



(51) International Patent Classification:

A61F 5/44 (2006.01) A61F 5/453 (2006.01)
A61F 5/442 (2006.01) A61F 5/455 (2006.01)
A61F 5/451 (2006.01)

(21) International Application Number:

PCT/US2016/022565

(22) International Filing Date:

16 March 2016 (16.03.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/135,585 19 March 2015 (19.03.2015) US

(71) Applicant: **RESTORE HEALTH, INC.** [US/US]; 166 Prospect Place, Brooklyn, NY 11238 (US).

(72) Inventor: **PARK, Joonhee**; 222 Pacific Street, Apt. 2B, Brooklyn, NY 11201 (US).

(74) Agents: **KOLE, Lisa B.** et al.; Baker Botts LLP, 30 Rockefeller Plaza, New York, NY 10112-4498 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available):

AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(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, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: TREATMENT FOR VESICOVAGINAL FISTULA

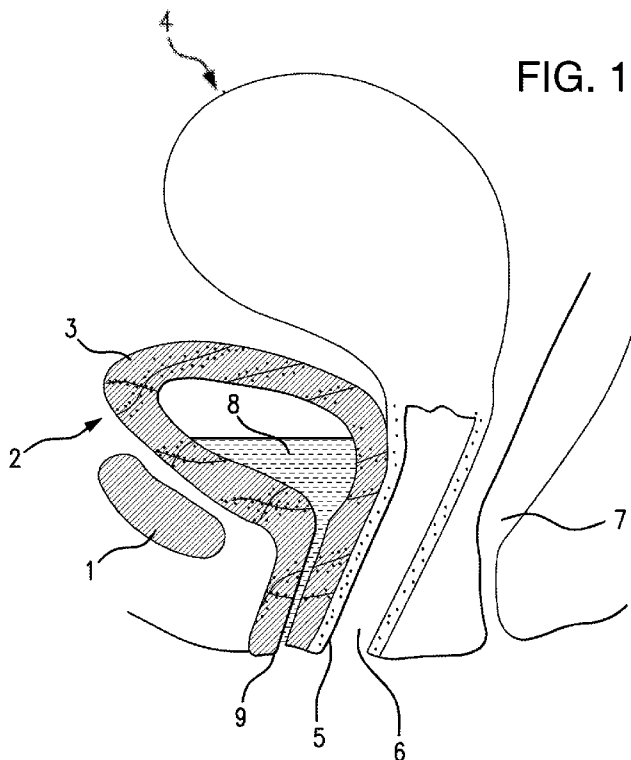


FIG. 1

(57) Abstract: The present invention relates to methods and compositions for the treatment of vesicovaginal fistula. It is based, at least in part, on the discovery that a menstrual cup may be used to collect urine and decrease or prevent urine leakage in certain women having vesicovaginal fistula and, in some cases, the menstrual cup was observed to at least partially occlude the fistula and permit normal micturition.

WO 2016/149317 A1

TREATMENT FOR VESICOVAGINAL FISTULA

CROSS REFERENCE TO RELATED APPLICATION

5 This application claims priority to United States Provisional Application No. 62/135,585, filed on March 19, 2015, which is incorporated herein by reference in its entirety and from which priority is claimed.

1. INTRODUCTION

 The present invention relates to compositions and methods for treating
10 vesicovaginal fistula.

2. BACKGROUND OF THE INVENTION

 Obstetric fistula is a communication, or channel, between the vagina and either the bladder (“vesicovaginal fistula”) or rectum (“rectovaginal fistula”). It may arise as a result of prolonged obstructed labor or rape. Obstetric fistula has a higher
15 incidence in low-income countries with fewer opportunities for surgical correction. According to Biadgilign et al. (2013, Reproductive Health 10:14), 10.6 per 1000 parous women in Ethiopia have experienced obstetric fistula.

 Vesicovaginal fistula (“VVF”) results in leakage of urine through the vagina and manifests as incontinence. VVF has been reported to have a number of
20 psychosocial consequences, including depression, feelings of shame, social and familial ostracism, and even divorce (Alio et al., 2011, Arch. Gynecol. Obstet. 284(2):371-378; Farid et al., 2013, J. Coll. Physicians Surg. Pak. 23(10):828-829). As many of the women suffering from VVF have limited or no access to surgical repair, there is a need for non-surgical treatment options.

Menstrual cups are known in the art. These are flexible cups that can be placed in the vaginal canal in order to collect menstrual fluid. Commercially available menstrual cups include the DivaCup®, the Mooncup®, the Instead Softcup™, the Ladycup, and the Lunette menstrual cup, among others. Patents and patent applications describing menstrual cups include United States Patent No. 5,827,248 to Crawford, Canadian Patent Application No. 2,579,454 to Chambers and Pickering, and International Patent Application Publication No. WO2006/058409 to Diva International.

10 3. SUMMARY OF THE INVENTION

The present invention relates to methods and compositions for the treatment of VVF. It is based, at least in part, on the discovery that a menstrual cup may be used to collect urine and decrease or prevent urine leakage in certain women having VVF and, in some cases, the menstrual cup was observed to at least partially occlude the fistula and permit normal micturition.

In various embodiments, the present invention provides for a method of treating VVF comprising placing a vaginal cup in the vaginal canal. In non-limiting subsets of embodiments, the vaginal cup, situated in the vaginal canal between the VVF and the entrance to the vagina, may collect urine and decrease or prevent urine leakage from the vagina. In various non-limiting embodiments, the vaginal cup, situated in the vaginal canal, may at least partially occlude the fistula and permit voiding by micturition through the urethra.

In a subset of embodiments, the vaginal cup is a menstrual cup such as those known in the art, but the invention is not limited to such menstrual cups and their uses. In non-limiting subsets of embodiments, the vaginal cup may have a

reversible means of occlusion that allows periodic drainage of urine without requiring removal of the device from the vagina. In non-limiting subsets of embodiments, the dimension of the vaginal cup may be elongated to increase the likelihood that it may occlude the fistula in a subject having a VVF. In non-limiting subsets of

5 embodiments, the vaginal cup may comprise means to connect to a urine collection bag which, for example, may be reversibly strapped to a leg of the subject.

FIGURE 1 is a diagram showing normal anatomy of the female pelvic cavity. The pubic symphysis **1** serves as the anterior landmark and the rectum **7** is the posterior landmark in the diagram. The bladder **2** is filled with urine **8** and the

10 bladder wall **3** is next to the vaginal wall **5**. The uterus **4** is located above the bladder. The urethra is structure **9**. Of note, the invention may also be used in a female from whom the uterous and/or cervix and/or a portion of the vagina has been removed.

FIGURE 2 is a diagram showing a VVF **10** connecting the bladder **2** and the vaginal canal **6**, which results in leakage of urine **8** from the vagina canal.

15 The VVF is located high in the vaginal wall, meaning closer to the cervix or the vaginal apex than to the vaginal entrance.

FIGURE 3 is a diagram showing a vaginal cup **11** positioned in the vaginal canal **6** below the fistula **10A** (“below” meaning between the VVF and the vaginal entrance) where it can collect urine **8** that has leaked through the fistula.

20 FIGURE 4 is a diagram showing a VVF **10B** located lower in the vaginal wall relative to the VVF **10A** shown in FIGURES 2 and 3 (“lower” meaning closer to the vaginal entrance). A vaginal cup **11** positioned in the vaginal canal **6** at least partially or completely occludes the fistula and allows urine to accumulate in the bladder **8**. In some instances, a subject in whom a vaginal cup at least partially or

25 completely occludes the fistula may be able to void via her urethra, although

sometimes the urethra is damaged or otherwise occluded, making voiding difficult or practicably impossible, and accumulated urine may be released by either draining the cup (for example, via an opening in the cup) or removing the cup (for example, and un-occluding the fistula).

5 FIGURE 5A-F. (A) Side view of vaginal cup **12A** having an open top end with a rim **13A**, a closed bottom end with a stem **14A**, and an outer surface **21A**. The top diameter is **15A**, the bottom diameter is **22A**, and the length is **16A**. (B) Side view of vaginal cup **12B** having an open top end with a rim **13B**, a bottom end with a stem having an open end **14B** over which a cap **17** may be placed to occlude the
10 opening, and an outer surface **21B**. The top diameter is **15B**, the bottom diameter is **22B**, and the length is **16B**. (C) Side view of vaginal cup **12C** having an open top end with a rim **13C**, a bottom end with a stem having an open end **14C** having an attached plug **18** that may be inserted into the open end of the stem to occlude the opening, and an outer surface **21C**. The top diameter is **15C**, the bottom diameter is
15 **22C**, and the length is **16C**. (D) Top view of vaginal cup **12A** showing the interior surface of the cup **19A**, the outer surface **21A**, the rim **13A** and the closed bottom end, showing the top of the stem **14A**. The diameter is **15A**. (E) Top views of vaginal cups **12B** or **12C** (which would be essentially the same) showing the interior surface of the cup **19B** or **19C**, the rim **13B** or **13C**, the outer surface **21B** or **21C**, and the top
20 of the stem **14B** or **14C** and showing the opening in the stem **20**. (F) Side view of the vaginal cup as depicted in FIGURE 5B, wherein the stem **14B** has means to connect the cup to a tubing **23** which may be connected to a collection bag **24**. The present invention further envisions embodiments in which the cup does not have a stem, where optionally there is a hole in the cup which may be reversibly occluded by a
25 stopper or a valve.

4. BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1. Schematic of normal female anatomy showing intact bladder and vaginal walls and accumulation of urine (gray) in the bladder.

5 FIGURE 2. Schematic showing vesicovaginal fistula resulting in leakage of urine through the vaginal canal.

FIGURE 3. Schematic showing vesicovaginal fistula with vaginal cup positioned in the vaginal canal to collect urine leaking through the fistula.

10 FIGURE 4. Schematic showing vesicovaginal fistula with vaginal cup positioned in the vaginal canal to at least partly occlude the opening of the fistula into the vaginal canal, thereby allowing collection of urine in the bladder.

FIGURE 5A-F. Views of vaginal cups for use according to the invention. (A) Side view of vaginal cup with closed stem. (B) Side view of vaginal cup with capped stem. (C) Side view of vaginal cup with plugged stem. (D) Top
15 view of vaginal cup with closed stem. (E) Top view of vaginal cup with open stem. (F) Side view of vaginal cup attached to collection bag.

5. DETAILED DESCRIPTION

The vaginal cup has an outer surface, at least a portion of which contacts the vaginal wall when positioned in the vaginal canal, and an inner surface
20 which defines a cavity. In configurations where the bottom end of the cup is closed or occluded, fluid may accumulate in the cavity of the vaginal cup.

The vaginal cup is flexible to facilitate insertion and withdrawal from the vagina.

In certain non-limiting embodiments the vaginal cup resembles a cone
25 and has a wider top diameter and a narrower bottom diameter.

In certain non-limiting embodiments the vaginal cup resembles a tube and the top diameter and bottom diameter are approximately equal.

In certain non-limiting embodiments the rim of the vaginal cup protrudes beyond the outer surface to form a lip, which aids in retaining position when the cup is placed in the vaginal canal. In certain non-limiting embodiments the rim has greater rigidity than the body of the vaginal cup, which aids in retaining position when the cup is placed in the vaginal canal.

In certain non-limiting embodiments, the vaginal cup may have one or a plurality of small holes, for example holes having a diameter of 0.5-2 mm, located in proximity of the rim (for example, within 1 cm of the rim) to aid in insertion and withdrawal by promoting pressure equalization.

In certain non-limiting embodiments, the vaginal cup is made of a biomedical grade polymer such as, but not limited to, latex, silicone, thermoplastic polymer, or polyethylene. In a specific, non-limiting embodiment, the vaginal cup is essentially made of silicone.

In certain non-limiting embodiments the top diameter is between about 3 and 8 centimeters, or between about 4 and 6 centimeters, or between about 4 and 5 centimeters, or between about 5 and 7 centimeters, or between about 5 and 6 centimeters, or about 3 centimeters, or about 3.5 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters, or about 5.5 centimeters, or about 6 centimeters, or about 6.5 centimeters, or about 7 centimeters, or about 7.5 centimeters, or about 8 centimeters.

In certain non-limiting embodiments, the bottom diameter is between about 1 and 5 centimeters, or between about 1 and 3 centimeters, or about 1 centimeter, or about 1.5 centimeters, or about 2 centimeters, or about 2.5 centimeters,

or about 3 centimeters, or about 3.5 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters.

In certain non-limiting embodiments, a vaginal cup may have dimensions wherein (i) the top diameter is between about 3 and 8 centimeters, or
5 between about 4 and 6 centimeters, or between about 4 and 5 centimeters, or between about 5 and 7 centimeters, or between about 5 and 6 centimeters, or about 3 centimeters, or about 3.5 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters, or about 5.5 centimeters, or about 6 centimeters, or about 6.5 centimeters, or about 7 centimeters, or about 7.5 centimeters, or about 8 centimeters;
10 and (ii) the bottom diameter is between about 1 and 5 centimeters, or between about 1 and 3 centimeters, or about 1 centimeter, or about 1.5 centimeters, or about 2 centimeters, or about 2.5 centimeters, or about 3 centimeters, or about 3.5 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters.

In certain non-limiting embodiments, the length of the vaginal cup is
15 between about 4 and 12 centimeters, or between about 5 and 10 centimeters, or between about 6 and 10 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters, or about 5.5 centimeters, or about 6 centimeters, or about 6.5 centimeters, or about 7 centimeters, or about 7.5 centimeters, or about 8 centimeters, or about 8.5 centimeters, or about 9 centimeters, or about 9.5 centimeters, or about 10
20 centimeters, or about 10.5 centimeters, or about 11 centimeters, or about 11.5 centimeters, or about 12 centimeters, where the stem may account for between about 0.5 and 3 centimeters or between about 0.5 and 2 centimeters or about 0.5 centimeters, or about 1 centimeter, or about 1.5 centimeters, or about 2 centimeters, or about 2.5 centimeters, or about 3 centimeters, of such length. In certain non-limiting
25 embodiments a vaginal cup having a longer length, for example a length greater than

7 centimeters or greater than 7.5 centimeters or greater than 8 cm (or greater than 6.5 centimeters excluding the stem or greater than 7 centimeters excluding the stem) may be chosen for a patient having a VVF located higher in the vaginal wall (i.e., closer to the cervix).

- 5 In certain non-limiting embodiments, a vaginal cup may have dimensions wherein (i) the top diameter is between about 3 and 8 centimeters, or between about 4 and 6 centimeters, or between about 4 and 5 centimeters, or between about 5 and 7 centimeters, or between about 5 and 6 centimeters, or about 3 centimeters, or about 3.5 centimeters, or about 4 centimeters, or about 4.5 centimeters, 10 or about 5 centimeters, or about 5.5 centimeters, or about 6 centimeters, or about 6.5 centimeters, or about 7 centimeters, or about 7.5 centimeters, or about 8 centimeters; (ii) the bottom diameter is between about 1 and 5 centimeters, or between about 1 and 3 centimeters, or about 1 centimeter, or about 1.5 centimeters, or about 2 centimeters, or about 2.5 centimeters, or about 3 centimeters, or about 3.5 centimeters, or about 4 15 centimeters, or about 4.5 centimeters, or about 5 centimeters; and (iii) the length is between about 4 and 12 centimeters, or between about 5 and 10 centimeters, or between about 6 and 10 centimeters, or about 4 centimeters, or about 4.5 centimeters, or about 5 centimeters, or about 5.5 centimeters, or about 6 centimeters, or about 6.5 centimeters, or about 7 centimeters, or about 7.5 centimeters, or about 8 centimeters, 20 or about 8.5 centimeters, or about 9 centimeters, or about 9.5 centimeters, or about 10 centimeters, or about 10.5 centimeters, or about 11 centimeters, or about 11.5 centimeters, or about 12 centimeters, where the stem may account for between about 0.5 and 3 centimeters or between about 0.5 and 2 centimeters or about 0.5 centimeters, or about 1 centimeter, or about 1.5 centimeters, or about 2 centimeters, or 25 about 2.5 centimeters, or about 3 centimeters, of such length.

In certain non-limiting embodiments the vaginal cup does not have a stem.

In certain non-limiting embodiments the vaginal cup has a stem, and the stem may be of a length and flexibility so that, when the vaginal cup is in place in the vagina, the stem protrudes from the vagina to facilitate release of urine and emptying of the cup.

In certain non-limiting embodiments the stem may be configured to reversibly attach to a tube which connects or may be connected to a collection bag (e.g., see FIGURE 5F). Medical tubing connectors are known in the art, for example but not limited to mating compatible connectors. Tubing that connects to urine collection bags are known in the art. In non-limiting embodiments a collection bag may be strapped to the leg of a subject for portability.

In certain non-limiting embodiments the vaginal cup is a menstrual cup, as known in the art, for example menstrual cups as described in United States Patent No. 5,827,248 to Crawford, Canadian Patent Application No. 2,579,454 to Chambers and Pickering, and International Patent Application Publication No. WO2006/058409 to Diva International, and or a commercially available menstrual cup such as the DivaCup®, the Mooncup®, the Instead Softcup™, the Ladycup, or the Lunette menstrual cup.

In certain non-limiting embodiments, the present invention provides for a method of treating a subject having a VVF comprising placing, in the vaginal canal of the subject, a vaginal cup as described above, wherein placement of the vaginal cup in the vaginal canal results in collection of urine.

The vaginal cup may be placed by a physician but the subject is desirably taught how to insert and remove the vaginal cup herself. The vaginal cup is

inserted by folding the cup by pressing facing portions of the rim together and then inserting it into the vagina using essentially the same technique as used for the insertion of a menstrual cup.

In certain non-limiting embodiments, the present invention provides
5 for a method of treating a subject having a VVF comprising placing, in the vaginal canal of the subject, a vaginal cup as described above, wherein placement of the vaginal cup in the vaginal canal results in collection of urine and decreases or prevents leakage of urine from the vaginal canal to the exterior of the subject.

In certain non-limiting embodiments, the present invention provides
10 for a method of treating a subject having a VVF comprising placing, in the vaginal canal of the subject, a vaginal cup as described above, wherein placement of the vaginal cup in the vaginal canal results in at least partial occlusion of the VVF. In a non-limiting subset of such embodiments, the vaginal cup essentially completely occludes the VVF.

In certain non-limiting embodiments, the present invention provides
15 for a method of treating a subject having a VVF comprising placing, in the vaginal canal of the subject, a vaginal cup as described above, wherein placement of the vaginal cup in the vaginal canal results in a decrease or prevention of leakage of urine from the vaginal canal to the exterior and an improvement in the ability of the subject
20 to void urine through the urethra.

In certain non-limiting embodiments, the method comprises emptying the vaginal cup after at least 2 hours, or after at least 4 hours, or after at least 6 hours, or after at least 12 hours, or after at least 24 hours. The vaginal cup may be emptied by either removing the cup, or by uncapping or unplugging the cup.

In certain non-limiting embodiments, the method comprises connecting the stem of the cup to a collection reservoir so that urine may flow from the cup to the collection reservoir.

In certain non-limiting embodiments, the vaginal cup may be removed
5 from the subject about once a day or about once a week.

In certain non-limiting embodiments, where the cup at least partially or completely obstructs the VVF (thus allowing the bladder of the subject to fill), the subject may learn to approximate how long it takes for her bladder to fill (for example, by recognizing the sensation of having a fully distended bladder) before
10 voiding through the urethra, releasing accumulated urine through the vagina cup, or releasing accumulated urine after withdrawing the vaginal cup.

As working examples, use of a Diva® menstrual cup in a small number of women with VVF resulted in reduction or correction of urine leakage, and in some instances insertion of a vaginal cup was observed to apparently occlude the
15 fistula hole and allowed urine to collect in the wearers' bladders.

Various publications and patents are set forth herein, the contents of which are hereby incorporated by reference in their entireties.

WHAT IS CLAIMED:

1. A method of treating a subject having a vesicovaginal fistula comprising placing, in the vaginal canal of the subject, a vaginal cup, wherein placement of the vaginal cup in the vaginal canal results in collection of urine.
2. A method of treating a subject having a vesicovaginal fistula comprising placing, in the vaginal canal of the subject, a vaginal cup, wherein placement of the vaginal cup in the vaginal canal results in collection of urine and decreases or prevents leakage of urine from the vaginal canal to the exterior of the subject.
3. A method of treating a subject having a vesicovaginal fistula comprising placing, in the vaginal canal of the subject, a vaginal cup, wherein placement of the vaginal cup in the vaginal canal results in at least partial occlusion of the vesicovaginal fistula.
4. The method of claim 3, wherein the vaginal cup essentially completely occludes the vesicovaginal fistula.
5. The method of claim 3, wherein placement of the vaginal cup in the vaginal canal results in a decrease or prevention of leakage of urine from the vaginal canal to the exterior and an improvement in the ability of the subject to void urine through the urethra.
6. The method of any of claims 1-5, further comprising emptying the vaginal cup after at least 4 hours.
7. The method of any of claims 1-5, where the vaginal cup comprises a stem and the method comprises connecting the stem to a collection reservoir so that urine may flow from the cup to the collection reservoir.

8. A vaginal cup as shown in FIGURE 5F, configured to connect to a collection bag.

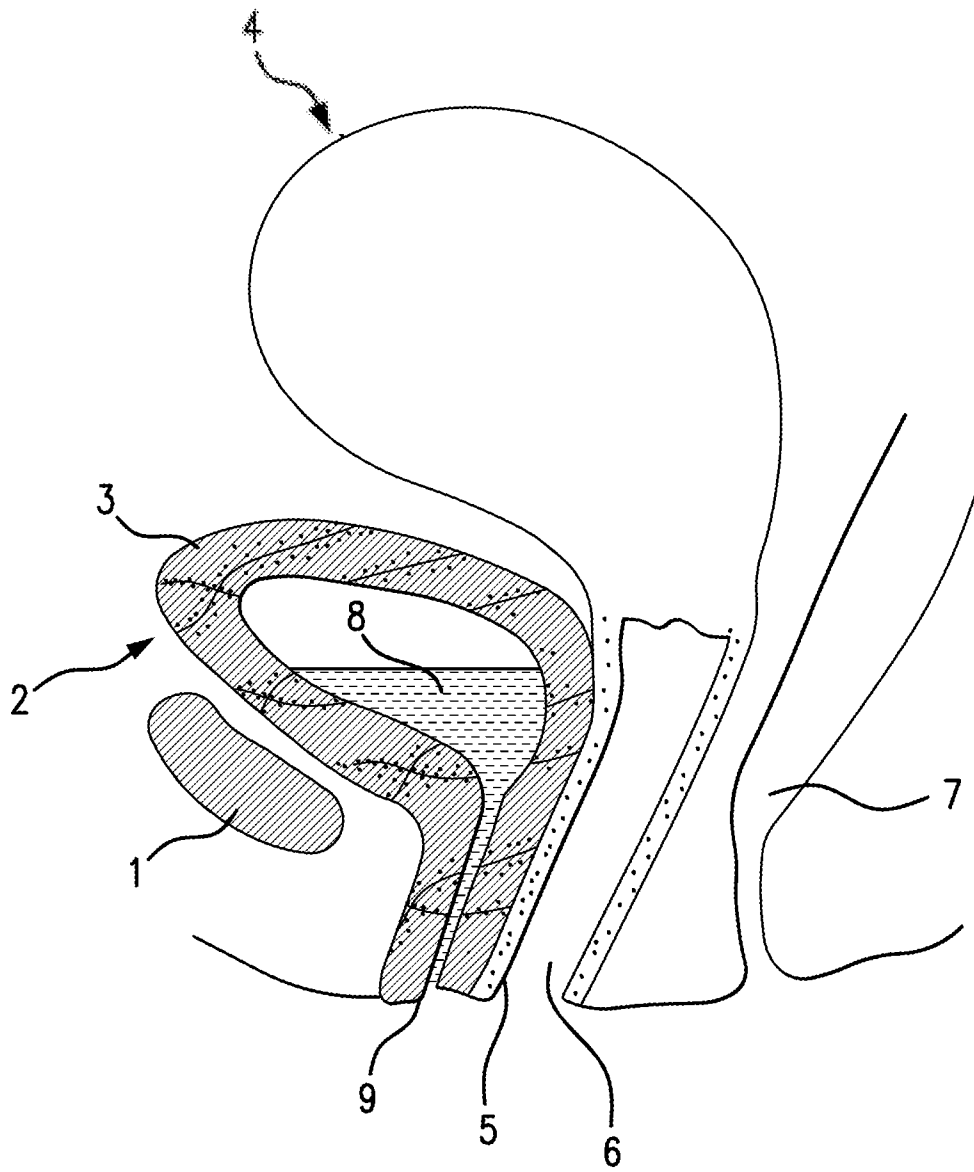


FIG. 1

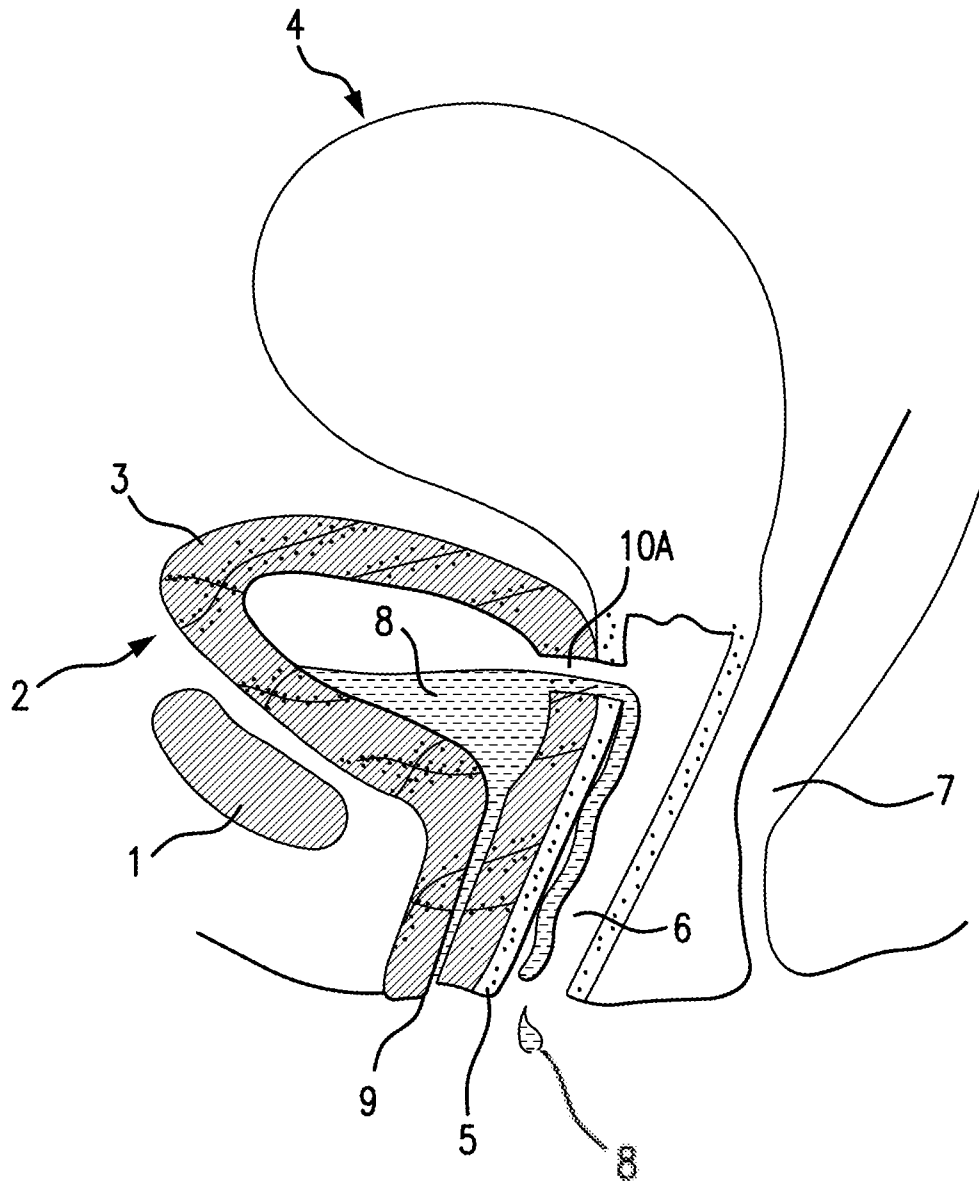


FIG. 2

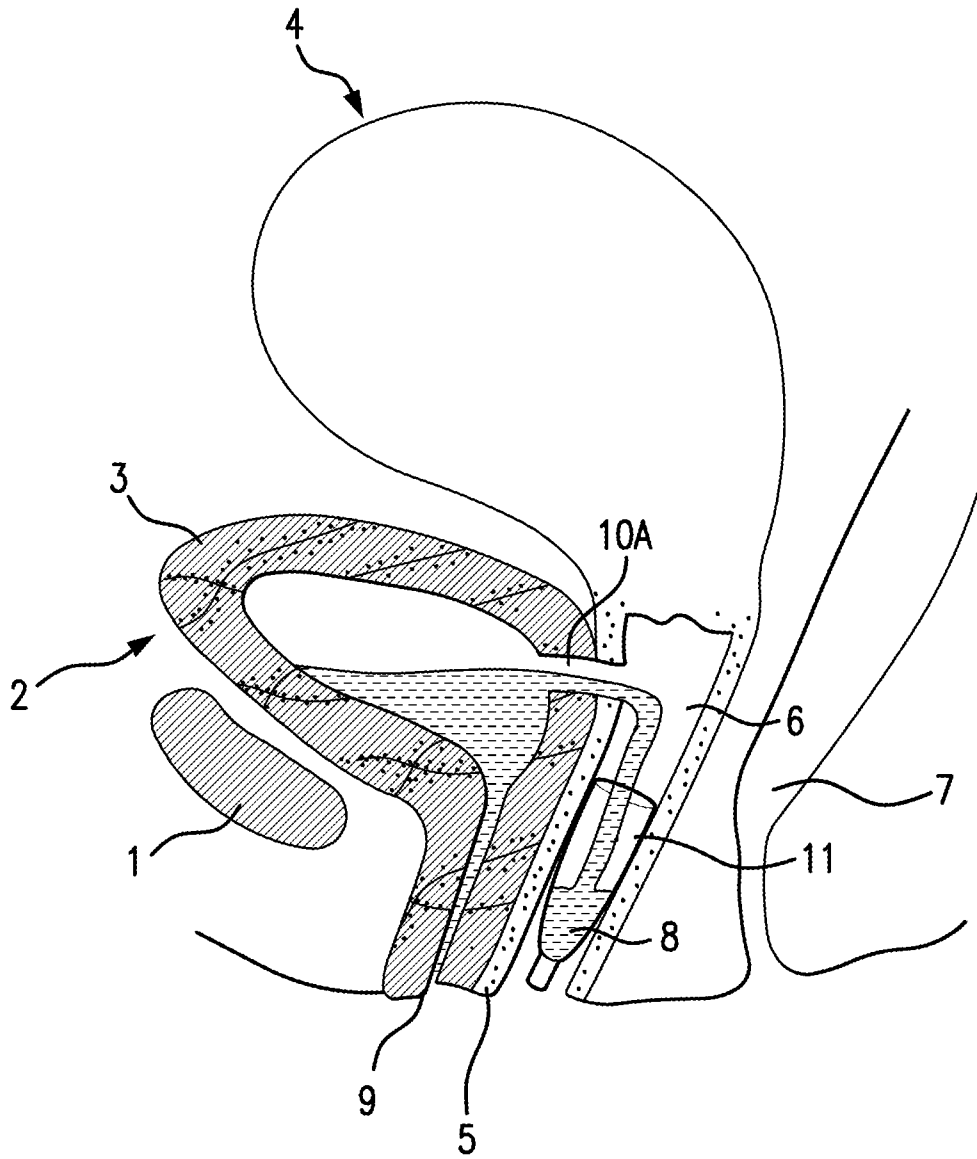


FIG. 3

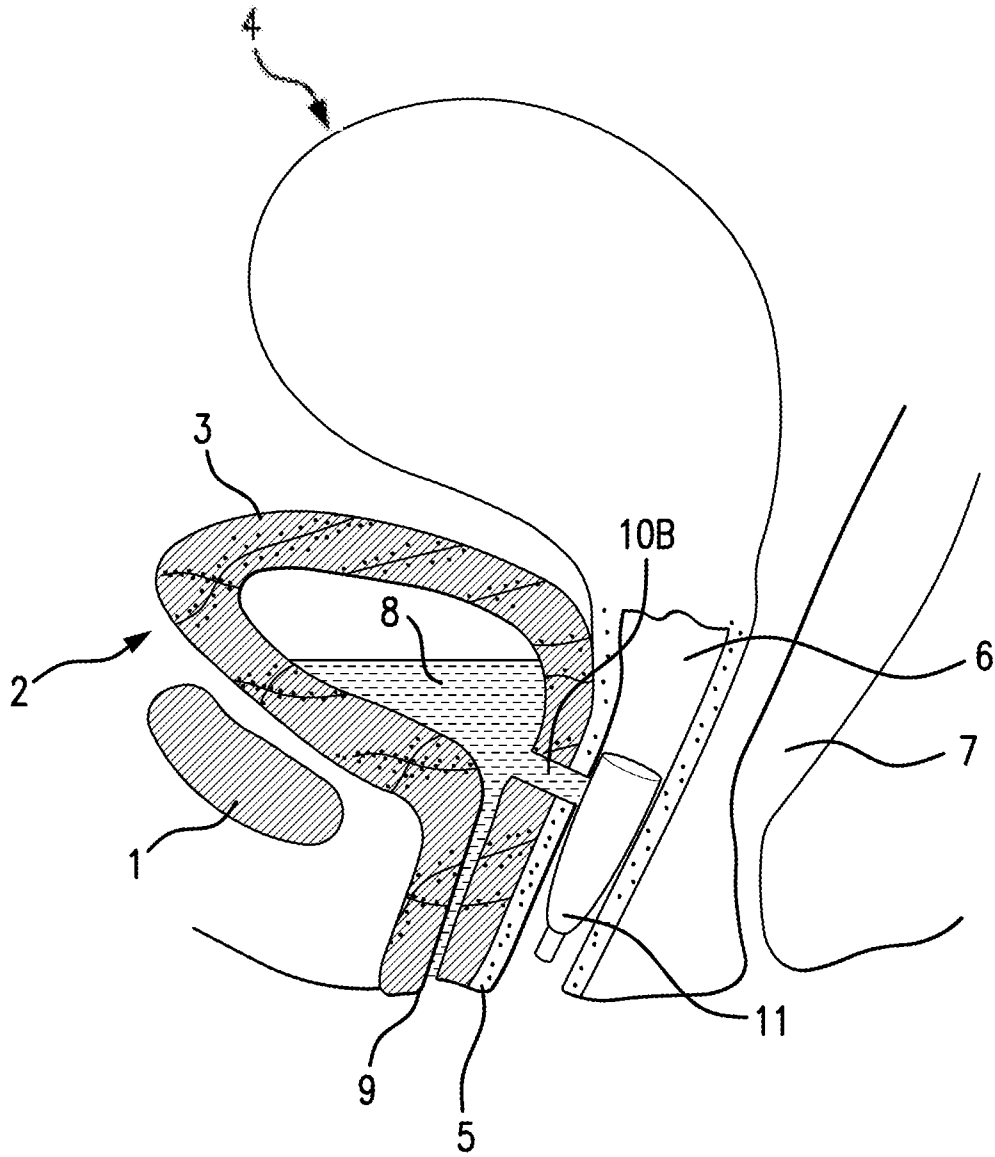


FIG. 4

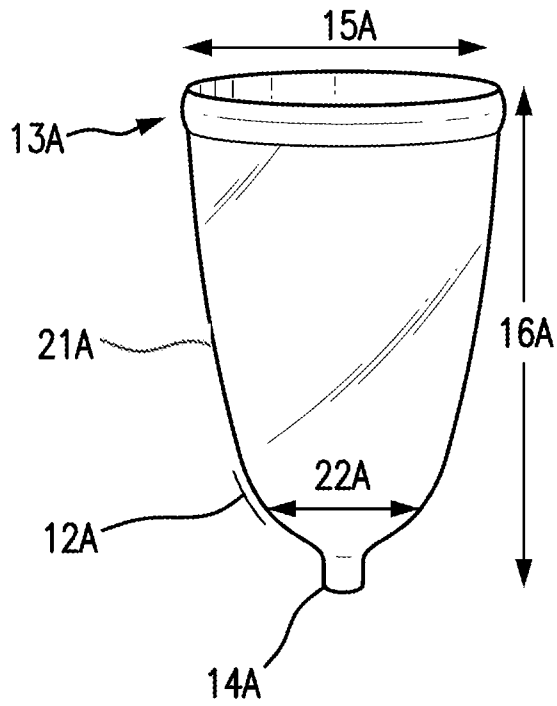


FIG. 5A

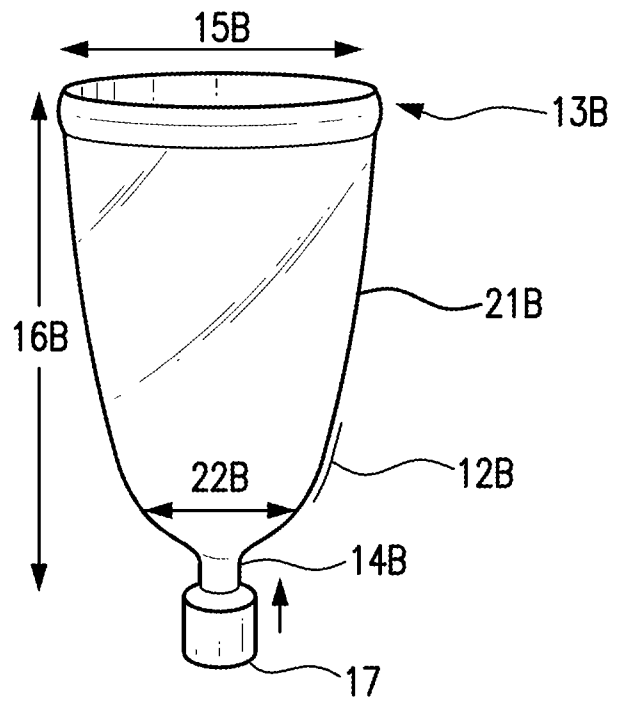


FIG. 5B

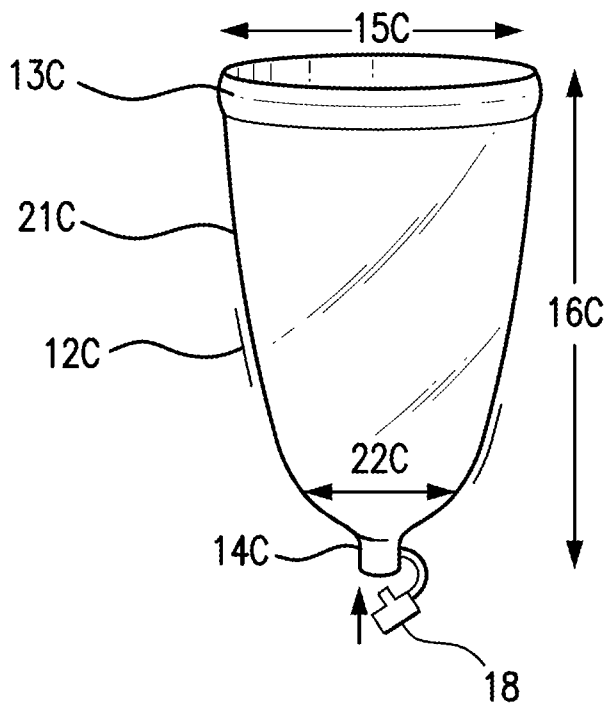


FIG. 5C

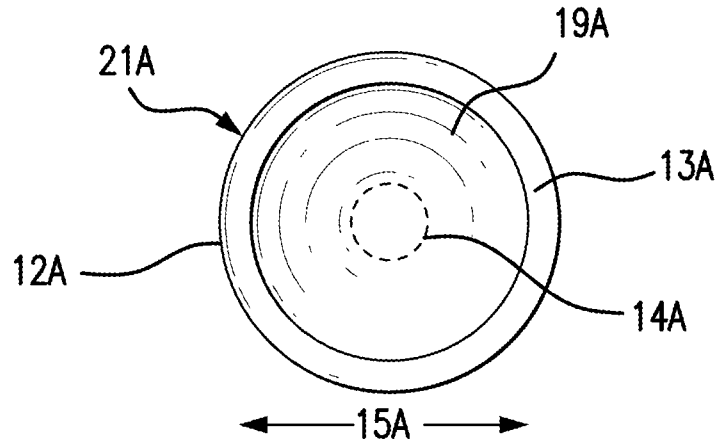


FIG. 5D

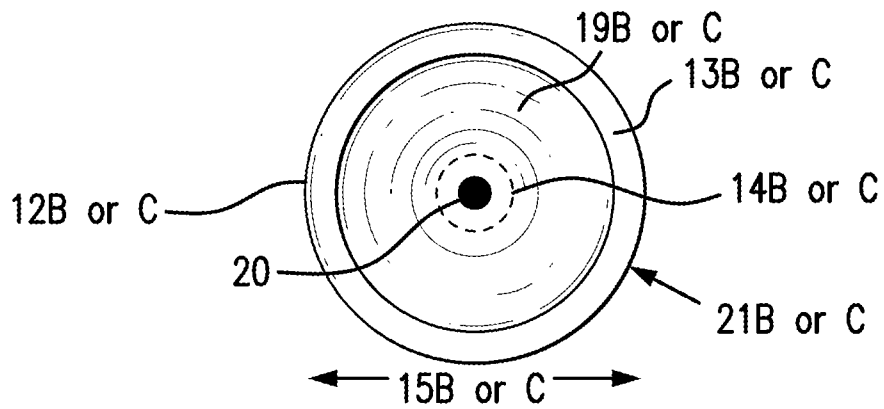


FIG. 5E

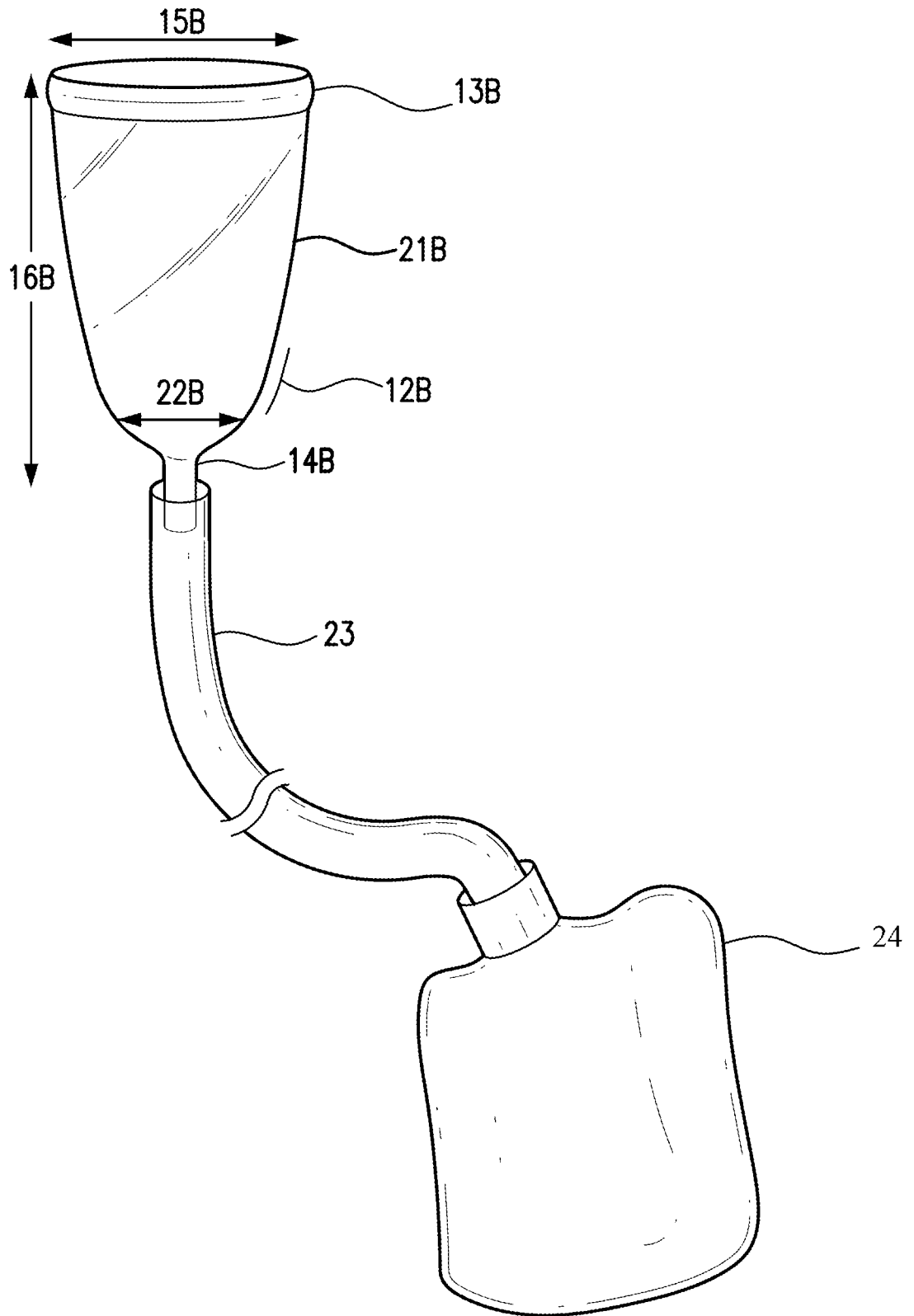


FIG. 5F

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/022565

| A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61F 5/44; A61F 5/442; A61F 5/451; A61F 5/453; A61F 5/455 (2016.01) CPC - A61F 5/4405; A61F 5/4408; A61F 5/451; A61F 5/453; A61F 5/455; A61F 5/4553 (2016.01) 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) - A61F 5/44; A61F 5/442; A61F 5/451; A61F 5/453; A61F 5/455 (2016.01) CPC - A61F 5/4405; A61F 5/4408; A61F 5/451; A61F 5/453; A61F 5/455; A61F 5/4553 (2016.01) | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 119/869; 604/323; 604/329; 604/330; 604/331; 604/349; 604/353 (keyword delimited) | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Google Patents, Google Search terms used: vesicovaginal, vagina, fistula, urine, urinary, incontinence, cup, collector, funnel, retainer, holder, empty, discard, remove | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | US 2007/0049879 A1 (GUTIERREZ) 01 March 2007 (01.03.2007) entire document | 1-7 |
| A | US 2008/0051831 A1 (DEAL et al) 28 February 2008 (28.02.2008) entire document | 1-7 |
| A | US 2008/0200888 A1 (GOOCH et al) 21 August 2008 (21.08.2008) entire document | 1-7 |
| A | US 3,116,734 A (TERMAN LOUIS A) 07 January 1964 (07.01.1964) entire document | 1-7 |
| A | US 2,483,079 A (WILLIAMS ALFRED J) 27 September 1949 (27.09.1949) entire document | 1-7 |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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 "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 13 May 2016 | | Date of mailing of the international search report 09 JUN 2016 |
| Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300 | | Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/022565

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.: 8
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:
Claim 8 has been held as an omnibus claim, as it refers to an invention "as shown in FIGURE 5F".

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:

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.:

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.