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ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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### (54) Title: SUBSTITUTION INFUSION FLUID AND CITRATE ANTICOAGULATION

(57) Abstract: The invention relates to a substitution infusion fluid for hemofiltration of a specific composition. The use of said substitution infusion fluid significantly reduces the risk of the occurrence of abnormalities in a patient undergoing hemofiltration. The invention also relates to a process for hemofiltration of blood wherein said substitution infusion fluid is used. The invention also relates to a citrate anticoagulation fluid of a specific composition. The invention also relates to a process for hemofiltration of blood wherein said substitution infusion fluid is used in combination with said citrate anticoagulation fluid. The use of said substitution infusion fluid in combination with said citrate anticoagulation fluid significantly further reduces the risk of the occurrence of abnormalities in a patient undergoing hemofiltration.

Inter anal Application No PCT/EP 00/03583

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K33/42 A61k A61K33/14 A61K33/06 A61K31/70 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)  $IPC \ 7 \qquad A61K$ 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) PAJ, CHEM ABS Data, EPO-Internal, EMBASE, WPI Data, BIOSIS, MEDLINE C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category 1 - 17SIEBERTH H.G.: "'Composition of the X rinsing water for extracorporeal hemodialysis in acute and chronic renal failure!. ZUSAMMENSETZUNG DES WASCHWASSERS FUR DIE EXTRACORPORALE HAMODIALYSE DER AKUTEN UND CHRONISCHEN NIERENINSUFFIZIENZ." MEDIZINISCHE TECHNIK, (1974) 94/2 (28-32). CODEN: METEAV, XP000856013 abstract page 31, column 2; table 1 -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C X Special categories of cited documents: "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 "A" document defining the general state of the art which is not considered to be of particular relevance invention \*E\* earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone \*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) "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 docu-O document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means document published prior to the international filing date but "&" document member of the same patent family later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 15 January 2001 10 January 2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

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		PC1/EF 00/03563				
C.(Continua	.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Helevani to claim No.				
X	VAN STONE J.C.: "Individualization of the dialysate prescription in chronic hemodialysis." DIALYSIS AND TRANSPLANTATION, (1994) 23/11 (624-625+628-635)., XP000856008 abstract the whole document page 634	1-17				
X	WO 93 24108 A (MINNTECH CORP) 9 December 1993 (1993-12-09) page 5, line 2-30; claims 9,24 page 7, line 25-35	1-12				
P,X	CHEMICAL ABSTRACTS, vol. 131, no. 19, 8 November 1999 (1999-11-08) Columbus, Ohio, US; abstract no. 262653, HARADA, MINORU ET AL: "Dialyzing compositions for hemodialysis in renal failure patients" XP002123553 abstract & JP 11 279051 A (NIKKISO CO., LTD., JAPAN) 12 October 1999 (1999-10-12)	1-17				
Y	PATENT ABSTRACTS OF JAPAN vol. 013, no. 579 (C-668), 20 December 1989 (1989-12-20) & JP 01 242531 A (NIPPON SEIYAKU KK), 27 September 1989 (1989-09-27) abstract	1-17				
Y	PATENT ABSTRACTS OF JAPAN vol. 016, no. 273 (C-0953), 18 June 1992 (1992-06-18) & JP 04 069341 A (OTSUKA PHARMACEUT FACTORY INC), 4 March 1992 (1992-03-04) abstract	1-19				
A	PATENT ABSTRACTS OF JAPAN vol. 006, no. 003 (C-086), 9 January 1982 (1982-01-09) & JP 56 128711 A (HIKARI SEIYAKU KK), 8 October 1981 (1981-10-08) abstract	1-17				

Intel anal Application No
PCT/EP 00/03583

etion) DOCLIMENTS CONSIDERED TO BE RELEVANT	101721 00703303	
	Relevant to claim No.	
ONO K. ET AL: "Glucose in the dialyzate does not reduce the free amino acid loss during routine hemodialysis of non-fasting patients."  CLINICAL NEPHROLOGY, (1984) 21/2 (106-109). CODEN: CLNHBI, XP000856986	7–12	
abstract  PALSSON R ET AL: "Regional citrate anticoagulation in continuous venovenous hemofiltration in critically ill patients with a high risk of bleeding."  KIDNEY INTERNATIONAL, (1999 MAY) 55 (5) 1991-7.,  XP000978115 abstract	18,19	
ASHTON D N ET AL: "Recent advances in continuous renal replacement therapy: citrate anticoagulated continuous arteriovenous hemodialysis."  ANNA JOURNAL, (1991 JUN) 18 (3) 263-7, 329.,  XP000978120 abstract page 265	18,19	
MACIAS W.L.: "Choice of replacement fluid/dialysate anion in continuous renal replacement therapy."  AMERICAN JOURNAL OF KIDNEY DISEASES, (1996) 28/5 SUPPL. 3 (S15-S20)., XP000978102  abstract page S15 -page S16 page S19	1-19	
WO 00 33853 A (GLOBAL HEMOSTASIS INST MGR AB ;RAANBY MATS (SE)) 15 June 2000 (2000-06-15) abstract	18,19	
WO 90 15612 A (UNIV JEFFERSON) 27 December 1990 (1990-12-27) abstract; claims 1-6	18,19	
	ONO K. ET AL: "Glucose in the dialyzate does not reduce the free amino acid loss during routine hemodialysis of non-fasting patients."  CLINICAL NEPHROLOGY, (1984) 21/2 (106-109). CODEN: CLNHBI, XP000856986 abstract  PALSSON R ET AL: "Regional citrate anticoagulation in continuous venovenous hemofiltration in critically ill patients with a high risk of bleeding." KIDNEY INTERNATIONAL, (1999 MAY) 55 (5) 1991-7. XP000978115 abstract  ASHTON D N ET AL: "Recent advances in continuous renal replacement therapy: citrate anticoagulated continuous arteriovenous hemodialysis."  ANNA JOURNAL, (1991 JUN) 18 (3) 263-7, 329. XP000978120 abstract page 265  MACIAS W.L.: "Choice of replacement fluid/dialysate anion in continuous renal replacement therapy."  AMERICAN JOURNAL OF KIDNEY DISEASES, (1996) 28/5 SUPPL. 3 (S15-S20). , XP000978102 abstract page S15 -page S16 page S19  WO 00 33853 A (GLOBAL HEMOSTASIS INST MGR AB ;RAANBY MATS (SE)) 15 June 2000 (2000-06-15) abstract  WO 90 15612 A (UNIV JEFFERSON) 27 December 1990 (1990-12-27)	

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## **INTERNATIONAL SEARCH REPORT**

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 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:						
	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:					
L	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:					
	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 II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)					
This Inter	rnational Searching Authority found multiple inventions in this international application, as follows:					
	see additional sheet					
1. X	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.					
	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.  X  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: 20 partially, 1-17 complete

Substitution infusion fluid for hemofiltration. Optionally in combination with citrate anticoagulation solution. Process for hemofiltration of blood using the same

- 1.1. Claims: 17 complete, 20 partially Substitution infusion fluid for hemofiltration in combination with citrate anticoagulation solution. Process for hemofiltration of blood using the same.
- 2. Claims: 20 partially, 18, 19 complete

Citrate anticoagulation solution for hemofiltration. Process for hemofiltration of blood using the same excluding the subject matter of invention  $\mathbf{1}$ 

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

information on patent family members

Inte. onal Application No PCT/EP 00/03583

Patent document cited in search report		Publication Patent fami date member(s)		Publication date	
WO 9324108	А	09-12-1993	AU 4239593 A CA 2137088 A EP 0647130 A HU 68062 A JP 7504591 T	09-12-1993 12-04-1995 29-05-1995	
JP 11279051	A	12-10-1999	NONE		
JP 01242531	Α	27-09-1989	JP 2720165 B	25-02-1998	
JP 04069341	Α	04-03-1992	NONE		
JP 56128711	Α	08-10-1981	NONE		
WO 0033853	Α	15-06-2000	AU 2017400 A	26-06-2000	
WO 9015612	Α	27-12-1990	US 4925665 A AU 5851590 A		