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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
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ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD,
SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT,
LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF,
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TD, TG)

Published:

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: INTERFERON VARIANTS WITH IMPROVED PROPERTIES

(57) Abstract: This invention relates to interferon variants with improved properties and methods for their use.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/009824

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/415 C07K14/56 C07K14/565

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 C07K

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, BIOSIS, 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	WO 02/074783 A (MERCK PATENT GMBH ; BAKER MATTHEW (GB); CARTER GRAHAM (GB); JONES TIM) 26 September 2002 (2002-09-26) page 9, line 1 - line 7; claim 39 -----	1-5
X	WO 98/48018 A (SCHNEIDER FRESENIUS CHRISTIAN ; OTTO BERND (DE); WASCHUETZA GERO (DE);) 29 October 1998 (1998-10-29) abstract ----- -/--	1-5

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
- "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

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/009824

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RUNKEL LAURA ET AL: "Differences in activity between alpha and beta type I interferons explored by mutational analysis" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 273, no. 14, 3 April 1998 (1998-04-03), pages 8003-8008, XP002160242 ISSN: 0021-9258 the whole document -----	1-5
A	MARSHALL SHANNON A ET AL: "Rational design and engineering of therapeutic proteins." DRUG DISCOVERY TODAY, vol. 8, no. 5, 1 March 2003 (2003-03-01), pages 212-221, XP002295833 ISSN: 1359-6446 the whole document -----	1-5

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2004/009824

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material
 - in written format
 - in computer readable form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in computer readable form
 - furnished subsequently to this Authority for the purpose of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/009824

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.: 1-5 (partially), 6-15 (completely)
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:

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.:
1-5 (partially)

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

International Application No. PCT/ US2004/ 009824

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

Invention 1

Claims 1-5 (partially): Variant type 1 intreferon-beta proteins exhibiting modified immunogenicity as shown in SEQ ID NO: 19

Inventions 2-7

Claims 1-5 (partially): As above, but relating to the protein shown in SEQ ID NO: 20, 21, 22, 23, 24 and 25

Invention 8

Claims 6-10: Variant type 1 interferon-alpha proteins exhibiting modified immunogenicity

Invention 9

Claims 11-15: Variant type 1 Interferon-kappa proteins exhibiting modified immunogenicity

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US2004 /009824

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-5 (partially), 6-15 (completely)

Present claims 1, 6 and 11 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. 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 can be carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to those interferon- β and interferon- κ variants which have actually been made and shown to be active (i.e. those proteins shown in SEQ ID NO: 19-30). Please note the objection as to lack of unity, however.

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

International Application No

PCT/US2004/009824

Patent document cited in search report		Publication date	Patent family member(s)	Publication date			
WO 02074783	A	26-09-2002	BR 0208041 A	25-02-2004			
			CA 2441095 A1	26-09-2002			
			WO 02074783 A2	26-09-2002			
			EP 1368377 A2	10-12-2003			
			HU 0303534 A2	28-01-2004			
			JP 2004529633 T	30-09-2004			
			MX PA03008310 A	11-12-2003			
<hr/>							
WO 9848018	A	29-10-1998	DE 19717864 A1	29-10-1998			
			AT 257859 T	15-01-2004			
			CA 2287521 A1	29-10-1998			
			DE 59810596 D1	19-02-2004			
			DK 975761 T3	16-02-2004			
			WO 9848018 A1	29-10-1998			
			EP 0975761 A1	02-02-2000			
			ES 2214709 T3	16-09-2004			
			JP 2001523957 T	27-11-2001			
			US 6572853 B1	03-06-2003			
			US 2004022763 A1	05-02-2004			
			<hr/>				