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(54) Title: LIQUID STABILIZED PROTEIN FORMULATIONS IN COATED PHARMACEUTICAL CONTAINERS

(57) Abstract: A container comprising a closure means coated by an inert fluorinated material and containing a liquid pharmaceutical composition. In particular, the container comprises a closure means coated by TEFLON and contains a HSA-free Interferon- β formulation having the following composition: 30 to 100 $\mu\text{g/ml}$ of interferon- β , an isotonicity agent, 0.1 to 2 mg/ml of Poloxamer 188, at least 0.12 mg/ml of L-Methionine and a buffer solution capable of maintaining the pH of the liquid formulation at a value between 3.0 and 4.0.



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INTERNATIONAL SEARCH REPORT

Inter | Application No
PCT/EP2004/050779

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/21 A61J1/00

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)
IPC 7 A61K A61J

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, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/28007 A (BIOGEN INC ;CHUNG WEN LI (US); DIBIASI MARY D (US); SCHARIN ERIC () 2 July 1998 (1998-07-02) page 2, lines 28-31 page 5, lines 22-24 page 10, lines 4-18 page 13, line 22 - page 14, line 2 page 16, lines 10-13; example 5 -----	1,3-7, 9-17
X	EP 0 736 303 A (HOFFMANN LA ROCHE) 9 October 1996 (1996-10-09) page 3, lines 49-52; claim 3; example 2 -----	1-3,5,6, 9-11,14, 15,17
X	EP 0 641 567 A (CIBA GEIGY AG) 8 March 1995 (1995-03-08) page 3, lines 9,10; examples ----- -/--	1-3, 9-11,14, 15,17



Further documents are listed in the continuation of box C.



Patent family members are listed in 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
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- *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

30 November 2004

Date of mailing of the international search report

13/12/2004

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INTERNATIONAL SEARCH REPORT

Intern  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.
X	WO 97/17087 A (GENENTECH INC) 15 May 1997 (1997-05-15) page 4, line 36 - page 5, line 27 page 10, lines 26-28; examples -----	1,2,5-7, 9-11,14, 15,17
X	US 5 661 125 A (STRICKLAND THOMAS WAYNE) 26 August 1997 (1997-08-26) examples 13-19 -----	1,2,5,6, 9-11,14, 15,17

INTERNATIONAL SEARCH REPORT

In international application No.
PCT/EP2004/050779

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:
see FURTHER INFORMATION sheet PCT/ISA/210
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: -

Present claims 1,2,5-7,9-17 relate to an extremely large number of possible compositions (comprising "proteins"). Support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC is to be found, however, for only a very small proportion of the compositions claimed (interferon). In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to claims 3, 4 and 8 and the compositions comprising interferon-beta as prepared in the examples.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr

Application No

PCT/EP2004/050779

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9828007	A	02-07-1998	AT 270899 T	15-07-2004
			AU 738362 B2	13-09-2001
			AU 5619198 A	17-07-1998
			BG 103594 A	28-04-2000
			BR 9714434 A	02-05-2000
			CA 2275890 A1	02-07-1998
			CN 1245434 A	23-02-2000
			CZ 9902282 A3	15-12-1999
			DE 69729880 D1	19-08-2004
			EA 2754 B1	29-08-2002
			EE 9900313 A	17-04-2000
			EE 200300127 A	16-06-2003
			EP 0948358 A1	13-10-1999
			HU 0000829 A2	28-07-2000
			JP 2001519770 T	23-10-2001
			NO 993121 A	24-08-1999
			NZ 336548 A	28-09-2001
			NZ 512792 A	26-11-2002
			PL 334365 A1	28-02-2000
			SK 85899 A3	18-01-2000
			TR 9901968 T2	21-12-1999
			WO 9828007 A1	02-07-1998
			US 2003190307 A1	09-10-2003
EP 0736303	A	09-10-1996	EP 0736303 A2	09-10-1996
			GR 3031775 T3	29-02-2000
			AT 183650 T	15-09-1999
			AU 685356 B2	15-01-1998
			AU 5044696 A	17-10-1996
			BR 9601276 A	13-01-1998
			CA 2172664 A1	07-10-1996
			CN 1141808 A , B	05-02-1997
			CY 2194 A	08-11-2002
			CZ 9600994 A3	16-10-1996
			DE 69603894 D1	30-09-1999
			DE 69603894 T2	20-04-2000
			DK 736303 T3	10-01-2000
			ES 2136910 T3	01-12-1999
			HK 1012232 A1	19-05-2000
			HU 9600857 A2	28-08-1997
			IL 117752 A	21-11-2000
			JP 2758154 B2	28-05-1998
			JP 8283176 A	29-10-1996
			KR 212346 B1	02-08-1999
			MA 23838 A1	31-12-1996
			NO 961322 A	07-10-1996
			NZ 286300 A	26-05-1997
			PL 313655 A1	14-10-1996
			RU 2113845 C1	27-06-1998
			SG 52806 A1	28-09-1998
			TR 970157 A2	21-03-1997
			TW 426523 B	21-03-2001
			US 5762923 A	09-06-1998
			ZA 9602553 A	07-10-1996
EP 0641567	A	08-03-1995	AT 190498 T	15-04-2000
			AU 679233 B2	26-06-1997
			AU 6893994 A	23-02-1995

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern I Application No
PCT/EP2004/050779

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0641567	A	CA 2129921 A1	14-02-1995
		CY 2230 A	18-04-2003
		DE 69423402 D1	20-04-2000
		DE 69423402 T2	03-08-2000
		DK 641567 T3	14-08-2000
		EP 0641567 A1	08-03-1995
		ES 2144034 T3	01-06-2000
		FI 943705 A	14-02-1995
		GR 3033239 T3	29-09-2000
		HU 68692 A2	28-07-1995
		IL 110566 A	22-12-1999
		JP 7145070 A	06-06-1995
		NO 942983 A	14-02-1995
		NZ 264218 A	26-07-1995
		PT 641567 T	31-08-2000
		US 5609868 A	11-03-1997
		ZA 9406073 A	14-02-1995
WO 9717087	A 15-05-1997	AT 255903 T	15-12-2003
		AU 721112 B2	22-06-2000
		AU 7518696 A	29-05-1997
		BR 9611571 A	30-03-1999
		CA 2234231 A1	15-05-1997
		CN 1201394 A ,B	09-12-1998
		DE 69631063 D1	22-01-2004
		DE 69631063 T2	30-09-2004
		DK 862452 T3	05-04-2004
		EP 0862452 A1	09-09-1998
		ES 2211991 T3	16-07-2004
		IL 124004 A	31-10-2003
		JP 2002502358 T	22-01-2002
		PT 862452 T	30-04-2004
		TR 9800811 T2	21-07-1998
		WO 9717087 A1	15-05-1997
		ZA 9609290 A	05-05-1998
US 5661125	A 26-08-1997	NONE	