 -----	1-48
Y	US 2004/191243 A1 (CHEN BEI [US] ET AL) 30 September 2004 (2004-09-30) paragraphs [0016], [0020], [0021] paragraphs [0036] - [0038] paragraph [0046] table 7 ----- -/--	1-48

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
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Date of the actual completion of the international search	Date of mailing of the international search report
23 June 2008	04/07/2008

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 <p style="text-align: center;">Villa Riva, A</p>
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International application No

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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>WO 03/039485 A (PROTEIN DESIGN LABS [US]; KAISHEVA ELIZABET A [US]; GUPTA SUPRIYA [US]) 15 May 2003 (2003-05-15) abstract page 4, lines 1-9 examples; tables</p>	1-48
Y	<p>WO 2006/096461 A (PHARMACIA & UPJOHN CO LLC [US]; CARROLL JAMES ALAN [US]; DAS TAPAN KAN) 14 September 2006 (2006-09-14) page 27, lines 7-13 page 28, lines 1-9 page 28, line 29 - page 30, line 12 page 30, lines 10-24 page 63, lines 25-32</p>	1-48
Y	<p>WO 2006/107854 A (AMGEN INC [US]; SIENA SALVATORE [IT]; MORONI MAURO [IT]; BARDELLI ALBE) 12 October 2006 (2006-10-12) abstract paragraphs [0042], [0045] paragraphs [0128] - [0131] paragraph [0135]</p>	1-48
E	<p>WO 2007/145862 A (GENENTECH INC [US]; HOFFMANN LA ROCHE [CH]; AMLER LUKAS C [US]; MOECKS) 21 December 2007 (2007-12-21) page 59, lines 7-30</p>	1-48

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2007/021475
--

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
wo 2004039826	A	13-05-2004	BR 0214168 A 14-09-2004
			CN 1694894 A 09-11-2005
			JP 2007528691 T 18-10-2007
US 2004191243	AI	30-09-2004	NONE
wo 03039485	A	15-05-2003	CA 2466034 AI 15-05-2003
			CN 1612689 A 04-05-2005
			EP 1441589 A2 04-08-2004
			HK 1074750 AI 08-06-2007
			JP 2005508981 T 07-04-2005
			KR 20050044365 A 12-05-2005
			NZ 532896 A 31-08-2007
wo 2006096461	A	14-09-2006	AR 053026 AI 18-04-2007
			AR 053553 AI 09-05-2007
			AR 054233 AI 13-06-2007
			AU 2006220828 AI 14-09-2006
			AU 2006220829 AI 14-09-2006
			CA 2600434 AI 14-09-2006
			CA 2600588 AI 14-09-2006
			CA 2600608 AI 14-09-2006
			CA 2600836 AI 14-09-2006
			EP 1858552 A2 28-11-2007
			EP 1871806 A2 02-01-2008
			EP 1865986 A2 19-12-2007
			EP 1868646 A2 26-12-2007
			JP 2006249081 A 21-09-2006
			JP 2006249083 A 21-09-2006
			JP 2006249084 A 21-09-2006
			JP 2006249085 A 21-09-2006
			KR 20070100922 A 12-10-2007
			KR 20070100848 A 11-10-2007
			wo 2006096488 A2 14-09-2006
wo 2006096490 A2 14-09-2006			
wo 2006096491 A2 14-09-2006			
wo 2006107854	A	12-10-2006	AU 2006232378 AI 12-10-2006
			CA 2602619 AI 12-10-2006
			EP 1869220 A2 26-12-2007
			KR 20080014745 A 14-02-2008
wo 2007145862	A	21-12-2007	US 2008038271 AI 14-02-2008