

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference GAL0032-PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2006/010247	International filing date (<i>day/month/year</i>) 17 March 2006 (17.03.2006)	Priority date (<i>day/month/year</i>) 17 March 2005 (17.03.2005)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant IVAX PHARMACEUTICALS S.R.O.			

<p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<p>3. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input checked="" type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application																						

	Date of issuance of this report 18 September 2007 (18.09.2007)
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)**

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2006/010247

International filing date (day/month/year)
17.03.2006

Priority date (day/month/year)
17.03.2005

International Patent Classification (IPC) or both national classification and IPC
INV. C07D491/06

Applicant
IVAX CORPORATION

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**


If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Date of completion of this opinion

see form PCT/ISA/210

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2006/010247

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed
 - a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - on paper
 - in electronic form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in electronic form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2006/010247

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-37
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-37
Industrial applicability (IA)	Yes: Claims	1-37
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1 Subject-matter of the independent claims

The present application is directed to a process for the isolation of galanthamine from plant sources by extraction of the biomaterial with an aqueous solution of an acid and further chromatographic work-up of the extract obtained.

2 Prior art documents

Reference is made to the following documents. The given numbering will be adhered to in the rest of the procedure:

D1: BERKOV S ET AL: "Intraspecific variability in the alkaloid metabolism of Galanthus elwesii" PHYTOCHEMISTRY, PERGAMON PRESS, GB, vol. 65, no. 5, March 2004 (2004-03), pages 579-586

D2: ABDALLAH O M: "NARCISINE AN ALKALOID FROM NARCISSUS TAZETTA" PHYTOCHEMISTRY, PERGAMON PRESS, GB, vol. 34, no. 5, 1993, pages 1447-1448

D3: US 2002/028802 A1 (HILLE THOMAS ET AL) 7 March 2002

3 Novelty (Article 33(2) PCT)

The presently claimed processes of independent claims 1 and 35 consists of two important steps a) extraction of the biomaterial and b) adsorption/desorption step i.e. a chromatographic work-up of the extract obtained in step a). This principle is also applied in D1 and D2 whereas D3 only uses liquid-liquid extraction steps.

Neither D1 and D2 uses the present chromatography technique involving a polymeric resin in combination with a water-miscible organic solvent. The present claims 1-37 are thus novel.

4 Inventive step (Article 33(3) PCT)

In the light of closest prior art D1 (which also uses an acidic aqueous solution to extract the biomaterial followed by a chromatographic step) the present technical problem resides in the provision of an alternative method for isolating galanthamine from plant sources. It does not appear that the choice of a certain chromatography technique leads to an inventive isolation process unless a surprising or advantageous effect is made credible for the present process. If, however, it could be convincingly argued that the choice of polystyrene copolymer resins in combination with water-miscible organic solvent as eluents forms indeed part of a non-obvious solution to the abovementioned problem, it is additionally remarked that this combination is missing from the content of present independent claims 1 and 35.

Thus, at present the subject-matter of the present set of claims is not inventive.

5 Industrial applicability (Article 33(4) PCT)

The subject-matter of the present claims 1-37 is in accordance with the requirements of Article 33(4) PCT.

Re Item VII

Certain defects in the international application

(1) The requirements of Rule 5.1(a)(ii) PCT are not met since the most relevant background art (document D1) has not been identified in the description.

(2) When entering the regional phase at the EPO, the Applicant is informed that an application may contain more than one independent claim in a particular category only certain circumstances. In the present case it appears that present claim 1 should be made

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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dependent on claim 35 which appears to be the broadest independent claim (and thus claim 35 should be renumbered as claim 1).

Re Item VIII

Certain observations on the international application

In steps b) of claims 1 and 35 it should presumably read "adsorbent" instead of "absorbent".