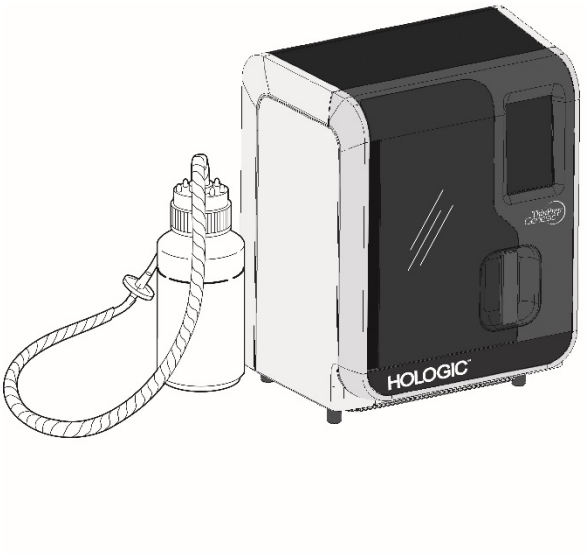
ThinPrep™ Genesis™ Processor



Instructions for Use

IVD

INTENDED USE

The ThinPrep™ Genesis™ 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*[1].

Also, for preparation of ThinPrep™ microscope slides from non-gynecologic (non-gyn) samples, including urine samples, and can be used to pipette an aliquot from the sample vial to the specimen transfer tube. For professional use.

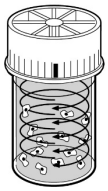
SUMMARY AND EXPLANATION OF THE SYSTEM

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 Genesis processor.

At the laboratory, the PreservCyt sample vial is placed into a ThinPrep Genesis processor. A laboratory can elect to set up the ThinPrep Genesis processor to track the chain of custody for the sample, and to set up printing IDs on each glass microscope slide. 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.

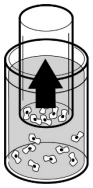
The cells are then captured on a gynecological ThinPrep Pap test filter that is specifically designed to collect cells. The ThinPrep Genesis processor constantly monitors the rate of flow through the ThinPrep Pap test filter during the collection process in order to prevent the cellular presentation 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



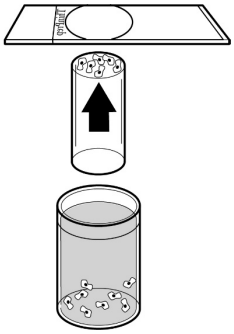
(1) Dispersion

The 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

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 Genesis 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® Genesis processor 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 Genesis processor is an alternative collection and transport medium for the testing of Human Papilloma Virus (HPV) and sexually transmitted infections (STIs) in gynecological specimens, including, but not limited to:

Chlamydia trachomatis and Neisseria gonorrhoeae (Aptima Combo 2® assay),
Chlamydia trachomatis (Aptima® CT assay),
Neisseria gonorrhoeae (Aptima® GC assay),
Mycoplasma genitalium (Aptima® Mycoplasma genitalium assay),
Trichomonas vaginalis (Aptima® Trichomonas vaginalis assay),
Human papillomavirus (Aptima® HPV assay), and
Human papillomavirus (Aptima® HPV 16 18/45 genotype assay)

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.

In addition to preparing a slide from a PreservCyt sample vial, the ThinPrep Genesis processor has the ability to remove a 1-ml aliquot from the sample vial and transfer the aliquot to a specimen transfer tube.

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 Genesis processor 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 Genesis processor 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 Genesis processor 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 Genesis processor are those designed and supplied by Hologic specifically for the ThinPrep Genesis processor. These include PreservCyt Solution vials, ThinPrep Pap test filters, ThinPrep microscope slides, and tubes for the aliquot. 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.
- A ThinPrep microscope slide can be used only once. The slide can only have cells transferred onto it once.
- Aliquots taken by the ThinPrep Genesis processor have not been evaluated for specific assays. Please refer to the instructions provided with a specific assay.
- The performance of HPV and STI ancillary testing on sample vials reprocessed using glacial acetic acid has not been evaluated.

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.
- Testing for certain sexually transmitted infections (STIs) and for Human Papilloma Virus (HPV) in conjunction with cytology may be performed. Refer to assay specific guidance for the collection, transport, and storage conditions of specimens for use in those systems.
- 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***
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

Organism	Initial Concentration	Log Reduction After 15 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 Genesis processor uses similar cell collection and slide preparation technology as the ThinPrep 2000 system. The performance characteristics of the ThinPrep Genesis processor are predicated on those of the ThinPrep 2000 system. Both clinical studies for the ThinPrep 2000 system and those comparing the ThinPrep Genesis processor to the ThinPrep 2000 system are described in the following sections.

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 system 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.

Since the time of the ThinPrep 2000 system study, terminology in The Bethesda System categories was revised. The data below retains the terminology from the original study.

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 (ThinPrep 2000 System Study)

	Laboratory Characteristics			Clinical Study Demographics			
Site	**Type of Patient Population**	**Laboratory Volume - Smears per Year**	**Cases**	**Patient Age Range**	**Post-Menopausal**	**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 (ThinPrep 2000 System Study)

		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 (ThinPrep 2000 System Study)

		Conventional			
		NEG	**ASCUS/AGUS+**	**LSIL+**	**TOTAL**
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 (ThinPrep 2000 System Study)

		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 (ThinPrep 2000 System Study)

		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 (ThinPrep 2000 System Study)

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	ThinPrep
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 = $\frac{\text{ThinPrep® LSIL+ - Conventional LSIL+}}{\text{Conventional LSIL+}} \times 100\%$*

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 (ThinPrep 2000 System Study)

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 = 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 (ThinPrep 2000 System Study)

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 (ThinPrep 2000 System Study)

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 (ThinPrep 2000 System Study)

Descriptive Diagnosis	ThinPrep		Conventional	
Number of Patients: 6747	**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 2000 System Study)

		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 (ThinPrep 2000 System Study)

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

Specimen Adequacy Number of Patients: 7223	ThinPrep		Conventional	
	N	%	N	%
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 (ThinPrep 2000 System Study)

		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 (ThinPrep 2000 System Study)

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 (ThinPrep 2000 System Study)

		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 (ThinPrep 2000 System Study)

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 (ThinPrep 2000 System)

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 Genesis Processor Compared to ThinPrep 2000 System

A prospective multi-center clinical study was conducted to evaluate the performance of the ThinPrep Genesis processor in direct comparison to the ThinPrep 2000 system. The objective of the ThinPrep clinical study was to demonstrate that gynecologic specimens prepared using the ThinPrep Genesis processor were at least as effective as specimens prepared using the ThinPrep 2000 system for the detection of atypical cells and cervical cancer or its precursor lesions.

CLINICAL STUDY DESIGN

This study was a prospective, multi–center, randomized, single–blinded, evaluation of pairs of ThinPrep slides generated from the control and investigational processor from the same residual cytological specimen. The study was conducted at three (3) laboratories in the United States. All study specimens were processed on both a ThinPrep 2000 system (TP-2000) and a ThinPrep Genesis processor (Genesis) and imaged on a ThinPrep Imaging System. All slides were read by three (3) cytotechnologists (CT) and three (3) pathologists at each site. The first review was performed utilizing ThinPrep Imaging Review Scopes (TIS) at each site, followed by a manual review arm of the same slides. To minimize reviewer bias, the CTs and pathologists were blinded to the initially reviewed TIS diagnosis. A two-week interval between the TIS review arm and the manual review arm minimized the potential for recognition bias. Following TIS and manual review, all slides were adjudicated by an independent site, the fourth site. All cytological diagnoses were determined in accordance with the Bethesda System criteria for all slides

1,260 patients' ThinPrep Pap Test specimens were enrolled in this study. 1,260 samples were enrolled from February 2019 through June 2020. Each study site enrolled 420 new specimens selected from their residual inventory (population of gynecological ThinPrep Pap Test specimens sent to the study sites' cytology laboratory). The samples for the study included specimens in each of the diagnostic categories being evaluated. Each study site produced 2 slides per specimen, 1 slide prepared on the ThinPrep Genesis processor and 1 slide prepared on the TP-2000 processor, yielding 840 slides (420 pairs of slides) per site for diagnostic review. A total of 2,520 slides were analyzed for the study.

LABORATORY AND PATIENT CHARACTERISTICS

Table 18 describes the patient populations at each of the study sites:

Table 18: Clinical Study Characteristics

Parameter	Statistic	Site 1 (N=412)	Site 2 (N=415)	Site 3 (N=415)	All Sites (N=1242)
Age (years)	n	412	415	415	1242
	Mean	38.7	39.7	38.6	39.0
	SD	12.93	12.67	13.96	13.20
	Median	36.0	37.0	34.0	36.0
	Min - Max	20 - 78	18 - 82	15 - 82	15 - 82
Postmenopausal					
Yes	n (%)	19 (4.6)	31 (7.5)	35 (8.4)	85 (6.8)
No	n (%)	393 (95.4)	384 (92.5)	380 (91.6)	1157 (93.2)
Hysterectomy					
Yes	n (%)	5 (1.2)	3 (0.7)	18 (4.3)	26 (2.1)
No	n (%)	407 (98.8)	412 (99.3)	397 (95.7)	1216 (97.9)

CLINICAL STUDY RESULTS

Results from the study comparing the performance of the ThinPrep Genesis processor and the ThinPrep 2000 system are presented here. The results for the slides that were manually reviewed by the CTs and pathologists in the study are followed by the results for slides that were reviewed by the CTs and pathologists with the Imager-assisted review.

A site diagnosis was the result of a CT and pathologist team's review, following clinical laboratory practices for CT review and pathologist referral.

After all study slides were reviewed, the 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 adjudication panels each consisting of one (1) cytotechnologist and three (3) independent pathologists. Each adjudication panel reviewed one-third of the slides prepared from each study site for a total of 840 slides per panel. Adjudication consensus agreement was obtained for each slide reviewed. Consensus agreement was achieved when at least two of the three pathologists from a panel rendered an identical diagnosis.

In cases where the pathologist review process did not obtain a consensus, the panel of pathologists was brought together at a multi-headed microscope to manually review those slides for consensus diagnosis. Hologic provided to each adjudication panel for review a list of the "non-consensus" slides for multi-head review. Each panel of pathologists participating in the multi-head review was blinded to all previous diagnoses obtained in the adjudication review.

Using the severity ordering of the diagnostic result (UNSAT, NILM, ASC-US, LSIL, ASC-H, AGUS, HSIL, Cancer), a single reference diagnosis was formed for each sample vial by choosing the more severe of the diagnoses in each pair to create the adjudication reference ("truth") result for each sample, or slide pair.

The 8 x 8 contingency tables for matched results are presented. In addition, diagnostic performance metric estimates along with their 95% confidence intervals are presented.

Table 19: Site Reviews: ThinPrep 2000 System vs ThinPrep Genesis Processor: Manual Review

		ThinPrep 2000 System								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep Genesis Processor	UNSAT	4	7	0	0	1	0	1	0	13
	NILM	10	2052	125	12	27	22	7	3	2258
	ASCUS	0	143	172	0	66	31	5	0	417
	AGUS	0	15	1	6	1	3	3	3	32
	LSIL	0	30	59	0	308	14	19	0	430
	ASC-H	0	18	24	1	8	49	41	2	143
	HSIL	0	12	13	1	24	30	282	17	379
	Cancer	0	0	1	1	0	4	17	64	87
	Total	14	2277	395	21	435	153	375	89	3759

Table 19 compares the results of the manual review of slides prepared on the ThinPrep 2000 system and slides from the same samples prepared on the ThinPrep Genesis processor.

Table 20: Site Reviews: ThinPrep 2000 System vs ThinPrep Genesis Processor: Imager-Assisted Review

		ThinPrep 2000 System								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep Genesis Processor	UNSAT	6	10	2	0	1	1	0	0	20
	NILM	10	2111	108	4	32	16	6	4	2291
	ASCUS	0	135	139	1	48	24	8	1	356
	AGUS	0	4	0	2	0	2	5	3	16
	LSIL	0	36	64	0	302	6	23	0	431
	ASC-H	0	20	20	2	11	65	43	5	166
	HSIL	0	10	15	3	21	43	288	10	390
	Cancer	0	3	0	3	0	3	12	68	89
	Total	16	2329	348	15	415	160	385	91	3759

Table 20 compares the results of the Imager-assisted review of slides prepared on the ThinPrep 2000 System and slides from the same samples prepared on the ThinPrep Genesis processor.

Table 21: Adjudicated ThinPrep 2000 System vs Adjudicated ThinPrep Genesis Processor

		Adjudicated Results (ThinPrep 2000 System)								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
Adjudicated Results (ThinPrep Genesis Processor)	UNSAT	2	2	0	0	0	0	1	0	5
	NILM	3	593	65	4	10	11	4	1	691
	ASCUS	1	69	48	2	25	2	2	1	150
	AGUS	0	2	0	0	0	1	1	1	5
	LSIL	0	10	27	0	143	2	18	0	200
	ASC-H	0	6	6	2	2	6	9	1	32
	HSIL	0	1	4	1	10	13	113	6	148
	Cancer	0	0	0	2	0	2	4	14	22
	Total	6	683	150	11	190	37	152	24	1253

Table 21 compares the results of the adjudication review of slides prepared on the ThinPrep 2000 system and the adjudication review of slides prepared on the ThinPrep Genesis processor.

Table 22: Adjudicated Results vs ThinPrep 2000 System: Manual Review, All Adjudicated Categories

		Adjudicated Results, All Sites								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep 2000 System	UNSAT	2	10	2	0	0	0	0	0	14
	NILM	4	1683	403	14	100	47	24	2	2277
	ASCUS	0	63	99	4	167	24	36	2	395
	AGUS	0	12	2	0	0	0	6	1	21
	LSIL	0	7	23	0	350	4	50	1	435
	ASC-H	0	15	17	3	19	20	74	5	153
	HSIL	0	2	3	1	9	18	323	19	375
	Cancer	0	2	0	2	0	1	18	66	89
	Total	6	1794	549	24	645	114	531	96	3759

Table 22 compares the results of the adjudication review of slides and the study sites' results of the same slides prepared on the ThinPrep 2000 system and reviewed manually.

Table 23: Adjudicated Results vs ThinPrep 2000 System: Imager-Assisted Review

		Adjudicated Results, All Sites								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep 2000 System	UNSAT	0	12	4	0	0	0	0	0	16
	NILM	5	1705	425	13	109	49	21	2	2329
	ASCUS	1	45	74	1	163	23	39	2	348
	AGUS	0	5	1	2	0	1	4	2	15
	LSIL	0	6	23	0	347	1	36	2	415
	ASC-H	0	16	17	5	17	24	77	4	160
	HSIL	0	2	5	1	9	16	333	19	385
	Cancer	0	3	0	2	0	0	21	65	91
	Total	6	1794	549	24	645	114	531	96	3759

Table 23 compares the results of the adjudication review of slides and the study sites' results of the same slides prepared on the ThinPrep 2000 system, reviewed with the ThinPrep Imaging System.

Table 24: Adjudicated Results vs ThinPrep Genesis Processor: Manual Review, All Adjudicated Categories

		Adjudicated Results, All Sites								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep Genesis Processor	UNSAT	1	6	4	0	1	0	1	0	13
	NILM	5	1696	388	14	89	49	15	2	2258
	ASCUS	0	65	112	2	174	28	35	1	417
	AGUS	0	11	3	5	0	2	6	5	32
	LSIL	0	1	22	0	352	4	49	2	430
	ASC-H	0	12	16	1	15	13	81	5	143
	HSIL	0	2	4	2	14	17	322	18	379
	Cancer	0	1	0	0	0	1	22	63	87
	Total	6	1794	549	24	645	114	531	96	3759

Table 24 compares the results of the adjudication review of slides and the study sites' results of the same slides prepared on the ThinPrep Genesis processor and reviewed manually.

Table 25: Adjudicated Results vs ThinPrep Genesis Processor: Imager-Assisted Review, All Adjudicated Categories

		Adjudicated Results, All Sites								
		UNSAT	NILM	ASCUS	AGUS	LSIL	ASC-H	HSIL	Cancer	Total
ThinPrep Genesis Processor	UNSAT	1	8	8	0	2	0	1	0	20
	NILM	5	1708	399	16	102	46	14	1	2291
	ASCUS	0	52	95	0	155	26	26	2	356
	AGUS	0	1	1	0	0	1	10	3	16
	LSIL	0	2	25	0	354	2	45	3	431
	ASC-H	0	17	16	3	12	23	90	5	166
	HSIL	0	4	4	3	20	13	323	23	390
	Cancer	0	2	1	2	0	3	22	59	89
	Total	6	1794	549	24	645	114	531	96	3759

Table 25 compares the results of the adjudication review of slides and the study sites' results of the same slides prepared on the ThinPrep Genesis processor, reviewed with the ThinPrep Imaging System.

Table 26: Performance Summary: ThinPrep Genesis Processor Results vs ThinPrep 2000 System Results for Slides with Manual Review: Sensitivity and Specificity

Manual Review						
	Sensitivity			Specificity		
Threshold	TP-2000 (95% CI)	Genesis (95% CI)	Difference (95% CI)	TP-2000 (95% CI)	Genesis (95% CI)	Difference (95% CI)
ASCUS+	70% (66% to 75%)	72% (68% to 75%)	2% (0% to 3%)	94% (92% to 97%)	95% (92% to 98%)	1% (0% to 1%)
LSIL+	70% (65% to 76%)	71% (66% to 75%)	0% (-2% to 2%)	97% (96% to 98%)	97% (97% to 98%)	1% (0% to 1%)
ASC-H+	73% (65% to 81%)	73% (66% to 80%)	0% (-2% to 2%)	98% (96% to 99%)	98% (97% to 99%)	0% (0% to 1%)
HSIL+	68% (63% to 73%)	68% (61% to 74%)	0% (-4% to 4%)	99% (98% to 99%)	99% (98% to 99%)	0% (-1% to 0%)

The sensitivity and specificity of the ThinPrep Genesis processor are similar to that of the ThinPrep 2000 system for slides reviewed manually. In the study, there were no statistically significant differences in performance between the ThinPrep Genesis and the ThinPrep 2000 system.

Table 27: Performance Summary: ThinPrep Genesis Processor Results vs ThinPrep 2000 System Results for Slides with Imager-Assisted Review: Sensitivity and Specificity

ThinPrep Imaging System Review						
	Sensitivity			Specificity		
Threshold	TP-2000 (95% CI)	Genesis (95% CI)	Difference (95% CI)	TP-2000 (95% CI)	Genesis (95% CI)	Difference (95% CI)
ASCUS+	68% (65% to 72%)	70% (66% to 74%)	2% (1% to 3%)	96% (95% to 97%)	96% (94% to 98%)	0% (-1% to 1%)
LSIL+	70% (64% to 76%)	72% (66% to 78%)	2% (0% to 4%)	97% (96% to 97%)	97% (96%to 98%)	0% (0% to 1%)
ASC-H+	75% (68% to 83%)	76% (68% to 84%)	0% (-3% to 4%)	97% (97% to 98%)	97% (96% to 98%)	0% (-1% to 0%)
HSIL+	70% (62% to 77%)	68% (59% to 77%)	-2% (-8% to 4%)	99% (98% to 99%)	98% (98% to 99%)	0% (-1% to 0%)

The sensitivity and specificity of the ThinPrep Genesis processor are similar to that of the ThinPrep 2000 system for slides reviewed with the ThinPrep Imaging System. The only category where there was a statistically significant difference was in the ASCUS+ category where the difference in sensitivity was 2%.

Reproducibility Studies

Intra- and Inter-instrument reproducibility of the ThinPrep Genesis processor was evaluated in laboratory studies using a split-sample technique.

INTRA-INSTRUMENT REPRODUCIBILITY

The study was designed to examine the ability of the ThinPrep Genesis processor to prepare reproducible slides from the same patient specimen using the same instrument. A total of 160 specimens were enrolled in the study. Each specimen was split into three portions and processed on three separate runs on a single instrument. The slides were stained, coverslipped, and then reviewed by cytotechnologists using Imager-assisted review according to the Bethesda System for Reporting Cervical Cytology. Six specimens were excluded from the analysis because at least one slide was unavailable for CT review. The resulting diagnoses are summarized in Table 28.

Table 28: Intra-instrument Reproducibility

	Specimen Diagnostic Level Number of specimens with three matching replicates			
Sample processing run on the ThinPrep Genesis processor	**NILM**	**ASCUS or ASC-H**	**LSIL or AGUS**	**HSIL or Cancer**
Run 1 (n = 154)	109	13	18	13
Run 2 (n = 154)	11	12	16	14
Run 3 (n = 154)	109	12	19	13

A chi-squared statistical test was conducted, yielding a p-value of 0.9989 indicating that the diagnosis is independent of run.

INTER-INSTRUMENT REPRODUCIBILITY

This study was designed to examine the ability of the ThinPrep Genesis processor to prepare reproducible slides from the same patient specimen using multiple instruments. A total of 160 specimens were enrolled in the study. Each specimen was split into three portions and processed on three different ThinPrep Genesis processors. The slides were stained, coverslipped, and then reviewed by cytotechnologists using Imager-assisted review according to the Bethesda System for Reporting Cervical Cytology. Ten specimens were excluded because at least one slide was unavailable for CT review. The resulting diagnoses are presented in Table 29.

Table 29: Inter-instrument Reproducibility

	Specimen Diagnostic Level Number of specimens with three matching replicates			
ThinPrep Genesis Processor	**NILM**	**ASCUS or ASC-H**	**LSIL or AGUS**	**HSIL or Cancer**
ThinPrep Genesis Processor 1 (n = 150)	112	5	22	11
ThinPrep Genesis Processor 2 (n = 150)	109	6	23	12
ThinPrep Genesis Processor 3 (n = 150)	111	6	21	12

A chi-squared statistical test was conducted, yielding a p-value of 0.9995 indicating that the diagnosis is independent of instrument.

Cell Count Study

A study was conducted to evaluate the quantity of cellular material transferred onto slides, comparing the ThinPrep Genesis processor to the ThinPrep 2000 system.

Two comparisons were made. Slides prepared on the ThinPrep 2000 system were compared to slides prepared using the “Aliquot + Slide” process on the ThinPrep Genesis processor. And, slides prepared on the ThinPrep 2000 system were compared to slides prepared using the “Slide” process on the ThinPrep Genesis processor.

A split-sample technique was used. A total of 300 specimens were enrolled in the study. Each specimen was split into three portions. Specimens processed by one of three methods (ThinPrep 2000, ThinPrep Genesis “Aliquot + Slide” or ThinPrep Genesis “Slide”). The slides were stained, coverslipped, and then imaged with the ThinPrep Imaging System in order to quantify the amount of cellular material on each slide. Figures 1 and 2 compare the cell counts between the ThinPrep 2000 and each Genesis processing method for each specimen.

Figure 1: Deming Regression
ThinPrep Genesis "Slide" Process vs. ThinPrep 2000 System

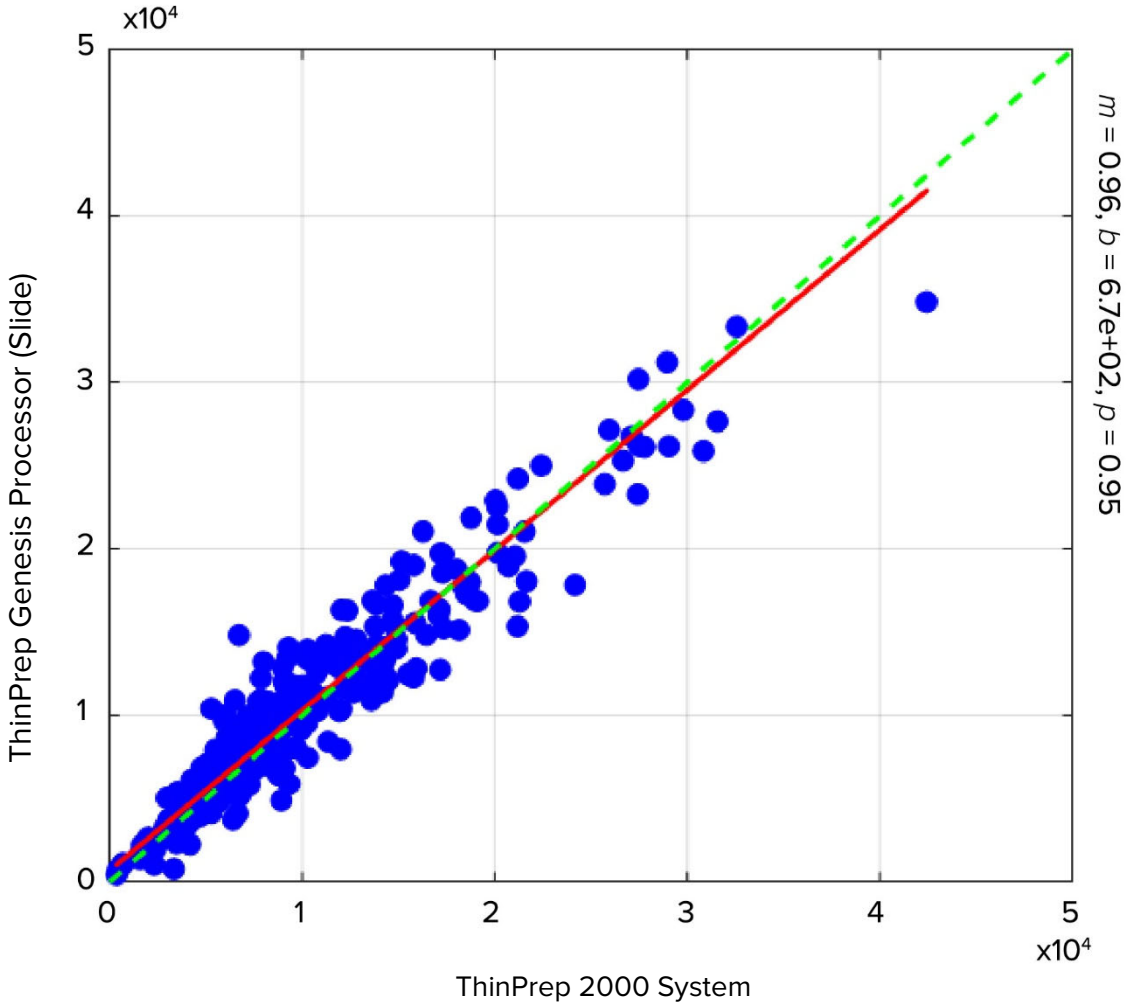
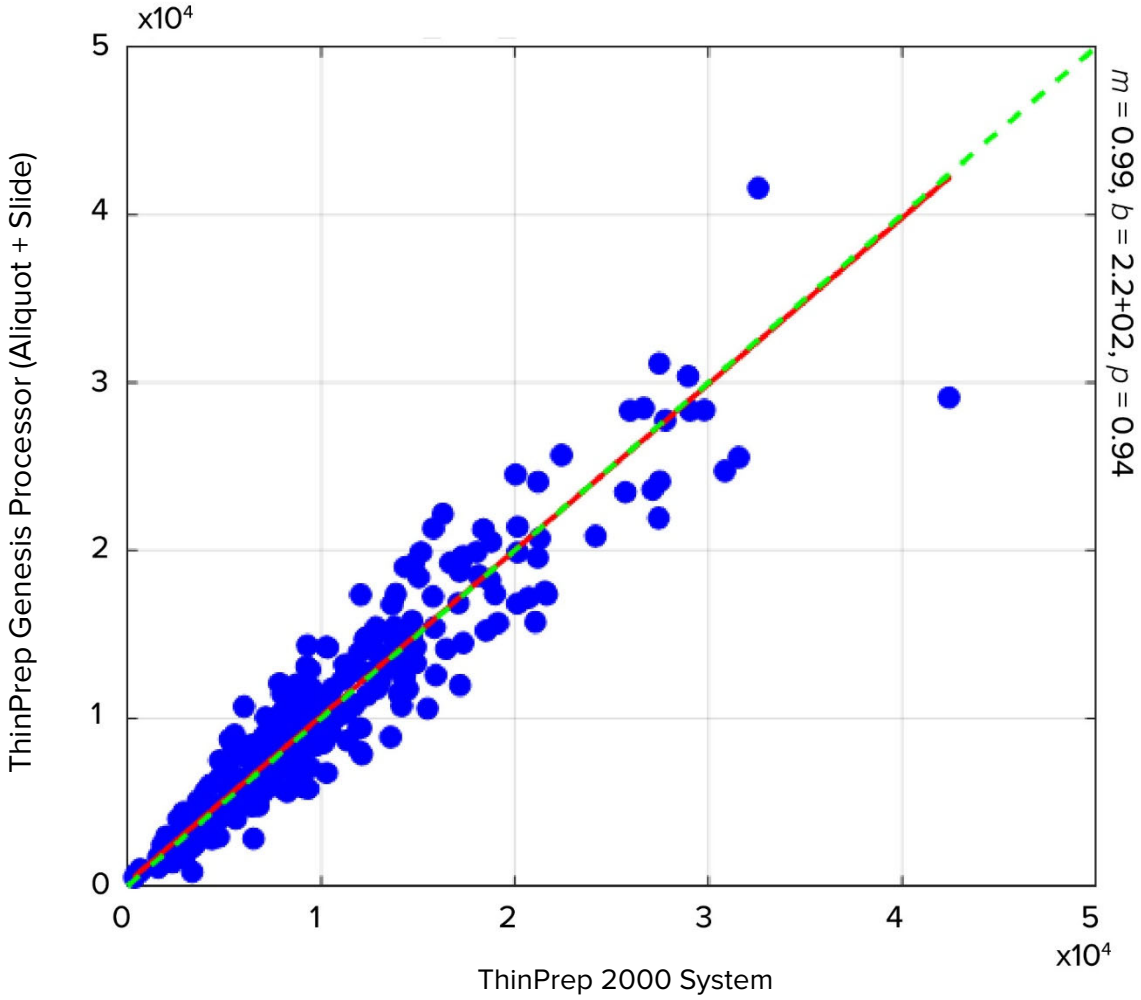


Figure 2: Deming Regression
ThinPrep Genesis "Aliquot + Slide" Process vs. ThinPrep 2000 System



The results of the study demonstrate that the slides produced by the ThinPrep Genesis processor, when operated in either "Slide" or "Aliquot + Slide" process, have epithelial cell counts comparable to the ThinPrep 2000 system.

DIAGNOSTIC COMPARISON FROM THE CELL COUNT STUDY

Furthermore, the slides prepared in the cell count study were reviewed by cytotechnologists and categorized according to the Bethesda System for Reporting Cervical Cytology. The resulting diagnosis determinates are presented in Tables 30 and 31.

Table 30: Diagnostic Comparison from Cell Count Study
Slides Processed on the ThinPrep Genesis Processor (Slide Process) vs. ThinPrep 2000 System

		ThinPrep 2000 System	
		ASCUS+	***<ASCUS***
ThinPrep Genesis Processor ("Slide" process)	***ASCUS+***	66	13
	<ASCUS	12	195

A statistical test for proportions was conducted, yielding a p-value $<10^{-4}$ demonstrating equivalence ASCUS+ between the two instruments.

Table 31: Diagnostic Comparison from Cell Count Study
Slides Processed on the ThinPrep Genesis Processor (Aliquot + Slide Process) vs. ThinPrep 2000 System

		ThinPrep 2000 System	
		ASCUS+	***<ASCUS***
ThinPrep Genesis Processor ("Aliquot + Slide" process)	***ASCUS+***	70	15
	<ASCUS	8	192

A statistical test for proportions was conducted, yielding a p-value $<10^{-4}$ demonstrating equivalence ASCUS+ between the two instruments.

Cellular Carry-over Study

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

On each system 350 abnormal clinical specimens were processed, alternating with 350 PreservCyt vials containing no cells ("acellular vials"). Specimens processed on the ThinPrep Genesis processor used the "Aliquot + Slide" process. After processing, slides made from the acellular vials were segregated from the cellular slides, stained and coverslipped and then reviewed by cytotechnologists. Any cells found on a slide were noted. Slides made from an acellular vial but containing at least one cell were considered to have cellular carry-over. One slide from the ThinPrep 2000 system was excluded due to operator error. Table 32 demonstrates the results.

Table 32: Cellular Carry-over

	ThinPrep 2000 System	ThinPrep Genesis Processor
Total # of Slides	349	350
# of Slides with carry-over	89	20
% of Slides with carry-over	25.5%	5.7%
Number of cells on the slides with carry-over: Median (Min, Max)	2 (1, 96)	2 (1, 43)

The study demonstrated that the cellular cross-contamination from slide to slide on the ThinPrep Genesis is not inferior to the performance of the ThinPrep 2000 system.

Molecular Carry-over Study

A study was designed to evaluate carry-over of the aliquot feature of the ThinPrep Genesis processor. A target-amplified assay was used. The study compared molecular results between specimen aliquots prepared manually to results from aliquots prepared on the ThinPrep Genesis processor, both before and after cytological slide preparation. A total of 600 specimen vials were prepared from either clinical specimen pools spiked with 1×10^4/ml SiHa and 1×10^4/ml HeLa cells (300 HPV^{pos} vials), or from unspiked clinical specimen pools (300 HPV^{neg} vials). Manual aliquots were prepared from HPV^{neg} specimen vials followed by HPV^{pos} specimen vials. Vials were then processed on Genesis processors in alternating positive/negative fashion. Each specimen was first processed in “Aliquot + Slide” mode (aliquot prepared before cytology), and the remaining vial contents processed in “Aliquot” mode (aliquot prepared post cytology). All aliquots were tested with a molecular HPV assay for high risk sub-types, and a molecular assay for HPV 16, 18, and 45. One HPV^{neg} vial was excluded due to operator error. Tables 33 and 34 demonstrate the positivity rates for both HPV^{pos} and HPV^{neg} vials for each aliquot preparation method, for each molecular assay.

Table 33: Molecular Carry-over – HPV High Risk Assay

Aliquot Preparation Method	HPV Negative Specimens			HPV Positive Specimens		
	# Negative Results	# Positive Results	Percent Positivity	# Negative Results	# Positive Results	Percent Positivity
Manual aliquot	291	8	2.7%	0	300	100.0%
Genesis aliquot prepared before cytology	287	12	4.0%	0	300	100.0%
Genesis aliquot prepared after cytology	291	8	2.7%	0	300	100.0%

Table 34: Molecular Carry-over – HPV 16/18/45 Specific Assay

Aliquot Preparation Method	HPV Negative Specimens			HPV Positive Specimens		
	# Negative Results	# Positive Results	Percent Positivity	# Negative Results	# Positive Results	Percent Positivity
Manual aliquot	297	2	0.7%	0	300	100.0%
Genesis aliquot prepared before cytology	298	1	0.3%	0	300	100.0%
Genesis aliquot prepared after cytology	299	0	0.0%	0	300	100.0%

Statistical tests for positive percent agreement and negative percent agreement for matching pairs between Manual and either Genesis (pre-cytology) or Genesis (post-cytology) were conducted. The tests yielded p-values of $<10^{-3}$ for both specimen groups tested with both assays, indicating that the Genesis does not contribute to target or inhibitor contamination.

Aliquots taken by the ThinPrep Genesis processor have not been evaluated for specific assays. Please refer to the instructions provided with a specific assay.

Aliquot Delivery Study

The ability for the ThinPrep Genesis processor to dispense an aliquot from a ThinPrep vial into an output tube was evaluated in a laboratory study. The data generated for this study demonstrate that the ThinPrep Genesis processor dispenses 1 mL ± 4% from the ThinPrep vial to an output tube.

Conclusions

The results of the study comparing the performance of the ThinPrep Genesis processor to the ThinPrep 2000 system demonstrate that the ThinPrep Genesis processor is at least as effective as the ThinPrep 2000 system for preparing slides from gynecologic specimens for the detection of atypical cells, cervical cancer or its precursor lesions, as well as all other cytologic categories, including adenocarcinoma, as defined by *The Bethesda System for Reporting Cervical Cytology*.

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 Genesis processor uses similar cell collection and slide preparation technology as the ThinPrep 2000 system, the ThinPrep Genesis processor 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 Genesis processor uses similar cell collection and slide preparation technology as the ThinPrep 2000 system, the ThinPrep Genesis processor 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 Genesis processor uses similar cell collection and slide preparation technology as the ThinPrep 2000 system, the specimen quality with the ThinPrep Genesis processor is also significantly improved over that of conventional Pap smear preparation in a variety of patient populations.

MATERIALS REQUIRED

MATERIALS PROVIDED

- ThinPrep Genesis processor
- ThinPrep Genesis processor operator's manual
- Power cord
- Waste bottle assembly with tubing harness and transport cover
- Fixative baths (10)
- Pipette tip disposal cup (2)
- Absorbent pad for filter plug (4)
- Absorbent pad for filter puncture area (4)
- Pipette tip holder (2, for customers performing aliquot removal)

- Multi-channel pipette tip gripper (for customers performing aliquot removal)
- Slide printer (optional)
- Tube printer (optional)
- USB key (1)

MATERIALS REQUIRED BUT NOT PROVIDED

- 20 ml PreservCyt® Solution vial
- ThinPrep® Pap Test filter
- ThinPrep® microscope slide
- Pipette tips (conductive, disposable, plastic pipette tips with an aerosol-resistant filter, 1 mL, for customers performing aliquot removal)
- Specimen transfer tube (for customers performing aliquot removal)
- Cervical collection device
- Slide staining system and reagents
- Standard laboratory fixative
- Coverslips and mounting media
- Lint-free wipes
- Personal protective equipment
- Sodium hypochlorite solution (0.5% solution, for customers performing aliquot removal)

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.

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TECHNICAL SERVICE AND PRODUCT INFORMATION

For technical service and assistance related to use of the ThinPrep Genesis processor, 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

Revision History	Date	Description
AW-23047-001 Rev. 001	11-2021	Add Clinical Study information. Add data in microbial/viral organism table. Add UK CA mark.