European Patent Office

SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

under Rule 46, paragraph 1 of the European Patent Convention

Application Number EP 02 71 9386

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	POLLACK V A ET AL: "INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR-ASSOCIATED TYROSINE PHOSPHORYLATION IN HUMAN CARCINOMAS WITH CP-358,774: DYNAMICS OF RECEPTOR INHIBITION IN SITU AND ANTITUMOR EFFECTS IN ATHYMIC MICE" JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, AMERICAN SOCIETY FOR PHARMACOLOGY AND, US, vol. 291, no. 2, 1999, pages 739-748, XP001014737 ISSN: 0022-3565 * page 741; figure 2 * ----- -/--	1,2,5-8, 11,12	C12Q1/00 C12Q1/68 G01N33/53 G01N33/567 C07K1/00 C07K14/00 C07K17/00 C07H21/02 C07H21/04

TECHNICAL FIELDS SEARCHED (Int.Cl.7)

C12Q
G01N

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

The present partial 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.

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Place of search	Date of completion of the search	Examiner
Munich	2 March 2005	Knudsen, H

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

EPO FORM 1503 03.82 (P04C23)

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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	MENDEL D B ET AL: "The angiogenesis inhibitor SU5416 has long-lasting effects on vascular endothelial growth factor receptor phosphorylation and function." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. DEC 2000, vol. 6, no. 12, December 2000 (2000-12), pages 4848-4858, XP002319665 ISSN: 1078-0432 * page 4850, left-hand column * * page 4853, right-hand column * * page 4856, left-hand column, paragraph 4 *	1-12	
	---		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	VINCENT P W ET AL: "Anticancer efficacy of the irreversible EGFr tyrosine kinase inhibitor PD 0169414 against human tumor xenografts." CANCER CHEMOTHERAPY AND PHARMACOLOGY. 2000, vol. 45, no. 3, 2000, pages 231-238, XP002319666 ISSN: 0344-5704 * figure 2 *	1,2,5-8, 11,12	

	-/--		

1

EPO FORM 1503 09.98 (P04C26)

European Patent Office

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Application Number
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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	
P,X	CHRISTENSEN J G ET AL: "High levels of HER-2 expression alter the ability of epidermal growth factor receptor (EGFR) family tyrosine kinase inhibitors to inhibit EGFR phosphorylation in vivo." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. DEC 2001, vol. 7, no. 12, December 2001 (2001-12), pages 4230-4238, XP009044605 ISSN: 1078-0432 * page 4232, left-hand column, last paragraph - page 4232, right-hand column, paragraph 1 *	1,2,5-8, 11,12	
	---		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
T	SEPP-LORENZINO L ET AL: "A Novel Orally Bioavailable Inhibitor of Kinase Insert Domain-Containing Receptor Induces Antiangiogenic Effects and Prevents Tumor Growth in Vivo" CANCER RESEARCH 15 JAN 2004 UNITED STATES, vol. 64, no. 2, 15 January 2004 (2004-01-15), pages 751-756, XP001205456 ISSN: 0008-5472 * page 752, left-hand column *	1-12	

EPO FORM 1503 09.98 (P04C25)

European Patent Office

LACK OF UNITY OF INVENTION SHEET B

Application Number
EP 02 71 9386

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: 1-12

In-vivo method for determining inhibition of a specific kinase receptor in which the compound is administered to a non-human test animal the concentration of the compound is determined in a blood or plasma sample and the phosphorylation of the kinase receptor is determined in a blood or tissue sample. The phosphorylation inhibition as a function of the plasma concentration indicates the inhibitory effect of the compound.

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2. claims: 13-17

Method for predicting the in-vivo IC50 of a compound in a second species in which in-vitro enzymatic IC50 for a first and a second species is measured and an in-vitro cellular or kinase receptor IC50 of the first species is measurede and multiplying the values.

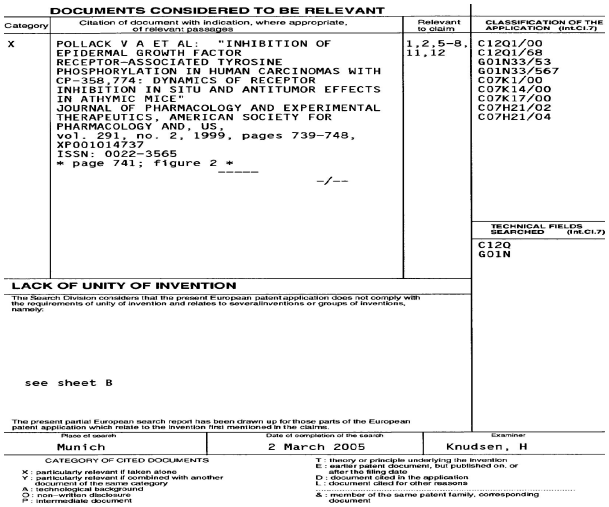
The claimed subject-matter contain two entirely different methods of predicting the in-vivo inhibitory effects of a test compound. The first method concerns an-vivo method taking samples from the test animal whereas the second method employs enzymatic and cellular methods. Thus, the only common concept is that the methods concern the prediction of the in-vivo inhibitory effects of a test compound on a kinase receptor.

However, this is a purpose of most methods studying the effects of potential therapeutic compounds (see eg the document "Pollack et al., J. Pharm. Exp. Therap., vol.291, p.739-748, (1999)" which disclose an in-vivo based method for determining the inhibitory effect of CP-358,774 which is an inhibitor of EGF receptor tyrosine kinase. Thus, the common concept is not novel and the claimed subject-matter is considered to contain two independent and separate inventions which are not linked by a common patentable concept.

专利名称(译)	在VIVO中测定受体型激酶抑制剂活性的方法		
公开(公告)号	EP1385983A4	公开(公告)日	2005-11-16
申请号	EP2002719386	申请日	2002-03-29
申请(专利权)人(译)	MERCK & CO. , INC.		
当前申请(专利权)人(译)	MERCK & CO. , INC.		
[标]发明人	THOMAS KENNETH A JR MAO XIANZHI KENDALL RICHARD L		
发明人	THOMAS, KENNETH, A., JR. MAO, XIANZHI KENDALL, RICHARD, L.		
IPC分类号	C12Q1/48 G01N33/567 C12Q1/00 C07H21/02 C07H21/04 C07K1/00 C07K14/00 C07K17/00 C12Q1/68 G01N33/53		
CPC分类号	C12Q1/485 G01N2333/912		
优先权	60/280771 2001-04-02 US		
其他公开文献	EP1385983A1		
外部链接	Espacenet		

摘要(译)

公开了用于测量化合物对激酶受体活性的抑制的体内方法。提供的实施例显示KDR激酶抑制的体内抑制与抑制剂的循环血液和血浆水平之间的直接相关性。这些数据用于预测和验证不可量化的体外测量值，例如鼠内皮细胞IC 50值。通过本发明的测定确定的化合物的体内效力可用于选择剂量和频率用于进一步的临床前动物模型研究和旨在产生安全性，效力和功效谱的人临床研究。对于各自的抑制剂。



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