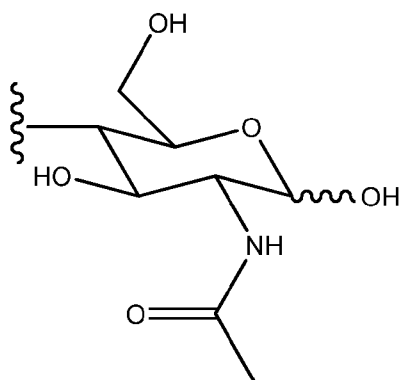




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[Continued on next page]

(54) Title: N-ACETYLHEXOSAMINE-CONTAINING N-GLYCANS IN GLYCOPROTEIN PRODUCTS



(57) Abstract: The present invention provides methods of evaluating a glycoprotein preparation for the absence, pres-
ence or amount of an N-acetylhexosamine glycan, e.g., an N-
acetylglucosamine glycan.

FIG. 1



(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/28759

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 33/48 (2012.01)

USPC - 436/87, 86; 435/4

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) - G01N 33/48 (2012.01)

USPC - 436/87, 86; 435/4

Documentation 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)

WEST - DB=PGPB,USPT,USOC,EPAB,JPAB; PLUR=YES; OP=ADJ; Google Scholar

search terms: acetylhexosamine, acetylhexaamine, measur\$, detec\$, quantif\$, glycoprotein, glycan, carbohydrat\$, polysacch\$, sacchar\$, reference, control, standard, compar\$, amount, level,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0144553 A1 (BOSQUES et al.) 10 June 2010 (10.06.2010) para [0008]; [0009]; [0025]; [0029]; [0046]; [0048]; [0052]; [0059]; [0127]-[0130]; [0134]; [0161]; [0162]; [0170]; [0171]; [0177]; [0184]-[0187]; [0191]-[0193]; [0210]; [0211]; [0233]; [0244]; [0255]; [0271]; [0360].	1-11, 22-32
A	US 5,068,190 A (HORIUCHI et al.) 26 November 1991 (26.11.1991) abstract.	1-11, 22-32
A	US 20090317834 A1 (LAINE et al.) 24 December 2009 (24.12.2009) abstract; para [0085]-[0089].	1-11, 22-32

☐ 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" 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)

"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

07 August 2012 (07.08.2012)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/28759

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.:
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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1-11 and 22-32, directed to a method for evaluating a glycoprotein preparation, comprising: providing a glycoprotein preparation; determining the presence, absence, or amount of N-acetylhexosamine in the preparation; and optionally making a decision regarding the glycoprotein preparation based upon the absence, presence or amount of the N-acetylhexosamine in the preparation.

- Please see extra sheet for continuation -

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.: 1-11 and 22-32

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.

Continuation of Box III: Lack of Unity of Invention

Group II: claims 12-21, directed to a method for screening a cell for the ability to produce glycoproteins comprising N-acetylhexosamine glycans, comprising:

- a) providing a plurality of cell populations that express a glycoprotein;
- b) culturing each of the plurality of cell populations under conditions suitable for expression of a glycoprotein preparation;
- c) measuring for N-acetylhexosamine glycans produced by one or more of the plurality of cells; and
- d) selecting one or more of the plurality of cell preparations based on the presence of a target level of N-acetylhexosamine glycans produced by the cell preparation.

Group III: claim 33, directed to a method for modulating effector function of an antibody preparation, comprising:

- 1) providing an antibody preparation; and
- 2) modulating the N-acetylhexosamine glycan content of the antibody preparation to thereby modulate effector function of the antibody preparation.

Group IV: claims 34 and 35, directed to a method for manufacturing a glycoprotein preparation, comprising:

- i) culturing cells to produce a recombinant glycoprotein preparation;
- ii) determining the presence, absence, or amount of N-acetylhexosamine in the produced preparation; and
- iii) processing the glycoprotein preparation as a pharmaceutical product based upon the determination.

The inventions listed as Groups I - IV 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 features of the claims of Groups I-IV are indicated above in the Group descriptions.

The only common technical element shared by the above groups is that they are related to measurement or assessment of N-acetylhexosamine. Groups I, III and IV are related to assessment of N-acetylhexosamine in a glycoprotein preparation. Groups II and IV are related to assessment of N-acetylhexosamine produced by cultured cells. These common technical elements do not represent an improvement over the prior art of US 2010/0144553 A1 to Bosques et al., which teaches a method for evaluating a glycoprotein preparation (para [0008]), the method comprising:

providing a glycoprotein preparation (para [0130] and [0177]);
determining the absence, presence or amount of N-acetylhexosamine in the preparation (para [0127]-[0129] and [0186]-[0187]); and
optionally, making a decision regarding the glycoprotein preparation based upon the absence, presence or amount of the N-acetylhexosamine in the preparation (para [0127]-[0129], [0186]-[0187] and [0191]-[0193]). Bosques further teaches wherein the glycan-comprising proteins may be produced in cell culture, and assessing the glycans produced by the cultured cells (para [0241], [0244]). Although Bosques does not specifically recite determining the absence, presence, or amount of N-acetylhexosamine produced by the cells, it would have been obvious to a person skilled in the art to do so, since Bosques teaches the assessment of N-acetylhexosamine as a part of glycan characterization (para [0129]).

Therefore, the inventions of Groups I-IV lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.