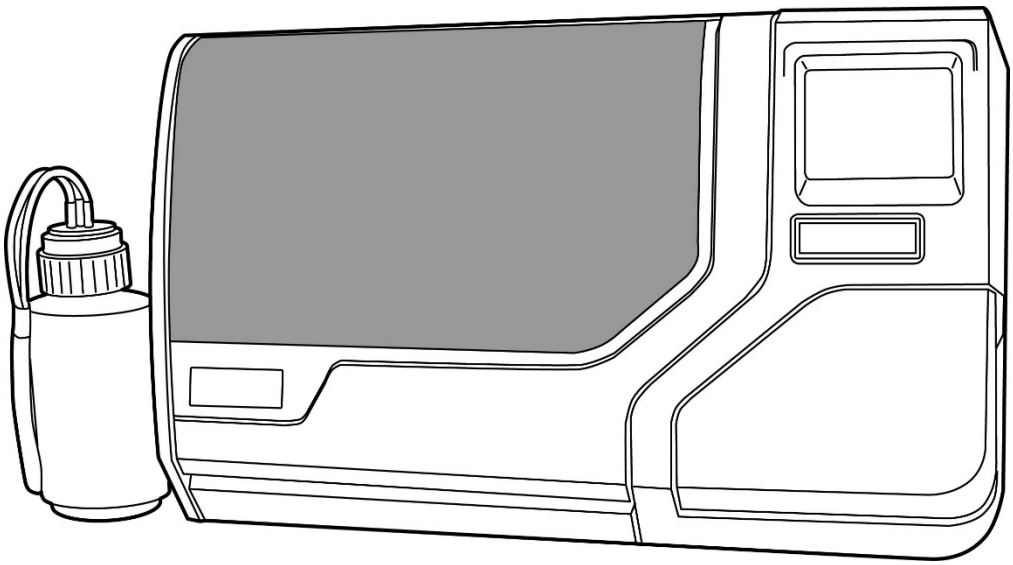
HOLOGIC®

ThinPrep™ 5000 System



Instructions for Use

IVD

INTENDED USE

The ThinPrep 5000 Processor is part of the ThinPrep System. It is used to prepare ThinPrep microscope slides from ThinPrep PreservCyt vials for use as a replacement for the conventional method of Pap smear preparations for 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 Cytology*. Also for preparation of ThinPrep slides from non-gynecologic (non-gyn) samples, including urine samples. For professional use.

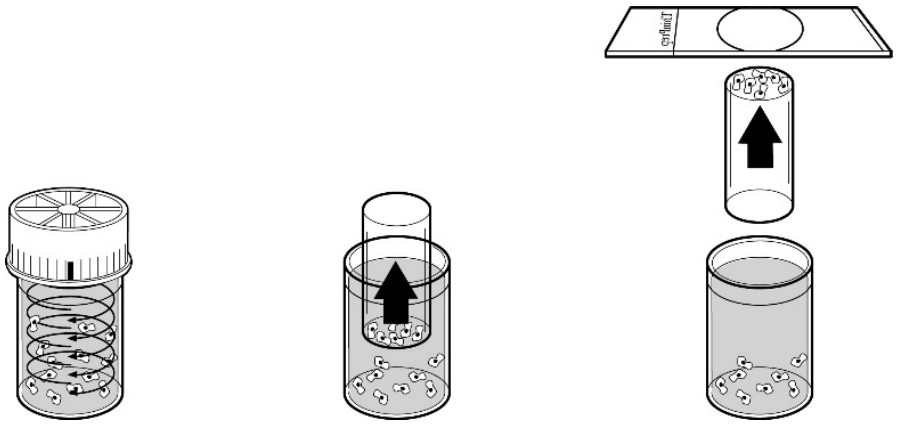
SUMMARY AND EXPLANATION OF THE SYSTEM

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

The sample vial is rotated, 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

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

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.

If any serious incident occurs related to this device, or any components used with this device, report it to Hologic Technical Support and the competent authority local to the user and/or patient.

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 by 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 5000 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. Other solutions cannot be substituted for PreservCyt Solution. 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.

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
Candida albicans	5.5 x 10^5 CFU/ml	≥4.7
Candida auris	2.6 x 10^5 CFU/ml	≥5.4
Aspergillus niger	4.8 x 10^5 CFU/ml	2.7*
Escherichia coli	2.8 x 10^5 CFU/ml	≥4.4
Staphylococcus aureus	2.3 x 10^5 CFU/ml	≥4.4
Pseudomonas aeruginosa	2.5 x 10^5 CFU/ml	≥4.4
Mycobacterium tuberculosis†	9.4 x 10^5 CFU/ml	4.9**
Rabbitpox virus	6.0 x 10^6 PFU/ml	5.5***

Organism	Initial Concentration	Log Reduction After 15 Minutes
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
** 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 ≥ 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.

ThinPrep 2000 System Compared to Conventional Pap Smear

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

	Laboratory Characteristics			Clinical Study Demographics			
Site	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%	18.2%	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							
		NEG	**ASCUS**	**AGUS**	**LSIL**	**HSIL**	**SQ CA**	**GL CA**	**TOTAL**
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			
		NEG	**ASCUS/AGUS+**	**LSIL+**	**TOTAL**
ThinPrep	NEG	5224	298	71	5593
	ASCUS/**AGUS+**	331	132	54	1154
	LSIL+	125	99	413	637
	TOTAL	5680	529	538	6747

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

		Conventional		
		NEG/ASCUS/ AGUS+	**LSIL+**	**TOTAL**
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 = ThinPrep™ LSIL+ - Conventional LSIL+ x 100%*
Conventional LSIL+

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	359	(9%)	0.102	Neither

**Increased detection = ThinPrep ASCUS+ - Conventional ASCUS+ x 100%*
Conventional ASCUS+

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	0.170	Neither
S2	65	48	33	0.042	ThinPrep
S3	77	54	33	<0.001	ThinPrep
H1	116	102	81	<0.001	ThinPrep
H2	115	86	90	0.876	Neither
H3	126	120	112	0.170	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	0.900	Neither
S2	101	85	59	0.005	ThinPrep
S3	109	95	65	<0.001	ThinPrep
H1	170	155	143	0.237	Neither
H2	171	143	154	0.330	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 ***Number of Patients: 6747***	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 **Number of Patients: 7223**	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**	**ThinPrep** SAT **Cases**	**Convent.** SAT **Cases**	**ThinPrep** SBLB **Cases**	**Convent.** SBLB **Cases**	**ThinPrep** UNSAT **Cases**	**Convent.** 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 publications[4-9] 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.

ThinPrep 5000 Processor Compared to ThinPrep 2000 System

A study was conducted to estimate the Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for specimens processed on the ThinPrep 5000 processor as compared with processing using the ThinPrep 2000 System.

Clinical Study Design

The study was a prospective, multi-center, split-sample, blinded evaluation of ThinPrep slides of known diagnoses generated from residual cytological specimens. The study was conducted at Hologic, Inc., Marlborough, MA and at two external laboratories in the United States.

One thousand two hundred sixty (1260) specimens were procured for and selected from Hologic's Residual Specimen Inventory for Hologic's laboratory. At the external study sites specimens were from residual cytological specimens from the clinical laboratory (after the laboratory has prepared a slide from the vial and has signed-out the case per standard practice). The laboratory's specimens were only supplemented from Hologic's inventory with the rarest cytologic diagnostic categories (AGUS and Cancer), if needed. Slides prepared for the study were from specimens processed within 6 weeks of specimen collection.

All study specimens were processed both on a ThinPrep 5000 processor and a ThinPrep 2000 system. The order in which the slides were processed was alternated in blocks of 20. All slides were stained, coverslipped, and read manually following standard laboratory procedures; all slides prepared at a site were reviewed independently by each of the three (3) pairs of cytotechnologists/pathologists. All cytologic diagnoses were determined in accordance with the Bethesda System 2001 criteria for all slides[1].

Table 18: Laboratory ThinPrep 5000 Diagnosis vs. Laboratory ThinPrep 2000 Diagnosis for First Pair of Cytotechnologist/Pathologist (Combined Sites)

Lab ThinPrep 5000 Diagnosis	Lab ThinPrep 2000 Diagnosis								
	UNSAT	NILM	ASC-US	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
UNSAT	31	9		1	1				42
NILM	9	624	32	2	4	3	2		676
ASC-US	3	23	59	3	33	10	1		132
AGUS	1	5		7		1	3	3	20
LSIL		6	19	1	111	9	14		160
ASC-H		6	7	2	9	27	12		63
HSIL			2		12	16	109	2	141
Cancer							3	23	26
Total	44	673	119	16	170	66	144	28	1260

Reference Diagnosis by Adjudication Review

After all slides in the study were reviewed, all ThinPrep 2000 and ThinPrep 5000 slides were subject to an adjudication review. Adjudication was done at a facility that was not one of the study sites conducting the study. Slides for adjudication were evenly divided between three (3) adjudication panels each consisting of one (1) cytotechnologist and three (3) independent pathologists. Each adjudication panel was blinded to the original review diagnosis for all slides and each independent pathologist within each panel was also blinded to other adjudicator's diagnoses for all slides. Adjudication consensus agreement was obtained for each slide reviewed. Consensus agreement was achieved when at least two (2) of the three (3) pathologists from a panel rendered an identical diagnosis. In cases where consensus agreement was not achieved the panel members were brought together at a multi-head microscope to review the slides together and come to a consensus diagnosis. For each specimen, an adjudicated diagnosis for the ThinPrep 2000 slide and an adjudicated diagnosis for the ThinPrep 5000 slide were obtained.

Table 19: Adjudicated ThinPrep 5000 Diagnosis vs. Adjudicated ThinPrep 2000 Diagnosis (Combined Sites)

Adjudicated ThinPrep 5000 Diagnosis	Adjudicated ThinPrep 2000 Diagnosis								
	UNSAT	NILM	ASC-US	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
UNSAT	14	8				1			23
NILM	12	696	39	8	9	2	4		770
ASC-US		33	48	4	26	7	4		122
AGUS		4	1	6			4	3	18
LSIL		12	20		135	3	10		180
ASC-H		7	4	2	6	7	11		37
HSIL			7	1	9	8	66	1	92
Cancer							2	16	18
Total	26	760	119	21	185	28	101	20	1260

For each specimen, the Reference Diagnosis (RD) was considered as the most abnormal diagnosis from the adjudicated diagnoses of the ThinPrep 2000 and ThinPrep 5000 slides. In the

study, there were 22 Cancer, 124 HSIL, 39 ASC-H, 202 LSIL, 23 AGUS, 120 ASC-US, and 696 NILM specimens. Thirty-four (34) specimens had UNSAT either with ThinPrep 2000 or with ThinPrep 5000 or with both. Clinical sensitivity and specificity (e.g., with reference to a histological diagnosis) cannot be measured in this study which relied on cytological examination alone. Instead, laboratory positive and negative diagnoses by both methods, ThinPrep 5000 and ThinPrep 2000, for the specimens with Reference Diagnosis of ASC-US+ (combined ASC-US, AGUS, LSIL, ASC-H, HSIL, and Cancer), LSIL+ (combined LSIL, ASC-H, HSIL, and Cancer), ASC-H+ (combined ASC-H, HSIL, and Cancer) and HSIL+ (combined HSIL and Cancer) were compared.

Clinical Study Results

Tables 20 through 23 present the comparison of Laboratory true positive and negative rates for ASC-US+, LSIL+, ASC-H+, and HSIL+.

Table 20: Laboratory ThinPrep 5000 Results vs Laboratory ThinPrep 2000 Results for the Specimens with Reference Diagnosis of ASC-US+

In the study, there were 530 specimens with Reference Diagnosis of ASC-US+ (combined ASC-US, AGUS, LSIL, ASC-H, HSIL, and Cancer) and 696 specimens with Reference Diagnosis of NILM.

In this table, “Positive” means ASC-US+ or UNSAT, and “Negative” means NILM. All percentages are rounded to the nearest 0.1%.

ASC-US+	Positive Percent Agreement			Negative Percent Agreement		
Lab CT/ Pathologist	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**
#1	90.9% (482/530) (88.2% to 93.1%)	89.4% (474/530) (86.5% to 91.8%)	1.5% (8/530) (-0.7% to 3.8%)	89.1% (620/696) (86.5% to 91.2%)	87.9% (612/696) (85.3% to 90.1%)	1.1% (8/696) (-1.1% to 3.5%)
#2	87.0% (461/530) (83.8% to 89.6%)	86.6% (459/530) (83.4% to 89.2%)	0.4% (2/530) (-2.7% to 3.4%)	88.6% (617/696) (86.1% to 90.8%)	90.7% (631/696) (88.3% to 92.6%)	-2.0% (-14/696) (-4.4% to 0.3%)
#3	87.5% (464/530) (84.5% to 90.1%)	88.5% (469/530) (85.5% to 90.9%)	-0.9% (-5/530) (-3.7% to 1.8%)	87.6% (610/696) (85.0% to 89.9%)	88.1% (613/696) (85.5% to 90.3%)	-0.4% (-3/696) (-2.9% to 2.0%)

Table 21: Laboratory ThinPrep 5000 Results vs Laboratory ThinPrep 2000 Results for the Specimens with Reference Diagnosis of LSIL+

In the study, there were 387 specimens with Reference Diagnosis of LSIL+ (combined LSIL, ASC-H, HSIL, and Cancer) and 839 specimens with Reference Diagnosis of (combined NILM, ASC-US, and AGUS).
In this table, “Positive” means LSIL+ or UNSAT, and “Negative” means NILM or ASC-US/AGUS. All percentages are rounded to the nearest 0.1%.

LSIL+	Positive Percent Agreement			Negative Percent Agreement		
Lab CT/ Pathologist	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**
#1	84.8% (328/387) (80.8% to 88.0%)	86.8% (336/387) (83.1% to 89.8%)	-2.1% (-8/387) (-5.9% to 1.7%)	90.3% (758/839) (88.2% to 92.2%)	89.5% (751/839) (87.3% to 91.4%)	0.8% (7/839) (-1.1% to 2.8%)
#2	84.0% (325/387) (80.0% to 87.3%)	83.5% (323/387) (79.4% to 86.8%)	0.5% (2/387) (-3.6% to 4.6%)	91.7% (769/839) (89.6% to 93.3%)	91.4% (767/839) (89.3% to 93.1%)	0.2% (2/839) (-1.7% to 2.2%)
#3	84.0% (325/387) (80.0% to 87.3%)	87.3% (338/387) (83.7% to 90.3%)	-3.4% (-13/387) (-7.4% to 0.6%)	88.6% (743/839) (86.2% to 90.5%)	89.4% (750/839) (87.1% to 91.3%)	-0.8% (-7/839) (-2.9% to 1.2%)

Table 22: Laboratory ThinPrep 5000 Results vs Laboratory ThinPrep 2000 Results for the Specimens with Reference Diagnosis of ASC-H+

In the study, there were 185 specimens with Reference Diagnosis of ASC-H+ (combined ASC-H, HSIL, and Cancer) and 1,041 specimens with Reference Diagnosis of (combined NILM, ASC-US/AGUS, and LSIL).
In this table, "Positive" means ASC-H+ or UNSAT, and "Negative" means NILM, ASC-US/AGUS, or LSIL. All percentages are rounded to the nearest 0.1%.

ASC-H+	Positive Percent Agreement			Negative Percent Agreement		
Lab CT/ Pathologist	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**
#1	81.6% (151/185) (75.4% to 86.5%)	84.3% (156/185) (78.4% to 88.9%)	-2.7% (-5/185) (-8.6% to 3.2%)	90.6% (943/1041) (88.7% to 92.2%)	90.6% (943/1041) (88.7% to 92.2%)	0.0% (0/1041) (-1.6% to 1.6%)
#2	81.6% (151/185) (75.4% to 86.5%)	81.1% (150/185) (74.8% to 86.1%)	0.5% (1/185) (-6.0% to 7.1%)	91.7% (955/1041) (89.9% to 93.3%)	91.1% (948/1041) (89.2% to 92.7%)	0.7% (7/1041) (-1.0% to 2.3%)
#3	85.4% (158/185) (79.6% to 89.8%)	84.9% (157/185) (79.0% to 89.3%)	0.5% (1/185) (-5.4% to 6.5%)	89.8% (935/1041) (87.8% to 91.5%)	90.6% (943/1041) (88.7% to 92.2%)	-0.8% (-8/1041) (-2.5% to 0.9%)

Table 23: Laboratory ThinPrep 5000 Results vs Laboratory ThinPrep 2000 Results for the Specimens with Reference Diagnosis of HSIL+

In the study, there were 146 specimens with Reference Diagnosis of HSIL+ (combined HSIL and Cancer) and 1,080 specimens with Reference Diagnosis of (combined NILM, ASC-US/AGUS, LSIL, and ASC-H).
In this table, "Positive" means HSIL+ or UNSAT, and "Negative" means NILM, ASC-US/AGUS, LSIL, or ASC-H. All percentages are rounded to the nearest 0.1%.

HSIL+	Positive Percent Agreement			Negative Percent Agreement		
Lab CT/ Pathologist	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**	**ThinPrep 5000 (95% CI)**	**ThinPrep 2000 (95% CI)**	**Difference (95% CI)**
#1	77.4% (113/146) (70.0% to 83.4%)	80.1% (117/146) (72.9% to 85.8%)	-2.7% (-4/146) (-9.8% to 4.3%)	93.2% (1007/1080) (91.6% to 94.6%)	93.2% (1007/1080) (91.6% to 94.6%)	0.0% (0/1080) (-1.4% to 1.4%)
#2	69.9% (102/146) (62.0% to 76.7%)	74.7% (109/146) (67.0% to 81.0%)	-4.8% (-7/146) (-11.8% to 2.3%)	94.3% (1018/1080) (92.7% to 95.5%)	94.7% (1023/1080) (93.2% to 95.9%)	-0.5% (-5/1080) (-1.9% to 1.0%)
#3	78.1% (114/146) (70.7% to 84.0%)	82.9% (121/146) (75.9% to 88.1%)	-4.8% (-7/146) (-12.6% to 3.1%)	91.9% (992/1080) (90.1% to 93.3%)	92.3% (997/1080) (90.6% to 93.8%)	-0.5% (-5/1080) (-2.1% to 1.2%)

In the study, there were 2.06% (26/1260) ThinPrep 2000 slides with UNSAT results by Adjudication and 1.83% (23/1260) ThinPrep 5000 slides with UNSAT results by Adjudication.

Agreement among Laboratory Cytotechnologists/Pathologists

The following tables indicate the extent to which the laboratory cytotechnologists / pathologists at a given site agreed amongst themselves on the diagnosis, comparing the ThinPrep 5000 processor to the ThinPrep 2000 system. Tables are provided for ASC-US+ and ASC-H+.

In Table 24 for ASC-H+, the number of specimens is shown for which various levels of agreement among the CTs occurred. Either all three CTs rated the slide as positive (ASC-H+), two out of three rated it positive, one out of three, or none of them.

Table 24: Laboratory Cytotechnologist/Pathologist Agreement, All Results, ASC-H+

		ThinPrep 2000 System Three lab CTs have read the same ThinPrep 2000 slide from a vial				
	ASC-H+	**Three CTs had ASC-H+**	**Two CTs had ASC-H+ & one had <ASC-H**	**One CT had ASC-H+ & two had <ASC-H**	**Three CTs had <ASC-H**	**Totals**
ThinPrep 5000 Processor Three lab CTs have read the same ThinPrep 5000 slide from a vial	**Three CTs had ASC-H+**	111	21	6	0	138
	Two CTs had ASC-H+ and one had <ASC-H	32	30	21	7	90
	One CT had ASC-H+ and two had <ASC-H	7	9	43	28	87
	Three CTs had <ASC-H	2	8	37	898	945
	Totals	152	68	107	933	1260

		ThinPrep 2000 System Three lab CTs have read the same ThinPrep 2000 slide from a vial		
	ASC-H+	**Three or two CTs had ASC-H+**	**Three or two CTs had <ASC-H**	**Totals**
ThinPrep 5000 Processor Three lab CTs have read the same ThinPrep 5000 slide from a vial	**Three or two CTs had ASC-H+**	194	34	242
	Three or two CTs had <ASC-H	26	1006	1032
	Totals	220	1040	1260

The rate of agreement between the ThinPrep 5000 result and the ThinPrep 2000 result from the previous table is presented below. PPA is the positive percent agreement, percent of specimens of ASC-H+ diagnosis with ThinPrep 5000 slides by a majority of laboratory CT/Pathologists among all specimens of ASC-H+ diagnosis with ThinPrep 2000 slides by a majority of laboratory CT/Pathologists. NPA is the negative percent agreement, percent of specimens of <ASC-H diagnosis with ThinPrep 5000 slides by a majority of laboratory CT/Pathologists among all specimens of <ASC-H diagnosis with ThinPrep 2000 slides by a majority of laboratory CT/Pathologists.

Table 25: Rate of CT/Pathologist Agreement, ASC-H+

ASC-H+				
	PPA	88.2%	(194/220)	(83.3% to 91.8%)
	NPA	96.7%	(1006/1040)	(95.5% to 97.7%)

In Table 26 for ASCUS+, the number of specimens is shown for which various levels of agreement among the CTs occurred. Either all three CTs rated the slide as positive (ASCUS+), two out of three rated it positive, one out of three, or none of them.

Table 26: CT Agreement, All Results, ASCUS+

		ThinPrep 2000 System Three lab CTs have read the same ThinPrep 2000 slide from a vial				
	ASCUS+	**Three CTs had ASC-H+**	**Two CTs had ASCUS+ & one had <ASCUS**	**One CT had ASCUS+ & two had <ASCUS**	**Three CTs had <ASCUS**	**Totals**
ThinPrep 5000 Processor Three lab CTs have read the same ThinPrep 5000 slide from a vial	**Three CTs had ASCUS+**	393	36	8	4	441
	Two CTs had ASCUS+ and one had <ASCUS	31	24	13	10	78
	One CT had ASCUS+ and two had <ASCUS	11	8	34	53	106
	Three CTs had <ASCUS	3	13	56	563	635
	Totals	438	81	111	630	1260

		ThinPrep 2000 System Three lab CTs have read the same ThinPrep 2000 slide from a vial		
	ASCUS+	**Three or two CTs had ASCUS**	**Three or two CTs had <ASCUS**	**Totals**
ThinPrep 5000 Processor Three lab CTs have read the same ThinPrep 5000 slide from a vial	**Three or two CTs had ASCUS+**	484	35	519
	Three or two CTs had <ASCUS	35	706	741
	Totals	519	741	1260

Table 27: Rate of CT/Pathologist Agreement, ASCUS+

ASCUS+			
PPA	93.3%	(484/519)	(90.8% to 95.1%)
NPA	95.3%	(706/741)	(93.5% to 96.6%)

The rate of agreement between the ThinPrep 5000 result and the ThinPrep 2000 result from the previous table is presented below. PPA is the positive percent agreement, percent of specimens of ASC-US+ diagnosis with ThinPrep 5000 slides by a majority of laboratory CT/Pathologists

among all specimens of ASC-US+ diagnosis with ThinPrep 2000 slides by a majority of laboratory CT/Pathologists. NPA is the negative percent agreement, percent of specimens of <ASC-US diagnosis with ThinPrep 5000 slides by a majority of laboratory CT/Pathologists among all specimens of <ASC-US diagnosis with ThinPrep 2000 slides by a majority of laboratory CT/Pathologists.

Precision Studies

Within- and between-instrument precision of the ThinPrep 5000 processor were evaluated in laboratory studies using a split-sample technique.

Within-Instrument Precision

The study was designed to examine the ability of the ThinPrep 5000 system to prepare reproducible slides from the same patient specimen using the same instrument. A total of 80 specimens were enrolled in the study. Each specimen was split into three portions and processed on three separate runs of one instrument. The slides were stained, coverslipped, and then reviewed by cytotechnologists. The resulting diagnoses and specimen adequacy determinates are presented below. Seventy eight (78) specimens had all three satisfactory ThinPrep 5000 slides and 2 specimens had all slides with UNSAT results. For comparison, the same procedure was carried out using a ThinPrep 2000 system, with results also presented below.

Table 28: Within-Instrument Precision

	ThinPrep 5000	ThinPrep 2000*
Percent of specimens that have three matching NILM replicates or three matching ASC-US+ replicates	97.4% (76/78) (91.1% to 99.3%)	97.2% (69/71) (90.3% to 99.2%)
Percent of specimens that have three matching <LSIL replicates or three matching LSIL+ replicates	98.7% (77/78) (93.1% to 99.8%)	97.2% (69/71) (90.3% to 99.2%)
Percent of specimens that have three matching <HSIL replicates or three matching HSIL+ replicates	98.7% (77/78) (93.1% to 99.8%)	100% (71/71) (94.9% to 100%)
Percent of specimens that have three matching Satisfactory replicates or three matching UNSAT replicates	100% (80/80) (95.4% to 100%)	100% (71/71) (94.9% to 100%)

** 80 specimens were enrolled, but 9 were excluded due to slide breakage and other errors.*

Between-Instrument Precision

The study was designed to examine the ability of the ThinPrep 5000 system to prepare reproducible slides from the same patient specimen using multiple instruments. A total of 120 specimens were enrolled in the study. Each specimen was split into three portions and processed on three instruments. The slides were stained, coverslipped, and then reviewed by cytotechnologists. The resulting diagnoses and specimen adequacy determinates are presented below. One hundred seventeen (117) specimens had all three satisfactory ThinPrep 5000 slides, one specimen had two slides with UNSAT result and one slide with Satisfactory result, one specimen had two slides with Satisfactory result and one slide with UNSAT result, and one specimen was excluded from analysis due to a broken slide. For comparison, the same procedure was carried out using a ThinPrep 2000 system, with results also presented below.

Table 29: Between-Instrument Precision

	ThinPrep 5000	**ThinPrep 2000***
Percent of specimens that have three matching NILM replicates or three matching ASC-US+ replicates	94.0% (110/117) (88.2% to 97.1%)	91.1% (102/112) (84.3% to 95.1%)
Percent of specimens that have three matching <LSIL replicates or three matching LSIL+ replicates	97.4% (114/117) (92.7% to 99.1%)	94.6% (106/112) (88.8% to 97.5%)
Percent of specimens that have three matching <HSIL replicates or three matching HSIL+ replicates	98.3% (115/117) (94.0% to 99.5%)	100% (112/112) (96.7% to 100%)
Percent of specimens that have three matching Satisfactory replicates or three matching UNSAT replicates	98.3% (117/119) (94.1% to 99.5%)	98.3% (113/115) (93.9% to 99.5%)

** 120 specimens were enrolled, but 5 were excluded due to slide breakage and other errors.*

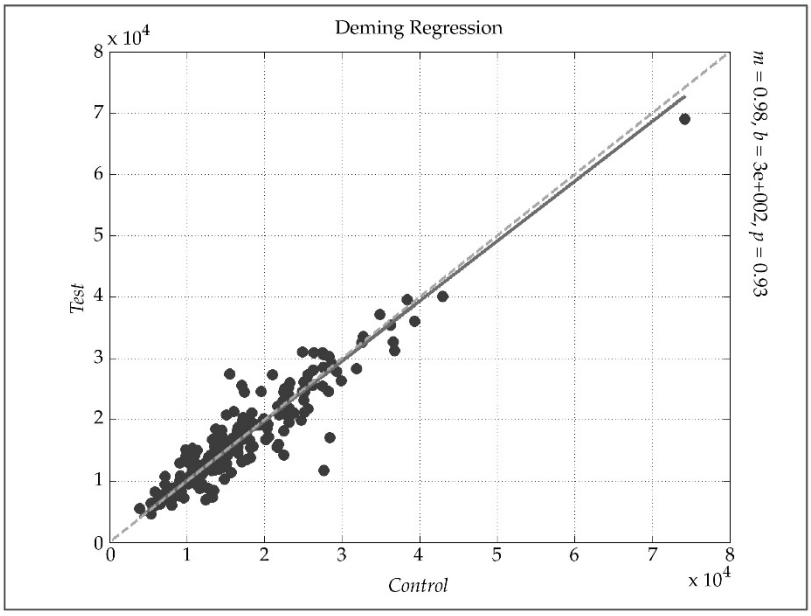
Cell Count Study

The quantity of cellular material transferred onto slides, comparing ThinPrep 5000 to the ThinPrep 2000, was evaluated in a laboratory study using a split-sample technique.

Two hundred ten (210) specimens were enrolled in the study (139 NILM, 28 ASC-US, 28 LSIL, and 15 HSIL). Each specimen was split into two parts, processed on a ThinPrep 2000 and ThinPrep

5000 system, then stained and coverslipped. All slides were run on a ThinPrep Imaging System to obtain Imager object count data, which has been demonstrated to correlate closely with cytotechnologist cell count estimates. Cellularity varies among clinical specimens, so a range of cell counts was obtained.

The chart below provides a scatter plot of the count data from the matched pairs of slides in this study. The *Control* axis is the ThinPrep 2000 slide's count value, and the *Test* axis is the matching ThinPrep 5000 slide's count.



Deming regression analysis was performed and the slope was 0.98 with 95% CI: 0.94 to 1.01 and the intercept was 300 with 95% CI: -300 to 897. The data demonstrate similar cell count values on the ThinPrep 2000 and ThinPrep 5000 slides.

Cellular Carry-Over Study

Cellular carry-over between slides was evaluated in a laboratory study, with comparison of the ThinPrep 5000 and ThinPrep 2000.

On each system, 200 abnormal clinical specimens were processed, alternating with 200 blank PreservCyt vials containing no cells. After processing, slides made from the blank vials were segregated from cellular slides, stained and coverslipped, then reviewed by cytotechnologists.

Any cells found on a slide were noted. Slides made from a blank vial but containing at least one cell were considered to have cellular carry-over.

The carry-over study results are presented in Table 30 below.

Table 30: Cellular Carry-Over

	ThinPrep 5000	ThinPrep 2000
Total # of Slides	200	200
# Slides with carry -over	4	38
% Slides with carry-over	2.0%	19.0%
Number of cells on the slides with carry-over: Median (Min, Max)	1 (1,5)	2 (1,28)

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
- Power cord
- ThinPrep 5000 Processor Operator's Manual
- Fixative baths with evaporation covers (3)
- Carousel (1)
- Carousel cover (1)
- Waste bottle assembly - includes bottle, bottle cap, tubing set, fittings, waste filter
- Staining Racks (pkg of 10)
- Absorbent pad for filter plug
- 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
- 20 ml PreservCyt™ Solution vial
- ThinPrep™ Pap Test Filter for Gynecologic Applications
- Standard laboratory fixative
- Coverslips and mounting media
- Cervical collection device
- ThinPrep microscope slides

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.

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TECHNICAL SERVICE AND PRODUCT INFORMATION

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

Telephone: 1-800-442-9892

Fax: 1-508-229-2795

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

Email: info@hologic.com

Hologic, Inc., 250 Campus Drive, Marlborough, MA 01752
1-800-442-9892, www.hologic.com

EC REP Hologic BV, Da Vincilaan 5, 1930 Zaventem, Belgium

UK Responsible Person Hologic, Ltd., Oaks Business Park, Crewe Road, Wythenshawe
Manchester M23 9HZ United Kingdom

Part No.AW-22289-001 Rev 003

Revision History

Revision	Date	Description
AW-22289-001 Rev. 001	11-2020	Add Precision Study and Cell Count Study Information. Add data in microbial/viral organism table.
AW-22289-001 Rev. 002	4-2021	Replace the CE mark. Correct Figure 1-2. Add UKCA mark.
AW-22289-001 Rev. 003	11-2021	Administrative change.