

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 038602-1087	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US01/04813	International filing date (day/month/year) 15/02/2001	Priority date (day/month/year) 15/02/2000
International Patent Classification (IPC) or national classification and IPC C07D403/00		
Applicant SUGEN, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 10/09/2001	Date of completion of this report 04.04.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Deutsch, W Telephone No. +49 89 2399 8281 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US01/04813

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-45 as originally filed

**Claims, No.:**

1-60 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
  - the language of publication of the international application (under Rule 48.3(b)).
  - the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

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*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. 52-59 in respect of IA.

because:

- the said international application, or the said claims Nos. 52-59 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims 3-32,35-51,60
	No: Claims 1,2,33,34,50,51
Inventive step (IS)	Yes: Claims
	No: Claims 1-51,60
Industrial applicability (IA)	Yes: Claims 1-51,60

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No: Claims

2. Citations and explanations  
**see separate sheet**

Reference is made to the following documents:

- D1: US-A-5 886 020 (PENG CHO TANG ET AL.) 23 March 1999 (1999-03-23)  
D2: WO 98 50356 A (SUGEN, INC.) 12 November 1998 (1998-11-12)  
D3: LI SUN ET AL.: 'Synthesis and biological evaluations of 3-substituted indolin-2-ones: a novel class of tyrosine kinase inhibitors that exhibit selectivity toward particular receptor tyrosine kinases' JOURNAL OF MEDICINAL CHEMISTRY., vol. 41, no. 14, - 1998 pages 2588-2603, XP002181002 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623  
D4: WO 99 61422 A (SUGEN, INC.) 2 December 1999 (1999-12-02)  
D5: WO 01 37820 A (SUGEN, INC.) 31 May 2001 (2001-05-31)  
D6: WO 00 38519 A (SUGEN, INC.) 6 July 2000 (2000-07-06)  
D7: WO 00 35908 A (F. HOFFMANN-LA ROCHE AG) 22 June 2000 (2000-06-22)

III

Claims 52-59 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V

**Novelty**

The following compounds from D1 to D3 are novelty destroying to the present claim 1

The compounds of D1 at column 22, lines 30-39 (SU5408); column 25, line 66 - column 26, line 2 (SU5455).

The compound at page 30, lines 1,2 and the 10718/HO2 on page 44 disclosed in D2.

Compounds 44 and 48 disclosed on pages 2594 and 2601 of D3.

**Inventive Step**

The closest prior art is considered to be D1 to D3.

In view of the novelty destroying subject matter, which D1-D3 contain and the fact that the compounds disclosed in these documents modulate the activity of kinase, the skilled person would having regard for qualitative activity expected this to be retained in the claimed compounds.

The problem underlying the present invention must therefore be the provision of further compounds with unexpected properties compared with the closest prior art. In the absence of any evidence for these unexpected properties, an inventive step cannot at present be acknowledged either for products or intermediates of the present claims.

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The following documents do not constitute prior art within the meaning of Rule 64.1 (b).

	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
D5	31.05.2001	22.11.2000	24.11.2000
D6	06.07.2000	30.12.1999	31.12.1998
D7	22.06.2000	08.12.1999	17.12.1998 16.08.1999

It may be noted that the filing date of D5 and D6 is earlier than the priority date of the present application. D5 -D7 contains subject matter which could anticipate the present claims.

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The following points could give rise to clarity objections at the regional stage of examination.

The present claims are unclear in view of inconsistencies between the claims and the description (see the PCT Guidelines for Examination, Chapter III, 4.2).

In the description it has been indicated that the terms "alkyl", "cycloalkyl", "aryl", "heteroaryl", "heteroalicyclic", "alkoxy", "aryloxy" etc. found in the claims may be substituted, but is not indicated in claim 1.

On page 14 of the description "cycloalkyl" is defined and indicates that "one or more of the rings may contain one or more double bond". and does not normally fall under the usual understanding of cycloalkyl.

The special meaning given in the description of the term "cycloalkyl" is not found in claim 1, leading to a discrepancy between the claims and the description.

Similar objections apply to "aryloxy", which would not be understood as including -O-heteroaryl (cf page 18 of the description); alkoxy, which would not be understood as being a cycloalkoxy group.

The term "lower" used for example in claim 8 leads to a lack of clarity, particularly in the upper number of carbon atoms.