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**SUPPLEMENTARY
EUROPEAN SEARCH REPORT**

Application Number
EP 03 75 1939

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
P,X	DERVIEUX T ET AL: "HPLC Determination of Erythrocyte Methotrexate Polyglutamates after Low-Dose Methotrexate Therapy in Patients with Rheumatoid Arthritis" CLINICAL CHEMISTRY, AMERICAN ASSOCIATION FOR CLINICAL CHEMISTRY, WASHINGTON, DC, vol. 49, no. 10, 1 January 2003 (2003-01-01), pages 1632-1641, XP002903601 ISSN: 0009-9147 * the whole document *	1-13	INV. C12N9/48 C12Q1/26 C12P13/14 C12P7/24 G01N33/53
X	COLE PETER D ET AL: "Effects of overexpression of gamma-glutamyl hydrolase on methotrexate metabolism and resistance" CANCER RESEARCH, vol. 61, no. 11, 1 June 2001 (2001-06-01), pages 4599-4604, XP002504003 ISSN: 0008-5472 * the whole document *	1-13	
X	RHEE M S ET AL: "CHARACTERIZATION OF HUMAN CELLULAR GAMMA-GLUTAMYL HYDROLASE" MOLECULAR PHARMACOLOGY, BALTIMORE, MD, US, vol. 53, no. 6, 1 June 1998 (1998-06-01), pages 1040-1046, XP001037321 ISSN: 0026-895X * the whole document *	1-13	TECHNICAL FIELDS SEARCHED (IPC) A61K C12Q
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The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search Munich		Date of completion of the search 14 November 2008	Examiner Seranski, Peter
CATEGORY OF CITED DOCUMENTS		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	
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			

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EPO FORM 1503 03.82 (P04C04)

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	PANETTA JOHN CARL ET AL: "Methotrexate intracellular disposition in acute lymphoblastic leukemia: a mathematical model of gamma-glutamyl hydrolase activity." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH JUL 2002, vol. 8, no. 7, July 2002 (2002-07), pages 2423-2429, XP002504004 ISSN: 1078-0432 * the whole document * -----	1-13	
			TECHNICAL FIELDS SEARCHED (IPC)
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
Place of search		Date of completion of the search	Examiner
Munich		14 November 2008	Seranski, Peter
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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EPO FORM 1503 03.82 (P04C04)

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due 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 those claims for which no payment was due.

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:
- The present supplementary 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 (Rule 164 (1) EPC).

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: 1-13

Method for efficiently converting methotrexate polyglutamates to methotrexates in a cellular extract using gamma glutamyl hydrolyse; Method for determining the level of said methotrexate polyglutamates.

2. claims: 14-20

Method for determining the level of methotrexate in cellular extract.

3. claims: 21-27

Method of optimizing therapeutic efficacy or reducing toxicity associated with methotrexate therapy.

4. claim: 28

An isolated composition produced by a disclosed method.

专利名称(译)	量化甲氨蝶呤代谢物的方法		
公开(公告)号	EP1546317A4	公开(公告)日	2008-12-31
申请号	EP2003751939	申请日	2003-08-28
[标]申请(专利权)人(译)	普罗米修斯实验室		
申请(专利权)人(译)	普罗米修斯实验室, INC.		
当前申请(专利权)人(译)	普罗米修斯实验室, INC.		
[标]发明人	DERVIEUX THIERRY RICHERSON RUSSELL B		
发明人	DERVIEUX, THIERRY RICHERSON, RUSSELL, B.		
IPC分类号	A61K35/18 C12Q1/34 C12Q1/37 G01N33/50 C12N9/48 C12Q1/26 C12P13/14 C12P7/24 G01N33/53		
CPC分类号	G01N33/5014 A61K35/18 C12Q1/34 C12Q1/37		
优先权	10/232760 2002-08-30 US		
其他公开文献	EP1546317A1		
外部链接	Espacenet		

摘要(译)

本发明提供了一种通过在适合于将甲氨蝶呤多谷氨酸酯有效转化为甲氨蝶呤的条件下使细胞提取物与γ-谷氨酰水解酶接触而将细胞提取物中的甲氨蝶呤多谷氨酸酯有效地转化为甲氨蝶呤的方法。

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Munich		14 November 2008	Seranski, Peter
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