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(54) Title: METHODS AND COMPOSITIONS FOR TREATING *CLOSTRIDIODES DIFFICILE* INFECTIONS

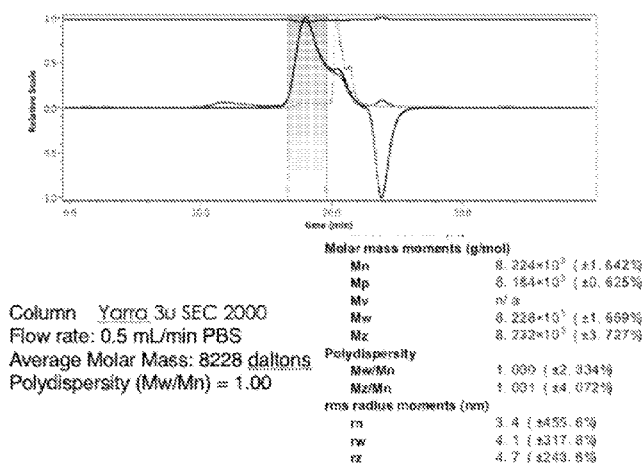


FIG. 1

(57) Abstract: Provided herein are immunogenic compositions for treating *Clostridiodes difficile* infections.



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
- *with sequence listing part of description (Rule 5.2(a))*

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10 November 2022 (10.11.2022)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 22/23029

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 31/702, A61P 31/04, C07H 17/04 (2022.01)

CPC - C08B 37/006, A61K 39/08, A61K 47/6415, A61K 37/646, A61P 31/04, C07H 1/00, C07H 17/04

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)

See Search History document

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

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	OBERLI et al. "A Possible Oligosaccharide-Conjugate Vaccine Candidate for Clostridium difficile Is Antigenic and Immunogenic" Chemistry & Biology, 27 May 2011, Vol. 18, pp 580-588; abstract, pg 580, col 1, para 2, pg 581, col 1, para 1 to col 2, para 2, pg 583, col 1, para 4, pg 583, col 2, para 1, pg 584, col 1, para 1, pg 585, col 2, para 1, pg 586, col 1, para 2, pg 586, col 2, para 1, pg 586, col 2, para 3, pg 587, col 1, para 3, Figure 1	1, 8-9, 15-22, 27-30, 33-49, 50/(1, 8-9, 15-22, 27-30, 33-49) ----- 2-7, 10-14, 23-26, 31-32, 50/(2-7, 10-14, 23-26, 31-32)
Y	WO 2020/102717 A2 (MATRIVAX, INC.) 22 May 2020 (22.05.2020) abstract, para [0021], [0074], [00171]	2-7, 10-14, 50/(2-7, 10-14)
Y	US 2019/0325991 A1 (NATIONAL INSTITUTES OF BIOMEDICAL INNOVATION, HEALTH AND NUTRITION) 24 October 2019 (24.10.2019) para [0521], [0545]	23-26, 50/(23-26)
Y	US 2018/0369406 A1 (VELOS BIO, INC.) 27 December 2018 (27.12.2018) para [0139], Claim 11	31-32, 50/(31-32)
A	WO 2020/104697 A1 (VAXXILON AG) 28 May 2020 (28.05.2020) whole doc.	1

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"D" document cited by the applicant in the international application	"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
"E" earlier application or patent but published on or after the international filing date	"&" document member of the same patent family
"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	

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 22/23029

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.: 52
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:

- see extra sheet for Box No. III Observations where unity of invention is lacking -

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.:
1-50

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 No. III. Observations where unity of invention is lacking

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 searched, the appropriate additional search fees must be paid.

Group I: claims 1-50, drawn to a composition comprising: a cell-surface polysaccharide of *Clostridiodes difficile* (*C. difficile*) and a carrier protein.

Group II: claims 51, 53-74, drawn to a method of treating an infection.

Group III: claims 75-95, drawn to a method of enriching for a cell-surface polysaccharide of *C. Difficile*.

The inventions listed as Groups I through III 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:

Special Technical Features

Group I includes the special technical feature of a composition which differs from the special technical feature of a method, as disclosed by Groups II and III.

Group II includes the special technical feature of administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition, not required by Group III.

Group III includes the special technical feature of enriching cell-surface polysaccharide of *C. difficile* sample wherein the enriched sample comprises less than about 5% by weight of a *C. difficile* impurity, not required by Group II.

Common Technical Features

The inventions of Groups I-III share the technical feature of a cell-surface polysaccharide of *Clostridiodes difficile* (*C. difficile*) and a carrier protein.

However, these shared technical features do not represent a contribution over prior art in view of the article "A Possible Oligosaccharide-Conjugate Vaccine Candidate for *Clostridium difficile* Is Antigenic and Immunogenic" by Oberli et al. (hereinafter "Oberli") (Chemistry & Biology, 27 May 2011, Vol. 18, pp 580-588.).

Oberli teaches a composition comprising:

(a) a cell-surface polysaccharide of *Clostridiodes difficile* (*C. difficile*); and

(b) a first polypeptide comprising a carrier protein derived from an organism other than *C. Difficile* (abstract, Here, we present the chemical synthesis of a PS-II hapten of a cell wall polysaccharide of hypervirulent ribotype 027 of *C. difficile*. Mice were immunized with a conjugate consisting of the synthetic hexasaccharide and the diphtheria toxoid variant CRM197.; pg 583, col 1, para 4, The synthetic hapten 2 of the *C. difficile* glycopolymer PS-II was conjugated to the protein carrier CRM197. The diphtheria toxoid CRM197 was chosen as a carrier because it is a constituent of licensed vaccines.);

wherein the carrier protein and the cell-surface polysaccharide are present in the composition at a ratio of from about 10:1 to about 1:10 (pg 583, col 2, para 1, The mass analysis of CRM197 yielded a m/z ion at 58.6 kDa. The mass spectrum of the neoglycoconjugate revealed mass peaks between 59.9 and 67.3 kDa corresponding to mono- to heptavalent glycoconjugates. On average four haptens 2 were loaded on the diphtheria toxoid.).

As said technical features were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the groups.

Groups I through III therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Item 4 (continued)

Claim 52 is a dependent claim and is not drafted in accordance with the second and third sentences of Rule 6.4(a)