Title: INTERNAL POSITIVE CONTROL FOR NUCLEIC ACID ASSAYS

Abstract: Compositions and methods for detecting a non-specific nucleic acid amplification inhibitor in a reaction are disclosed. An internal positive control (IPC) may be included in samples to be tested for target nucleic acids as a means to monitor non-specific inhibition of nucleic acid amplification and provide confidence in negative results obtained in target-specific assays. Provided herein are an IPC polynucleotide, IPC control primers, and IPC probes. Also provided are methods of using an IPC polynucleotide, primers, and probes to detect a non-specific nucleic acid amplification inhibitor.
INTERNATIONAL SEARCH REPORT
PCT/US 08/71378

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12Q 1/68 (2009.01)
USPC - 435/6; 435/91.2; 536/24.3

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) C12Q 1/68 (2009.01)
USPC: 435/6; 435/91.2; 536/24.3

Documented searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB; USPT; EPAB; JPAB); internal positive control, assay, amplification, inhibitor, deoxyribonucleotide triphosphate, DNA polymerase, hemoglobin, heparin, EDTA; espi@cenet: amplification, internal, positive; Google Scholar: ribulose-1,5-bisphosphate carboxylase oxygenase large subunit N-methyltransferase; NCBI: BT0057

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>
| Y        | US 5,952,202 A (AOYAGI et al.) 14 September 1999 (14.09.1999), abstract; col. 6, 6
          | in 43-45; col 7, in 11-15; col 7, in 16-34; col 7, in 28-31; col 11, in 16-21; col 17, in 35-39; col 17, in 45-47; col 20, in 34-60; col 20, in 57-60 | 1-7, 9-12,16-18, 21-23 |
| Y        | US 2005/0095644 A1 (HARTMAN et al.) 5 May 2005 (05.05.2005), abstract; para [0025], [0073], [0096], [0100], [0115]-[0124]. | 1-7, 9-12, 21-23 |
| Y        | US 5,723,752 A (HOUTZ) 3 March 1998 (03.03.1998), abstract, col 6, 14-22; col 9, in 34-38; col 12, in 19-22; col 13, in 35-39; col 15, in 12-16 | 2, 5, 7, 12, 18 |
| Y        | GenBank Accession No. BT00579. Arabidopsis thaliana clone C105297 putative ribulose-1,5-bisphosphate carboxylase oxygenase large subunit N-methyltransferase (At1g14030) mRNA, complete cds - NCBI Entrez Nucleotide, 15 March 2003 [online]. [Retrieved on 2009 07 02] | 3-5, 7, 9-12, 16-18 |

D. Further documents are listed in the continuation of Box C.

- Special categories of cited documents
  - A document defining the general state of the art which is not considered to be of particular relevance
  - E document earlier application or patent but published on or after the international filing date
  - L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  - Q document referring to an oral disclosure, use, exhibition or other means
  - P document published prior to the international filing date but later than the priority date claimed
  - T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
  - X document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  - Y document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
  - Z document member of the same patent family

Date of the actual completion of the international search
2 July 2009 (02.07.2009)

Date of mailing of the international search report
14 JUL 2009

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. 571-273-3201

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PCT OSP 571-272-7774
**INTERNATIONAL SEARCH REPORT**

**Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. **☐** Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. **☐** Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. **☑** Claims Nos.: 8, 13-15, 19-20, 24-29
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Group I: Claims 1-7, 9-12, 16-18 and 21-23 drawn to methods and compositions for quantifying an amount of a target nucleic acid, comprising: a control primer comprising a sequence of SEQ ID NO: 5; and an oligonucleotide probe comprising a sequence of SEQ ID NO: 7.

Groups M-II: Claims 1-7, 9-12, 16-18 and 21-23 drawn to methods and compositions for quantifying an amount of a target nucleic acid, comprising: a control primer comprising a sequence of SEQ ID NO: 5; and an oligonucleotide probe comprising a sequence of SEQ ID NO: 10 or 11. If Applicant elects to have this group searched, Applicant must specify the specific oligonucleotide probe sequence to be searched. Each nucleic acid sequence constitutes an inventive concept.

—please see supplemental box—

1. **☐** As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. **☐** As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. **☐** As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. **☒** No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

   1-7, 9-12, 16-18 and 21-23, limited to SEQ ID NOs: 1, 2, 5 and 7

**Remark on Protest**

**☐** The additional search fees were accompanied by the applicant’s protest and, where applicable, the payment of a protest fee.

**☐** The additional search fees were accompanied by the applicant’s protest but the applicable protest fee was not paid within the time limit specified in the invitation.

**☐** No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Continuation of Box No. III: Observations where unity of invention is lacking

Groups I-VI: Claims 1-7, 9-12, 16-18 and 21-23 drawn to methods and compositions for quantifying an amount of a target nucleic acid, comprising: a control primer comprising a sequence of SEQ ID NO: 6; and an oligonucleotide probe comprising a sequence of SEQ ID NO: 7, 10 or 11. If Applicant elects to have this group searched, Applicant must specify the specific oligonucleotide probe sequence to be searched. Each nucleic acid sequence constitutes an inventive concept.

Groups VII-IX: Claims 1-7, 9-12, 16-18 and 21-23 drawn to methods and compositions for quantifying an amount of a target nucleic acid, comprising: a control primer comprising a sequence of SEQ ID NO: 8; and an oligonucleotide probe comprising a sequence of SEQ ID NO: 7, 10 or 11. If Applicant elects to have this group searched, Applicant must specify the specific oligonucleotide probe sequence to be searched. Each nucleic acid sequence constitutes an inventive concept.

Groups X-XII: Claims 1-7, 9-12, 16-18 and 21-23 drawn to methods and compositions for quantifying an amount of a target nucleic acid, comprising: a control primer comprising a sequence of SEQ ID NO: 9; and an oligonucleotide probe comprising a sequence of SEQ ID NO: 7, 10 or 11. If Applicant elects to have this group searched, Applicant must specify the specific oligonucleotide probe sequence to be searched. Each nucleic acid sequence constitutes an inventive concept.

The inventions listed as Groups I-XII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature shared by the inventions listed as Groups I-XII is the specific nucleic acid sequence recited therein. In the instant case, because no significant structural similarities can readily be ascertained, the inventions do not share a special technical feature. Without a shared special technical feature, the inventions lack unity with one another.