The present disclosure provides methods for biosynthesis of acetaminophen. The present disclosure provides host cells genetically modified to provide for production of acetaminophen. The present disclosure provides a recombinant host cell that is genetically modified with one or more heterologous nucleic acids comprising nucleotide sequences encoding 4-aminobenzoate hydroxylase (4ABH) and N-hydroxy-L-tryptophan O-acetyltransferase (NhoA). The present disclosure provides a recombinant prokaryotic host cell that is genetically modified with one or more heterologous nucleic acids comprising nucleotide sequences encoding 4ABH and NhoA.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C08G 73/22 (2016.01)
CPC - C08G 73/22 (2016.05)

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

8. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - C08G 73/22; C12N 1/15, 1/19, 1/21 (2016.01)
CPC - C08G 73/22; C12N 9/104; C12P 13/005, 13/02; Y02P 20/52 (2016.05)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 435/129, 252.3, 252.32, 252.33 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Search terms used: 4ABH NhoA N-acetyl-p-aminophenol paracetamol vector host cell recombinant expression

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>
<tbody>
<tr>
<td>Y</td>
<td>US 2005/01 18665 A1 (ZHOU et al) 02 June 2005 (02.06.2005) entire document</td>
<td>1-9</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents.
“A” document defining the general state of the art which is not considered to be of particular relevance
“B” earlier application or patent but published on or after the international filing date
“D” document which may throw doubts on priority claims or which is cited to establish the publication date of another citation or other special reason (as specified)
“O” 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
“&” document member of the same patent family

Date of the actual completion of the international search
11 May 2016

Date of mailing of the international search report
02 JUN 2016

Name and mailing address of the ISA/
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Blaine R. Copenheaver
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PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)
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.: 10-29
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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.;

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.