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26.09.2003 US 506579 P
19.12.2003 US 531377 P
19.03.2004 US 804592
19.08.2004 US 922560**

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(54) **Apparatuses and methods for reducing albumin in samples**

(57) The present invention is directed to apparatuses and methods for reducing the content of albumin in serum, plasma and/or blood samples. The apparatuses comprise an insoluble support with a ligand attached thereto. According to certain embodiments of the invention, the ligand is a bromosulphophthalein, Cibacron Blue

or Warfarin ligand or salts or esters thereof. Also provided are methods of making the apparatus, as well as kits and albumin-depleted samples produced by the methods of the present invention.

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PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention EP 04 10 4644 shall be considered, for the purposes of subsequent proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WOLKOFF A W ET AL: "Purification of ligandin by affinity chromatography on sulfobromophthalein-agarose gel." PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE. SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE (NEW YORK, N. Y.) FEB 1979, vol. 160, no. 2, February 1979 (1979-02), pages 150-153, XP008040124 ISSN: 0037-9727 * page 150, left-hand column, last paragraph - right-hand column, paragraph 1; table 1 *	1-8,13, 20,22, 24-27	G01N33/68
D,X	TRAVIS J ET AL: "Isolation of albumin from whole human plasma and fractionation of albumin-depleted plasma." THE BIOCHEMICAL JOURNAL. 1 AUG 1976, vol. 157, no. 2, 1 August 1976 (1976-08-01), pages 301-306, XP008040119 ISSN: 0264-6021 * page 302, left-hand column, paragraph 1 - paragraph 4 *	13-17,38	
Y		18,19	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			G01N
INCOMPLETE SEARCH			
The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.			
Claims searched completely :			
Claims searched incompletely :			
Claims not searched :			
Reason for the limitation of the search: see sheet C			
Place of search The Hague		Date of completion of the search 9 December 2004	Examiner Marttin, E
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 04 10 4644

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	US 4 093 612 A (TRAVIS JAMES ET AL) 6 June 1978 (1978-06-06)	13-17,38	
Y	* column 1, line 23 - column 2, line 58 * * column 5, line 67 - column 6, line 4 * * column 7, line 1 - column 8, last line ; claim 1; examples 1-5 *	1-12, 20-27, 32-34,37	
Y	EP 0 469 519 A (TOSOH CORP) 5 February 1992 (1992-02-05) * column 3, line 23 - line 26; claims 1,8 *	1-12, 18-27, 32-37, 39-49	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	STEEL LAURA F ET AL: "Efficient and specific removal of albumin from human serum samples." MOLECULAR & CELLULAR PROTEOMICS : MCP. APR 2003, vol. 2, no. 4, April 2003 (2003-04), pages 262-270, XP002309638 ISSN: 1535-9476	32-37	
A	* page 263, left-hand column, paragraph 1 - right-hand column, paragraph 1 *	7-12, 24-31	
Y	ANONYMOUS: "Montage Albumin Deplete Kit" MILLIPORE DATA SHEET, [Online] 2002, pages 1-4, XP002309532 Retrieved from the Internet: URL:http://www.millipore.com/publications. nsf/dda0cb48c91c0fb6852567430063b5d6/93fb1 49395b1e8df85256c0d003d41a0/\$FILE/PF1770EN 00.pdf> [retrieved on 2004-12-08] * the whole document *	39-49	



Claim(s) searched incompletely:
28,32-38,47,48

Claim(s) not searched:
-

Reason for the limitation of the search:

Present claims 28,32-38,47,48 relate to products defined by reference to desirable characteristics or properties, namely ligands capable of preferentially binding albumin (claims 35, 36, 37, 47, 48) and ligands capable of binding one or more non-albumin proteins (claims 28,32-38). The terms "ligands capable of preferentially binding albumin" or "ligands capable of binding one or more non-albumin proteins" as used in the present independent claims 32, 36-38, and 47 and in dependent claims 28,33-35, and 48 define a ligand by the compound it binds to. However, a ligand cannot be sufficiently characterised by the compound it binds to as it is done by expressions as "ligands capable of preferentially binding albumin" or "ligands capable of binding one or more non-albumin proteins", because it is impossible to know which substances are encompassed in this expression.

The claims cover all products having these characteristics or properties, whereas the application provides support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC for only a very limited number of such products. 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. Independent of the above reasoning, the claims also lack clarity (Article 84 EPC). An attempt is made to define the product by reference to results to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products mentioned in claims 39, 43 and 49 and the concept of "ligands capable of binding one or more non-albumin proteins".



CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

- No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

- None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:
1-35, 36 in part, 37 in part, 38, 39-49 in part



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-35, 36 in part, 37 in part, 38, 39-49 in part

Apparatus, comprising an insoluble support having a ligand comprising bromosulphophthalein attached thereto; a method for producing an albumin-depleted or protein-depleted sample comprising running the sample over said support; an albumin-depleted sample prepared by said method; a method of binding bromosulphophthalein to an insoluble support; a method for making said apparatus; a kit comprising said support; a spin column comprising an inner column comprising bromosulphophthalein; a method for producing an albumin-depleted sample comprising providing said spin column; a kit comprising an inner column comprising bromosulphophthalein.

2. claims: 36 in part, 37 in part, 39-49 in part

A method for producing a protein-depleted sample comprising running the sample over an insoluble support having a ligand comprising Cibracon Blue; a spin column comprising an inner column comprising Cibracon Blue; a method for producing an albumin-depleted sample comprising providing said spin column; a kit comprising an inner column comprising Cibracon Blue.

3. claims: 36 in part, 37 in part, 39-49 in part

A method for producing a protein-depleted sample comprising running the sample over an insoluble support having a ligand comprising Warfarin; a spin column comprising an inner column comprising Warfarin; a method for producing an albumin-depleted sample comprising providing said spin column; a kit comprising an inner column comprising Warfarin.

4. claims: 36 in part, 37 in part, 47 in part, 48 in part

A method for producing a protein-depleted sample comprising running the sample over an insoluble support having a ligand capable of preferentially binding albumin insofar as not comprised in subjects 1-3; a kit comprising an inner column comprising a ligand capable of preferentially binding albumin insofar as not comprised in subjects 1-3.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 04 10 4644

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-12-2004

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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EP 0469519	A	05-02-1992	JP 4086554 A EP 0469519 A2	19-03-1992 05-02-1992

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82