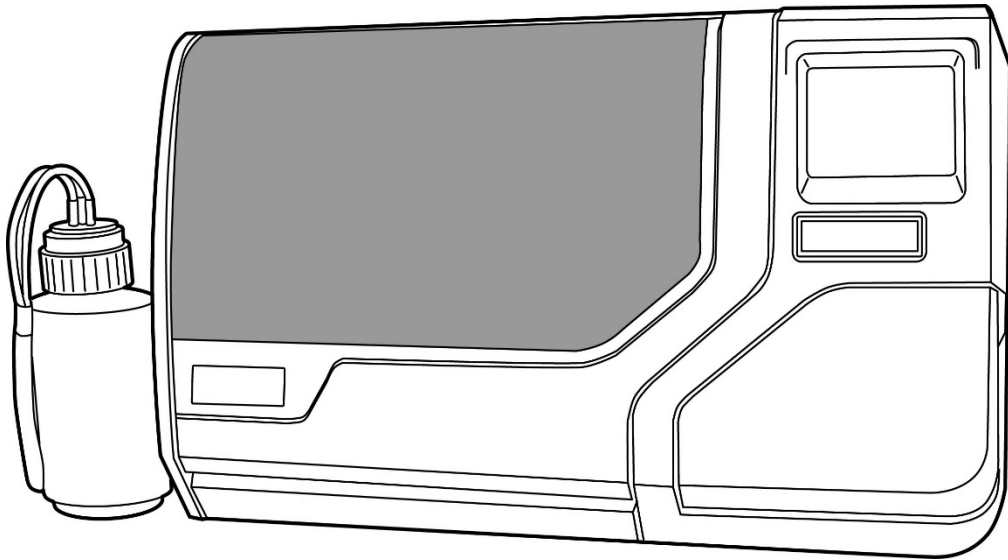


ThinPrep[®] 5000 System



Instructions For Use

CE

INTENDED USE

The ThinPrep® 5000 System is intended as a replacement for the conventional method of Pap smear preparation for use in screening for the presence of atypical cells, cervical cancer, or its precursor lesions (Low-grade Squamous Intraepithelial Lesions, High-grade Squamous Intraepithelial Lesions), as well as all other cytologic categories as defined by *The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses*¹.

SUMMARY AND EXPLANATION OF THE SYSTEM

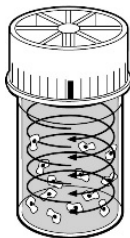
The ThinPrep process begins with the patient's gynecologic sample being collected by the clinician using a cervical sampling device which, rather than being smeared on a microscope slide, is immersed and rinsed in a vial filled with 20 ml of PreservCyt® Solution (PreservCyt). The ThinPrep sample vial is then capped, labeled, and sent to a laboratory equipped with a ThinPrep 5000 Processor.

At the laboratory, the PreservCyt sample vial is bar-coded along with the test request form to establish a sample chain of custody and is placed into a ThinPrep 5000 Processor. A glass slide bearing the same sample identification number as on the sample vial is loaded into the Processor. A gentle dispersion step mixes the cell sample by currents in the fluid that are strong enough to separate debris and disperse mucus, but gentle enough to have no adverse effect on cell appearance.

The cells are then captured on a Gynecological ThinPrep Pap Test Filter that is specifically designed to collect cells. The ThinPrep 5000 constantly monitors the rate of flow through the ThinPrep Pap Test Filter during the collection process in order to prevent the cellular presentation from being too scant or too dense. A thin layer of cells is then transferred to a glass slide in a 20 mm-diameter circle, and the slide is automatically deposited into a fixative solution.

The ThinPrep Sample Preparation Process

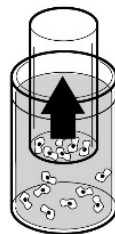
1. Dispersion



(1) Dispersion

The ThinPrep Pap Test Filter rotates within the sample vial, creating currents in the fluid that are strong enough to separate debris and disperse mucus, but gentle enough to have no adverse effect on cell appearance.

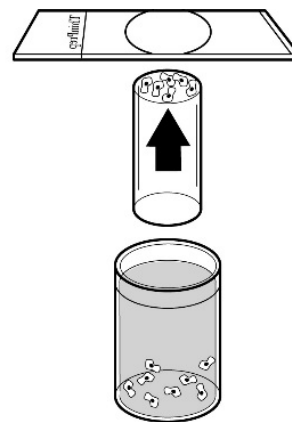
2. Cell Collection



(2) Cell Collection

A gentle vacuum is created within the ThinPrep Pap Test Filter, which collects cells on the exterior surface of the membrane. Cell collection is controlled by the ThinPrep 5000 Processor's software that monitors the rate of flow through the ThinPrep Pap Test Filter.

3. Cell Transfer



(3) Cell Transfer

After the cells are collected on the membrane, the ThinPrep Pap Test Filter is inverted and gently pressed against the ThinPrep Microscope Slide. Natural attraction and slight positive air pressure cause the cells to adhere to the ThinPrep Microscope Slide resulting in an even distribution of cells in a defined circular area.

As with conventional Pap smears, slides prepared with the ThinPrep® 5000 System are examined in the context of the patient's clinical history and information provided by other diagnostic procedures such as colposcopy, biopsy, and human papillomavirus (HPV) testing, to determine patient management.

The PreservCyt® Solution component of the ThinPrep 5000 System is an alternative collection and transport medium for gynecologic specimens tested with the Digene Hybrid Capture™ System HPV DNA and Hologic APTIMA COMBO 2® CT/NG Assays. Refer to the respective manufacturer's package inserts for instructions for using PreservCyt Solution for collection, transport, storage, and preparation of specimens for use in those systems.

The PreservCyt Solution component of the ThinPrep 5000 System is also an alternative collection and transport medium for gynecologic specimens tested with the Roche Diagnostics COBAS AMPLICOR™ CT/NG assay. Refer to Hologic's labeling (Document #MAN-02063-001) for instructions for using PreservCyt Solution for collection, transport, storage, and preparation of specimens and to the Roche Diagnostics COBAS AMPLICOR CT/NG package insert for instructions for use of that system.

LIMITATIONS

- Gynecologic samples collected for preparation using the ThinPrep 5000 System should be collected using a broom-type or endocervical brush/plastic spatula combination collection devices. Refer to the instructions provided with the collection device for warnings, contraindications, and limitations associated with specimen collection.
- Preparation of microscope slides using the ThinPrep 5000 System should be performed only by personnel who have been trained by Hologic or by organizations or individuals designated by Hologic.
- Evaluation of microscope slides produced with the ThinPrep 5000 System should be performed only by cytotechnologists and pathologists who have been trained to evaluate ThinPrep prepared slides by Hologic or by organizations or individuals designated by Hologic.
- Supplies used in the ThinPrep 5000 System are those designed and supplied by Hologic specifically for the ThinPrep 5000 System. These include PreservCyt Solution vials, ThinPrep Pap Test Filters, and ThinPrep Microscope Slides. Alternative collection media, filters, and slides have not been validated by Hologic and may lead to erroneous results. Hologic does not provide a warranty for results using any of these alternatives. Product performance may be compromised if supplies that have not been validated by Hologic are used. After use, supplies should be disposed of in accordance with local, state, and federal regulations.
- A ThinPrep Pap Test Filter must be used only once and cannot be reused.
- The performance of HPV DNA and CT/NG testing on sample vials reprocessed with glacial acetic acid (GAA) has not been evaluated.

CONTRAINDICATIONS

- *Chlamydia trachomatis* and *Neisseria gonorrhoeae* testing using the Hologic APTIMA COMBO 2[®] CT/NG and the Roche Diagnostics COBAS AMPLICOR assays should not be performed on a sample that has already been processed using the ThinPrep 3000 processor.

WARNINGS

- For In Vitro Diagnostic Use
- Danger. PreservCyt Solution contains methanol. Toxic if swallowed. Toxic if inhaled. Causes damage to organs. Flammable liquid and vapor. Keep away from heat, sparks, open flames and hot surfaces. PreservCyt Solution should be stored and disposed of in accordance with all applicable regulations.
- Alternative collection media, filters and slides have not been validated by Hologic and may lead to erroneous results. Hologic does not provide a warranty for results using any of these alternatives.

PRECAUTIONS

- This equipment generates, uses and can radiate radio frequency energy, and if not installed and used in accordance with the Operator's Manual, may cause interference to radio communications. Operation of this equipment in a residential area is likely to cause harmful interference, in which case the user will be required to correct the interference at his/her own expense.
- PreservCyt Solution *with* cytologic sample intended for ThinPrep Pap testing must be stored between 15°C (59°F) and 30°C (86°F) and tested within 6 weeks of collection.
- PreservCyt Solution *with* cytologic sample intended for CT/NG testing using the Roche Diagnostics COBAS AMPLICOR CT/NG test must be stored between 4°C (39°F) and 25°C (77°F) and tested within 6 weeks of collection.
- PreservCyt Solution was challenged with a variety of microbial and viral organisms. The following table presents the starting concentrations of viable organisms, and the log reduction of viable organisms found after 15 minutes in the PreservCyt Solution. As with all laboratory procedures, universal precautions should be followed.

Organism	Initial Concentration	Log Reduction After 15 Minutes
<i>Candida albicans</i>	5.5 x 10 ⁵ CFU/ml	≥4.7
<i>Candida auris</i>	2.6 x 10 ⁵ CFU/ml	≥5.4
<i>Aspergillus niger</i>	4.8 x 10 ⁵ CFU/ml	2.7*
<i>Escherichia coli</i>	2.8 x 10 ⁵ CFU/ml	≥4.4
<i>Staphylococcus aureus</i>	2.3 x 10 ⁵ CFU/ml	≥4.4
<i>Pseudomonas aeruginosa</i>	2.5 x 10 ⁵ CFU/ml	≥4.4
<i>Mycobacterium tuberculosis</i> [†]	9.4 x 10 ⁵ CFU/ml	4.9**
Rabbitpox virus	6.0 x 10 ⁶ PFU/ml	5.5***
HIV-1	3.2 x 10 ⁷ TCID ₅₀ /ml	≥7.0***
Hepatitis B virus [†]	2.2 x 10 ⁶ TCID ₅₀ /ml	≥4.25
SARS-CoV-2 virus	1.8 x 10 ⁶ TCID ₅₀ /ml	≥3.75
* After 1 hour 4.7 log reduction		

Organism	Initial Concentration	Log Reduction After 15 Minutes
**	After 1 hour 5.7 log reduction	
***	Data is for 5 minutes	
†	Organisms were tested with similar organisms from the same genus to assess antimicrobial effectiveness	
Note:	All log reduction values with a \geq designation yielded undetectable microbial presence after exposure to PreservCyt Solution. The listed values represent the minimum allowable claim given the initial concentration and the detection limit of the quantitative method.	

PERFORMANCE CHARACTERISTICS: REPORT OF CLINICAL STUDIES

The ThinPrep 5000 System is technologically similar to the ThinPrep 2000 System. A critical review of the ThinPrep 5000 System demonstrated that the clinical evaluation of the ThinPrep 2000 System applies to the ThinPrep 5000 System and is described below.

A prospective multi-center clinical study was conducted to evaluate the performance of the ThinPrep 2000 System in direct comparison to the conventional Pap smear. The objective of the ThinPrep clinical study was to demonstrate that gynecologic specimens prepared using the ThinPrep 2000 System were at least as effective as conventional Pap smears for the detection of atypical cells and cervical cancer or its precursor lesions in a variety of patient populations. In addition, an assessment of specimen adequacy was performed.

The initial clinical study protocol was a blinded, split sample, matched pair study, for which a conventional Pap smear was prepared first, and the remainder of the sample (the portion that normally would have been discarded) was immersed and rinsed into a vial of PreservCyt Solution. At the laboratory, the PreservCyt sample vial was placed into a ThinPrep 2000 Processor and a slide was then prepared from the patient's sample. ThinPrep and conventional Pap smear slides were examined and diagnosed independently. Reporting forms containing patient history as well as a checklist of all possible categories of The Bethesda System were used to record the results of the screening. A single independent pathologist reviewed all discrepant and positive slides from all sites in a blinded fashion to provide a further objective review of the results.

LABORATORY AND PATIENT CHARACTERISTICS

Cytology laboratories at three screening centers (designated as S1, S2, and S3) and three hospital centers (designated as H1, H2, and H3) participated in the clinical study. The screening centers in the study serve patient populations (screening populations) with rates of abnormality (Low-grade Squamous Intraepithelial Lesion [LSIL] and more severe lesions) similar to the United States average of less than 5%.² The hospital centers in the study serve a high risk referral patient population (hospital populations) characterized by high rates (>10%) of cervical abnormality. Data on race demographics was obtained for 70% of the patients that participated in the study. The study population consisted of the following race groups: Caucasian (41.2%), Asian (2.3%), Hispanic (9.7%), African American (15.2%), Native American (1.0%) and other groups (0.6%).

Table 1 describes the laboratories and the patient populations.

Table 1: Site Characteristics

Site	Laboratory Characteristics			Clinical Study Demographics			
	Type of Patient Population	Laboratory Volume - Smears per Year	Cases	Patient Age Range	Post-Meno-pausal	Previous Abnormal Pap Smear	Convent. Prevalence LSIL+
S1	Screening	300,000	1,386	18.0 - 84.0	10.6%	8.8%	2.3%
S2	Screening	100,000	1,668	18.0 - 60.6	0.3%	10.7%	2.9%
S3	Screening	96,000	1,093	18.0 - 48.8	0.0%	7.1%	3.8%
H1	Hospital	35,000	1,046	18.1 - 89.1	8.1%	40.4%	9.9%
H2	Hospital	40,000	1,049	18.1 - 84.4	2.1%	18.8%	12.9%
H3	Hospital	37,000	981	18.2 - 78.8	11.1%	38.2%	24.2%

CLINICAL STUDY RESULTS

The diagnostic categories of The Bethesda System were used as the basis of the comparison between conventional and ThinPrep® findings from the clinical study. The diagnostic classification data and statistical analyses for all clinical sites are presented in Tables 2 through 11. Cases with incorrect paperwork, patient's age less than 18 years, cytologically unsatisfactory slides, or patients with a hysterectomy were excluded from this analysis. Few cases of cervical cancer (0.02%³) were represented in the clinical study, as is typical in the United States patient population.

Table 2: Diagnostic Classification Table, All Categories

		Conventional							TOTAL
		NEG	ASCUS	AGUS	LSIL	HSIL	SQ CA	GL CA	
ThinPrep	NEG	5224	295	3	60	11	0	0	5593
	ASCUS	318	125	2	45	7	0	0	497
	AGUS	13	2	3	0	1	0	1	20
	LSIL	114	84	0	227	44	0	0	469
	HSIL	11	15	0	35	104	2	0	167
	SQ CA	0	0	0	0	0	1	0	1
	GL CA	0	0	0	0	0	0	0	0
	TOTAL	5680	521	8	367	167	3	1	6747

Abbreviations for Diagnoses: *NEG* = Normal or negative, *ASCUS* = Atypical Squamous Cells of Undetermined Significance, *AGUS* = Atypical Glandular Cells of Undetermined Significance, *LSIL* = Low-grade Squamous Intraepithelial Lesion, *HSIL* = High-grade Squamous Intraepithelial Lesion, *SQ CA* = Squamous Cell Carcinoma, *GL CA* = Glandular Cell Adenocarcinoma

Table 3: Three Category Diagnostic Classification Table

		Conventional			TOTAL
		NEG	ASCUS/AGUS+	LSIL+	
ThinPrep	NEG	5224	298	71	5593
	ASCUS/AGUS+	331	132	54	517
	LSIL+	125	99	413	637
	TOTAL	5680	529	538	6747

Table 4: Two Category Diagnostic Classification Table, LSIL and More Severe Diagnoses

		Conventional		TOTAL
		NEG/ASCUS/AGUS+	LSIL+	
ThinPrep	NEG/ASCUS/AGUS+	5985	125	6110
	LSIL+	224	413	637
	TOTAL	6209	538	6747

Table 5: Two Category Diagnostic Classification Table, ASCUS/AGUS and More Severe Diagnoses

		NEG	ASCUS/AGUS+	TOTAL
ThinPrep	NEG	5224	369	5593
	ASCUS/AGUS+	456	698	1154
	TOTAL	5680	1067	6747

The diagnostic data analysis from the sites is summarized in Table 6 and 7. When the p-value is significant (p < 0.05), the method favored is indicated in the tables.

Table 6: Results by Site, LSIL and More Severe Lesions

Site	Cases	ThinPrep LSIL+	Convent. LSIL+	Increased Detection*	p-Value	Method Favored
S1	1,336	46	31	48%	0.027	ThinPrep
S2	1,563	78	45	73%	<0.001	ThipPrep
S3	1,058	67	40	68%	<0.001	ThinPrep
H1	971	125	96	30%	<0.001	ThinPrep
H2	1,010	111	130	(15%)	0.135	Neither
H3	809	210	196	7%	0.374	Neither

$$*Increased\ detection = \frac{ThinPrep\ LSIL+ - Conventional\ LSIL+}{Conventional\ LSIL+} \times 100\%$$

For LSIL and more severe lesions, the diagnostic comparison statistically favored the ThinPrep® method at four sites and was statistically equivalent at two sites.

Table 7: Results by Site, ASCUS/AGUS and More Severe Lesions

Site	Cases	ThinPrep ASCUS+	Convent. ASCUS+	Increased Detection*	p-Value	Method Favored
S1	1,336	117	93	26%	0.067	Neither
S2	1,563	124	80	55%	<0.001	ThinPrep
S3	1,058	123	81	52%	<0.001	ThinPrep
H1	971	204	173	18%	0.007	ThinPrep
H2	1,010	259	282	(8%)	0.360	Neither
H3	809	327	358	(9%)	0.102	Neither

$$*Increased\ detection = \frac{ThinPrep\ ASCUS+ - Conventional\ ASCUS+}{Conventional\ ASCUS+} \times 100\%$$

For ASCUS/AGUS and more severe lesions, the diagnostic comparison statistically favored the ThinPrep method at three sites and was statistically equivalent at three sites.

One pathologist served as an independent reviewer for the six clinical sites, receiving both slides from cases where the two methods were either abnormal or discrepant. Since a true reference cannot be determined in such studies and therefore true sensitivity cannot be calculated, the use of an expert cytologic review provides an alternative to histologic confirmation by biopsy or human papillomavirus (HPV) testing as a means for determining the reference diagnosis.

The reference diagnosis was the more severe diagnosis from either of the ThinPrep or conventional Pap slides as determined by the independent pathologist. The number of slides diagnosed as abnormal at each site, compared to the reference diagnosis of the independent pathologist, provides the proportion of LSIL or more severe lesions (Table 8) and the proportion of ASCUS/AGUS or more severe lesions (Table 9). The statistical analysis allows a comparison of the two methods and a determination of which method is favored when using the independent pathologist for expert cytologic review as the adjudicator of the final diagnosis.

Table 8: Independent Pathologist Results by Site, LSIL and More Severe Lesions

Site	Cases Positive by Independent Pathologist	ThinPrep Positive	Conventional Positive	p-Value	Method Favored
S1	50	33	25	0.0614	Neither
S2	65	48	33	0.0119	ThinPrep
S3	77	54	33	<0.001	ThinPrep
H1	116	102	81	<0.001	ThinPrep
H2	115	86	90	0.607	Neither
H3	126	120	112	0.061	Neither

For LSIL and more severe lesions, the diagnostic comparison statistically favored the ThinPrep method at three sites and was statistically equivalent at three sites.

Table 9: Independent Pathologist Results by Site, ASCUS/AGUS and More Severe Lesions

Site	Cases Positive by Independent Pathologist	ThinPrep® Positive	Conventional Positive	p-Value	Method Favored
S1	92	72	68	0.0511	Neither
S2	101	85	59	0.001	ThinPrep
S3	109	95	65	<0.001	ThinPrep
H1	170	155	143	0.090	Neither
H2	171	143	154	0.136	Neither
H3	204	190	191	1.000	Neither

For ASCUS/AGUS and more severe lesions, the diagnostic comparison statistically favored the ThinPrep method at two sites and was statistically equivalent at four sites.

Table 10 below shows the summary for all sites of the descriptive diagnosis for all Bethesda System categories.

Table 10: Summary of Descriptive Diagnosis

Descriptive Diagnosis <i>Number of Patients: 6747</i>	ThinPrep		Conventional	
	N	%	N	%
Benign Cellular Changes:	1592	23.6	1591	23.6
Infection:				
Trichomonas Vaginalis	136	2.0	185	2.7
Candida spp.	406	6.0	259	3.8
Coccobacilli	690	10.2	608	9.0
Actinomyces spp.	2	0.0	3	0.0
Herpes	3	0.0	8	0.1
Other	155	2.3	285	4.2
Reactive Cellular Changes Associated with:				
Inflammation	353	5.2	385	5.7
Atrophic Vaginitis	32	0.5	48	0.7
Radiation	2	0.0	1	0.0
Other	25	0.4	37	0.5
Epithelial Cell Abnormalities:	1159	17.2	1077	16.0
Squamous Cell:				
ASCUS	501	7.4	521	7.7
favor reactive	128	1.9	131	1.9
favor neoplastic	161	2.4	140	2.1
undetermined	213	3.2	250	3.7
LSIL	469	7.0	367	5.4
HSIL	167	2.5	167	2.5
Carcinoma	1	0.0	3	0.0
Glandular Cell:				
Benign Endometrial cells in Postmenopausal Women	7	0.1	10	0.1
Atypical Glandular Cells (AGUS)	21	0.3	9	0.1
favor reactive	9	0.1	4	0.1
favor neoplastic	0	0.0	3	0.0
undetermined	12	0.2	2	0.0
Endocervical Adenocarcinoma	0	0.0	1	0.0

Note: Some patients had more than one diagnostic subcategory.

Table 11 shows the rates of detection for infection, reactive changes, and the total benign cellular changes for both the ThinPrep® and conventional methods at all sites.

Table 11: Benign Cellular Changes Results

	ThinPrep		Conventional	
	N	%	N	%
Benign Cellular Changes				
Infection	1392	20.6	1348	20.0
Reactive Changes	412	6.1	471	7.0
Total*	1592	23.6	1591	23.6

* Total includes some patients that may have had both an infection and reactive cellular change.

Tables 12, 13, and 14 show the specimen adequacy results for the ThinPrep method and conventional smear method for all of the study sites. Of the 7,360 total patients enrolled, 7,223 are included in this analysis. Cases with patient's age less than 18 years or patients with a hysterectomy were excluded from this analysis.

Two additional clinical studies were conducted to evaluate specimen adequacy results when samples were deposited directly into the PreservCyt® vial, without first making a conventional Pap smear. This specimen collection technique is the intended use for the ThinPrep 2000 System. Tables 15 and 16 present the split sample and direct to vial results.

Table 12: Summary of Specimen Adequacy Results

Specimen Adequacy <i>Number of Patients: 7223</i>	ThinPrep		Conventional	
	N	%	N	%
Satisfactory	5656	78.3	5101	70.6
Satisfactory for Evaluation but Limited by:	1431	19.8	2008	27.8
Air-Drying Artifact	1	0.0	136	1.9
Thick Smear	9	0.1	65	0.9
Endocervical Component Absent	1140	15.8	681	9.4
Scant Squamous Epithelial Component	150	2.1	47	0.7
Obscuring Blood	55	0.8	339	4.7
Obscuring Inflammation	141	2.0	1008	14.0
No Clinical History	12	0.2	6	0.1
Cytolysis	19	0.3	119	1.6
Other	10	0.1	26	0.4
Unsatisfactory for Evaluation:	136	1.9	114	1.6
Air-Drying Artifact	0	0.0	13	0.2
Thick Smear	0	0.0	7	0.1
Endocervical Component Absent	25	0.3	11	0.2
Scant Squamous Epithelial Component	106	1.5	47	0.7
Obscuring Blood	23	0.3	58	0.8
Obscuring Inflammation	5	0.1	41	0.6
No Clinical History	0	0.0	0	0.0
Cytolysis	0	0.0	4	0.1
Other	31	0.4	9	0.1

Note: Some patients had more than one subcategory.

Table 13: Specimen Adequacy Results

		Conventional			
		SAT	SBLB	UNSAT	TOTAL
ThinPrep	SAT	4316	1302	38	5656
	SBLB	722	665	44	1431
	UNSAT	63	41	32	136
	TOTAL	5101	2008	114	7223

SAT=Satisfactory, SBLB=Satisfactory But Limited By, UNSAT=Unsatisfactory

Table 14: Specimen Adequacy Results by Site

Site	Cases	Thin Prep SAT Cases	Con-vent. SAT Cases	Thin Prep SBLB Cases	Con-vent. SBLB Cases	Thin Prep UNSAT Cases	Con-vent. UNSAT Cases
S1	1,386	1092	1178	265	204	29	4
S2	1,668	1530	1477	130	178	8	13
S3	1,093	896	650	183	432	14	11
H1	1,046	760	660	266	375	20	11
H2	1,049	709	712	323	330	17	7
H3	981	669	424	264	489	48	68
All Sites	7,223	5656	5101	1431	2008	136	114

The Satisfactory But Limited By (SBLB) category can be broken down into many subcategories, one of which is the absence of Endocervical Component. Table 15 shows the Satisfactory But Limited By category “No ECC’s” for ThinPrep® and conventional slides.

Table 15: Specimen Adequacy Results by Site, SBLB Rates for no Endocervical Component.

SBLB Due to No ECC's					
Site	Cases	ThinPrep SBLB-no ECC's	ThinPrep SBLB-no ECC's (%)	Conventional SBLB-no ECC's	Conventional SBLB-no ECC's (%)
S1	1,386	237	17.1%	162	11.7%
S2	1,668	104	6.2%	73	4.4%
S3	1,093	145	13.3%	84	7.7%
H1	1,046	229	21.9%	115	11.0%
H2	1,049	305	29.1%	150	14.3%
H3	981	120	12.2%	97	9.9%
All Sites	7,223	1140	15.8%	681	9.4%

For the results of the clinical study involving a split-sample protocol, there was a 6.4 percent difference between conventional and ThinPrep methods in detecting endocervical component. This is similar to previous studies using a split sample methodology.

DIRECT-TO-VIAL ENDOCERVICAL COMPONENT (ECC) STUDIES

For the intended use of the ThinPrep® 2000 System, the cervical sampling device will be rinsed directly into a PreservCyt® vial, rather than splitting the cellular sample. It was expected that this would result in an increase in the pick-up of endocervical cells and metaplastic cells. To verify this hypothesis, two studies were performed using the direct-to-vial method and are summarized in Table 16. Overall, no difference was found between ThinPrep and conventional methods in these two studies.

Table 16: Summary of Direct-to-vial Endocervical Component (ECC) Studies

Study	Number of Evaluable Patients	SBLB due to No Endocervical Component	Comparable Conventional Pap Smear Percentage
Direct-to-Vial Feasibility	299	9.36%	9.43% ¹
Direct-to-Vial Clinical Study	484	4.96%	4.38% ²

1. Direct-to-Vial Feasibility study compared to overall clinical investigation conventional Pap smear SBLB-No Endocervical Component rate.

2. Direct-to-Vial Clinical study compared to site S2 clinical investigation conventional Pap smear SBLB-No Endocervical Component rate.

DIRECT-TO-VIAL HSIL+ STUDY

Following initial FDA approval of the ThinPrep System, Hologic conducted a multi-site direct-to-vial clinical study to evaluate the ThinPrep 2000 System versus conventional Pap smear for the detection of High Grade Squamous Intraepithelial and more severe lesions (HSIL+). Two types of patient groups were enrolled in the trial from ten (10) leading academic hospitals in major metropolitan areas throughout the United States. From each site, one group consisted of patients representative of a routine Pap test screening population and the other group made up of patients representative of a referral population enrolled at the time of colposcopic examination. The ThinPrep specimens were collected prospectively and compared against a historical control cohort. The historical cohort consisted of data collected from the same clinics and clinicians (if available) used to collect the ThinPrep specimens. These data were collected sequentially from patients seen immediately prior to the initiation of the study.

The results from this study showed a detection rate of 511 / 20,917 for the conventional Pap smear versus 399 / 10,226 for the ThinPrep slides. For these clinical sites and these study populations, this indicates a 59.7% increase in detection of HSIL+ lesions for the ThinPrep specimens. These results are summarized in Table 17.

Table 17: Summary of Direct-to-Vial HSIL+ Study

Site	Total CP (n)	HSIL+	Percent (%)	Total TP (n)	HSIL+	Percent (%)	Percent Change (%)
S1	2,439	51	2.1	1,218	26	2.1	+2.1
S2	2,075	44	2.1	1,001	57	5.7	+168.5
S3	2,034	7	0.3	1,016	16	1.6	+357.6
S4	2,043	14	0.7	1,000	19	1.9	+177.3
S5	2,040	166	8.1	1,004	98	9.8	+20.0
S6	2,011	37	1.8	1,004	39	3.9	+111.1
S7	2,221	58	2.6	1,000	45	4.5	+72.3
S8	2,039	61	3.0	983	44	4.5	+49.6
S9	2,000	4	0.2	1,000	5	0.5	+150.0
S10	2,015	69	3.4	1,000	50	5.0	+46.0
Total	20,917	511	2.4	10,226	399	3.9	59.7 (p<0.001)

Percent Change (%) = ((TP HSIL+/TP Total)/(CP HSIL+/CP Total)-1) *100

GLANDULAR DISEASE DETECTION – PUBLISHED STUDIES

The detection of endocervical glandular lesions is an essential function of the Pap test. However, abnormal glandular cells in the Pap sample may also originate from the endometrium or from extrauterine sites. The Pap test is not intended to be a screening test for such lesions.

When suspected glandular abnormalities are identified, their accurate classification as true glandular versus squamous lesions is important for proper evaluation and subsequent treatment (*e.g.* choice of excisional biopsy method versus conservative follow-up). Multiple peer-reviewed publications⁴⁻⁹ report on the improved ability of the ThinPrep 2000 System to detect glandular disease versus the conventional Pap smear. Although these studies do not consistently address sensitivity of different Pap testing methods in detecting specific types of glandular disease, the reported results are consistent with more frequent biopsy confirmation of abnormal glandular findings by the ThinPrep Pap Test compared to conventional cytology.

Thus, the finding of a glandular abnormality on a ThinPrep Pap Test slide merits increased attention for definitive evaluation of potential endocervical or endometrial pathology.

CONCLUSIONS

The ThinPrep® 2000 System is as effective as the conventional Pap smear in a variety of patient populations and may be used as a replacement for the conventional Pap smear method for the detection of atypical cells, cervical cancer, or its precursor lesions, as well as all other cytologic categories as defined by The Bethesda System. Since the ThinPrep 5000 System is technologically similar to the ThinPrep 2000 System, we conclude that the ThinPrep 5000 System is also as effective as the conventional Pap smear in a variety of patient populations and may be used as a replacement for the conventional Pap smear method for the detection of atypical cells, cervical cancer, or its precursor lesions, as well as all other cytologic categories as defined by the Bethesda System.

The ThinPrep 2000 System is significantly more effective than the conventional Pap smear for the detection of Low-grade Squamous Intraepithelial (LSIL) and more severe lesions in a variety of patient populations. Since the ThinPrep 5000 System is technologically similar to the ThinPrep 2000 System, we conclude that the ThinPrep 5000 is also significantly more effective than the conventional Pap smear for the detection of Low-grade Squamous Intraepithelial (LSIL) and more severe lesions in a variety of patient populations.

Specimen quality with the ThinPrep 2000 System is significantly improved over that of conventional Pap smear preparation in a variety of patient populations. Since the ThinPrep 5000 System is technologically similar to the ThinPrep 2000 System, we conclude that the specimen quality with the ThinPrep 5000 System is also significantly improved over that of conventional Pap smear preparation in a variety of patient populations.

MATERIALS REQUIRED

MATERIALS PROVIDED

ThinPrep 5000 Processor

- ThinPrep 5000 Processor Instrument
- ThinPrep 5000 Processor Operator's Manual
- Fixative baths with evaporation covers (3)
- Carousel (1)
- Waste bottle assembly - includes bottle, bottle cap, tubing set, fittings, waste filter
- Power cord
- Staining Racks (pkg of 10)
- Carousel cover (1)
- Absorbent pad for filter
- Absorbent pad for evaporative cover

ThinPrep 5000 Processor with AutoLoader

- ThinPrep 5000 Processor with AutoLoader
- ThinPrep 5000 Processor with AutoLoader Operator's Manual
- Power cord
- System Accessory Kit
- Optional items (printer, LIS networking)

MATERIALS REQUIRED BUT NOT PROVIDED

- Slide staining system and reagents
- Standard laboratory fixative
- Coverslips and mounting media
- ThinPrep microscope slides
- 20 ml PreservCyt® Solution vial
- ThinPrep® Pap Test Filter for Gynecologic Applications
- Cervical collection device

STORAGE

- Store PreservCyt Solution between 15°C (59°F) and 30°C (86°F). Do not use beyond the expiration date printed on the container.
- Store PreservCyt Solution with cytologic sample intended for ThinPrep Pap testing between 15°C (59°F) and 30°C (86°F) for up to 6 weeks.
- Store PreservCyt Solution with cytologic sample intended for CT/NG testing using the Roche Diagnostics COBAS AMPLICOR CT/NG test between 4°C (39°F) and 25°C (77°F) for up to 6 weeks.

BIBLIOGRAPHY

1. Solomon D., Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, Raab S, Sherman M, Wilbur D, Wright T, Young N, for the Forum Group Members and the 2001 Bethesda Workshop. The 2001 Bethesda System Terminology for Reporting Results of Cervical Cancer. *JAMA*. 2002;287:2114-2119.
2. Jones HW. Impact of The Bethesda System, *Cancer* 77 pp. 1914-1918, 1995.
3. American Cancer Society. Cancer Facts and Figures, 1995.
4. Ashfaq R, Gibbons D, Vela C, Saboorian MH, Iliya F. ThinPrep Pap Test. Accuracy for glandular disease. *Acta Cytol* 1999; 43: 81-5
5. Bai H, Sung CJ, Steinhoff MM: ThinPrep Pap Test promotes detection of glandular lesions of the endocervix. *Diagn Cytopathol* 2000;23:19-22
6. Carpenter AB, Davey DD: ThinPrep Pap Test: Performance and biopsy follow-up un a university hospital. *Cancer Cytopathology* 1999; 87: 105-12
7. Guidos BJ, Selvaggi SM. Detection of endometrial adenocarcinoma with the ThinPrep Pap test. *Diagn Cytopathol* 2000; 23: 260-5
8. Schorge JO, Hossein Saboorian M, Hynan L, Ashfaq R. ThinPrep detection of cervical and endometrial adenocarcinoma: A retrospective cohort study. *Cancer Cytopathology* 2002; 96: 338-43
9. Wang N, Emancipator SN, Rose P, Rodriguez M, Abdul-Karim FW. Histologic follow-up of atypical endocervical cells. Liquid-based, thin-layer preparation vs. conventional Pap smear. *Acta Cytol* 2002; 46: 453-7

TECHNICAL SERVICE AND PRODUCT INFORMATION

For technical service and assistance related to use of the ThinPrep 5000 System, contact Hologic:

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Fax: 1-508-229-2795

For international or toll-free blocked calls, please contact 1-508-263-2900.

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