PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
JASON R. BOND
MEDLEN & CARROLL, LLP
101 HOWARD STREET, SUITE 350
SAN FRANCISCO, CA 94105

REC'D 24 OCT 2005
PCT
WIPO PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant' s or agent's file reference FORS-09468	Date of mailing (*day/month/year*) 21 OCT 2005 **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US05/00452	07 January 2005 (07.01.2005)	07 January 2005 (07.01.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/68; C12N 7/00; C07H 21/04 and US Cl.: 435/6, 235.1; 536/24.32

Applicant

THIRD WAVE TECHNOLOGIES, INC.

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 43*bis*.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 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 66.1*bis*(*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/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Timothy M. Brown Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/00452

Box No. I Basis of this 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, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language ____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 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

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable 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:

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Box No. 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. 3,5,12 and 14

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ 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. 3,5,12 and 14 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. ____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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

1. Statement

Novelty (N)	Claims 8-11,13 and 15-21	YES
	Claims 1, 2, 4 and 7	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1, 2, 4, 6-11, 13, 15-21	NO
Industrial applicability (IA)	Claims 1, 2, 4, 6-11, 13, 15-21	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1, 2, 4 and 7 lack novelty under PCT Article 33(2) as being anticipated by Zhang et al. (US 5,942,391).

Claims 1, 2, 4 and 7 are drawn to a composition comprising a pair of DNA oligonucleotides that are capable of binding the 5' untranslated region (UTR) region of HCV. Zhang et al. disclose a composition comprising pair of probes that hybridize to the 5' UTR of HCV (col. 32, lines 25-29). Zhang et al. therefore anticipate the subject matter of claims 1, 2, 4 and 7.

Claim 6, 8-11, 13, and 15-21 lack an inventive step under PCT Article 33(3) as being obvious over Fors et al. (US 2003/0152942) in view of Zhang et al. (US 5,942,391).

The invention of the claims listed above is drawn to a method for detecting single nucleotide polymorphisms in the 5' UTR of HCV. The method is performed by contacting a sample from a subject with a pair of HCV DNA 5' UTR probes. In summary, Applicant's invention is drawn to an INVADER assay for serotyping HCV in a sample using a probe for the 5' UTR of HCV. Fors et al. disclose many features of the claimed method including an INVADER assay for detecting HCV polymorphisms using a pair of oligonucleotide probes (¶¶ 0 010-0011, 0023; and Table 1). Fors et al. provide that the probes may be composed of RNA or DNA (Id.). Fors et al. do not expressly teach using probes comprising the 5' UTR of HCV. However, Zhang et al. overcome this deficiency by disclosing the detection of HCV target sequences using probes for the 5' UTR (col. 32, lines 25-29; and Examples 4 and 5). At the time of Applicants' invention, it would have been obvious to modify Fors et al. to include the 5' UTR probes taught by Zhang et al. This results because one skilled in the art would readily recognize that different polymorphisms could be detected simply by switching probes. Thus, one skilled in the art would have been motivated to apply Zhang et al.'s probes to the method of Fors et al. in order to detect polymorphisms in the 5' UTR of HCV.