510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K153128

B. Purpose for Submission:

New device

C. Measurand:

Not applicable

D. Type of Test:

Not applicable

E. Applicant:

KOLPLAST CI SA

F. Proprietary and Established Names:

Kolplast Cervical Sample Collection Kit

G. Regulatory Information:

1. Regulation section:

   21 CFR §884.4530 Obstetric-gynecologic specialized manual instrument

2. Classification:

   Class II

3. Product code:

   HHT – Spatula, cervical, cytological

4. Panel:

   Obstetrics/Gynecology

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   The Kolplast Cervical Sample Collection Kit is intended for collection of cytological specimens from the ectocervix and the endocervix for conventional Pap Smear Test or Liquid-Based ThinPrep® Pap Test with PreservCyt® solution.

3. Special conditions for use statement(s):

   For prescription use only.

   It is not intended for use in pregnant women and should be used by a clinical or other qualified health professional only.

4. Special instrument requirements:

   Not applicable

I. Device Description:

The Kolplast Cervical Sample Collection Kit is a single use, non-sterile, disposable manual gynecological device intended for collection of cervical cells from the cervix for Pap Test analysis. It is composed of a cervical brush and a plastic spatula.

- The cervical brush has a white nylon bristle head, which is secured by stainless steel to the plastic handle. It is intended for the collection of cytological specimens from the endocervix.
- The plastic spatula has a handle with a notched end that corresponds to the contour of the cervix. It is intended for the collection of cytological specimens from the ectocervix.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Pap Smear Kit

2. Predicate 510(k) number(s):

K861389

3. Comparison with predicate:

Similarities		
Item	Kolplast Cervical Sample Collection Kit (Candidate Device) k153128	Pap Smear Kit (Predicate) k861389
Intended Use	For collection of cytological specimens from the ectocervix and the endocervix for conventional Pap Smear Test or Liquid-Based ThinPrep® Pap Test with PreservCyt® solution. For prescription use only. It is not intended for use in pregnant women and should be used by a clinical or other qualified health professional only.	For collection and transportation of gynecological smears used in Papanicolaou's Exfolative Cytology Test.
Device components	Brush and spatula	Brush and spatula
Composition	Brush: Plastic handle and a head with woven nylon interlaced in a stainless steel twisted wire; Spatula: plastic.	Same
Material	Brush head: Nylon and stainless steel 304; Brush handle: plastic; Spatula: plastic.	Same
Spatula Dimensions	Overal length: 7.2 inches Concave edge length: 0.82 inches	Same
Supplied	Non-sterile, disposable	Same

Differences		
Item	Kolplast Cervical Sample Collection Kit (Candidate Device) k153128	Pap Smear Kit (Predicate) k861389
Brush Dimensions	Head length: 0.08 inches Head diameter: 0.27-0.19 inches overall length: 7.2 inches	Head length: 0.09 inches Head diameter: 0.27-0.19 inches Overall length: 7.7 inches

K. Standard/Guidance Document Referenced (if applicable):

ISO 10993-5: Biological evaluation of medical devices – Part 5: Tests for *in vitro* cytotoxicity (2009).

ISO 10993-10: Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization (2010)

ISO 10993-12: Biological evaluation of medical devices – Part 12: Sample preparation and reference material (2012).

L. Test Principle:

For collection of cytological specimens from the ectocervix, the plastic spatula notched end is placed against the ectocervix and rotated around the circumference of the ectocervix. For collection of cytological specimens from the endocervix, the head of the cervical brush is inserted into the cervix, rotated ¼ to ½ turn via the handle and removed from the cervix. The collected endocervical or ectocervical cell sample is then transferred to a glass slide by smearing, or to preservative fluid in a container by swirling.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Not applicable

   b. Linearity/assay reportable range:

   Not applicable

   c. Traceability, Stability, Expected values (controls, calibrators, or methods):

   i. Performance Testing

   To assess the safety of the device, the following performance tests were conducted on candidate devices:

Test	Component	Acceptance Criteria	Number of items tested	Number of items failed	Results
Traction Resistance	Brush	Should not break with 7 kg force applied	315	0	Passed
	Spatula		315	0	Passed
Bending Resistance	Brush	Should not break when bend and pass through a guide tube*	315	0	Passed
	Spatula		315	0	Passed
Head-Stem Fixing Strength	Brush	Should not break with 7 kg force applied	315	0	Passed
Nylon Bristles Decoupling Rotation**	Brush	Bristles should not detach from the head	315	0	Passed

* The tube is about 2.25 inches in length and 1.375 inch in diameter.

** Brush head is inserted into rubber block (two stached rubber pieces) with 2.85 kgf applied, rotated 10 times clockwise and removed from the rubber block while pressure still applied.

ii. Shelf-life stability

To assess a shelf-life of five years, the same performance bench tests as summarized above in section (M.1.*c.i*) were conducted on real time aged devices.

Test	Component	Acceptance Criteria	Number of items tested	Number of items failed	Results
Traction Resistance	Brush	Should not break with 7 kg force applied	315	0	Passed
	Spatula		315	0	Passed

Bending Resistance	Brush	Should not break when bend and pass through a guide tube*	315	0	Passed
	Spatula		315	0	Passed
Head-Stem Fixing Strength	Brush	Should not break with 7 kg force applied	500	0	Passed
Nylon Bristles Decoupling Rotation**	Brush	Bristles should not detach from the head	500	0	Passed

* The tube is about 2.25 inches in length and 1.375 inch in diameter.

** Brush head is inserted into rubber block (two stached rubber pieces) with 2.85 kgf applied, rotated 10 times clockwise and removed from the rubber block while pressure still applied.

iii. Biocompability

Cytotoxicity, sensitization and irritation potential of the device were assessed for biocompatibility. The material specifications are shown in the table below.

Component	Material Name	Function	Patient Contact (Direct/Indirect)
Kolplast Cervical Brush Protected Tip			
Handle	Polystyrene	Handle	Indirect
	Polystyrene High Impact	Handle	Indirect
Head	Polycarbonate Adhesive	Protection of tip	Direct
	Nylon	Collecting of endocervical cells	Direct
	Stainless Steel	Nylon support	Direct
Kolplast Cervical Plastic Spatula			
Spatula (curve and long edge + handle)	Polypropylene	Handle and collecting samples	Direct

Cytotoxicity

Cytotoxicity testing was conducted on the Kolplast Cervical Brush Protected Tip and the Kolplast Cervical Plastic Spatula, per ISO 10993-5:2009, using the MEM Elution Method. A single preparation of the test extract was extracted in single strength Minimum Essential Medium (1x MEM) at 37°C for 24 hours, along with negative control, reagent control and positive control extracted similarly. Triplicate monolayers of L-929 mouse fibroblast cells were dosed with test extract and controls and incubated at 37°C (5% CO_2) for 48 hours. Following incubation, the cell monolayers were examined microscopically for abnormal cell morphology and cellular degeneration. The cell monolayers treated with test extract and controls showed no evidence of causing cell lysis or toxicity. The testing results demonstrated the candidate device is non-cytotoxic.

Sensitization

Sensitization testing was conducted on the Kolplast Cervical Brush Protected Tip and the Kolplast Cervical Plastic Spatula, per ISO 10993-10:2010, using the Guinea Pig Maximization Test (GPMT) on both polar and non-polar extracts. In each test, 15 male animals were used with 10 in the test group and 5 in the control group. The test substance was extracted in an incubator shaker (100 RPM) at 121°C for 1 hour at concentration of 0.2 g/ml in 0.9% Sodium Chloride solution (polar extract) or cotton seed oil (non-polar extract). The test substance was injected intradermally, 0.1 mL, and later topically on the dermis of the test animals. No change was observed on the test area (Magnusson and Klingman score = 0) 48 and 72 hours for polar extraction or 24 hours and 48 hours for non-polar extraction after application of test substance. After 7 days of the injection, gauzes saturated (0.5 mL) with the test substance and control substance was applied on the skin of test animal and control animal respectively. The animals appeared normal with no death. The testing results demonstrated the candidate device is non-sensitizing.

Irritation

Irritation testing was conducted on the Kolplast Cervical Brush Protected Tip and the Kolplast Cervical Spatula, per ISO 10993-10:2010, using the vaginal mucosal irritation test on both polar and non-polar extracts. In each test, 15 nulliparous and non-pregnant female rats (*Rattus norvegicus,* aged 4-6 weeks, weighted about 200 g) were used with 10 in the test group and 5 in the control group. The test extract was extracted in an incubator at 121°C for 1 hour in purified water (polar extract) or cotton seed oil (non-polar extract). The test extract and control substance (purified water for polar test and cotton seed oil for non-polar test) were applied to the middle part of the animals vagina, through a urethral probe. The application was repeated three times a day for four consecutive days. Necropsies were performed to examine the genital tract of test and control animals and vaginal irritation indices were

calculated. In a scale of 4.00, the irritation index of the test group is 0.17 for polar extract and 0.00 for non-polar extract. The testing results demonstrated the candidate device is non-irritant.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

To assess clinical performance, cytological specimens collected by using the subject device and slides were prepared for both conventional Pap Smear method and ThinPrep® liquid-based Pap Test.

i. Conventional Pap Smear testing

Cytological specimens from 422 patients were collected and slides were prepared for conventional Pap Smear, according to the Instructions for Use of the Kolplast

Cervical Sample Collection Kit. Prepared slides were analyzed by two certified cytotechnologists and reviewed by one pathologist. The inclusion criteria were women older than 21 years of age who are scheduled for routine gynecological evaluations. Patients were excluded if they refused to sign informed consent and denied participating in the study, or if they had a history using ointments, creams, vaginal douches or transvaginal ultrasound within the two days prior to the gynecological examination. The study results are shown in the table below:

Results	Cases (%)
Total number	422 (100%)
Normal	199 (47.1%)
Positive Atypical Cells	10 (2.37%)
Inflammatory	213 (50.4%)
ASC-US	5 (1.4%)
ASC-H	1 (0.2%)
LSIL	1 (0.2%)
HSIL	3 (0.7%)
Cancer	0
AGS-US	0
AGC-H	0
Unsatisfactory	0

Specimen adequacy evaluation is summarized in the table below:

Criteria for inadequacy	Number of cases (%)
Total number	422 (100%)
Insufficient cellular material present	0
Separated superfacial cells suggesting vaginal sampling only	0
Obscured by blood and/or inflammatory exudates	10 (2.37%)
Too thickly spread for assessment	13 (3.08%)
EC/TZ component not identified: absence of columnar cells	131 (31.04%)

ii. Liquid-based Pap Test

Cytological specimens from 579 patients were collected and preserved in ThinPrep® PreservCyt® solution, according to the Instructions for Use of the candidate device and ThinPrep® PreservCyt® solution. Slides were prepared by using the ThinPrep® Liquid-based method and analyzed by two certified cytotechnologists and reviewed by one pathologist. The inclusion criteria were women older than 21 years of age who are scheduled for routine gynecological evaluations. Patients were excluded if they did not want to participate in the study

or if there was a history using ointments, creams, vaginal douches or transvaginal ultrasound within two days prior to the gynecological examination. The first 214 patients were selected for the evaluation of specimen adequacy. Out of 579 collected cases, eight cases had sampling artifacts and were excluded from the study. The results from 571 cases are shown in the table below:

Results	Cases (%)
Total number	571 (100%)
Normal	408 (71.5%)
Positive Atypical Cells	19 (3.3%)
Inflammatory	144 (25.2%)
ASC-US	11 (1.9%)
ASC-H	0 (0%)
LSIL	7 (1.2%)
HSIL	1 (0.2%)
Cancer	0
AGS-US	0
AGC-H	0
Unsatisfactory	0

Specimen adequacy evaluation is summarized in the table below:

Criteria for inadequacy	Number of cases (%)
Total number	214 (100%)
Insufficient cellular material present	0
Separated superficial cells suggesting vaginal sampling only	0
Obscued by blood and/or inflammatory exudates	2 (0.93%)
Too thickly spread	1 (0.47%)
EC/TZ component not identified: absence of columnar cells	17 (7.94%)

The study results summarized in this section demonstrate that the cervical samples collected with the Kolplast Cervical Sample Collection Kit are adequate for cytological evaluation with conventional Pap Smear method and liquid-based Pap test method.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.