Part Number: 500029690	BALTSO0191 Version 13.0 Template 4 Inserts
Category and Description: Package Insert, BD FocalPoint™ Slide Profiler RoHS Product Insert	**Rev from:** 00 **Rev to:** 01
	Job Number: 469-18

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Blank (Sheet) Size: Length: 11" Width: 8.5"

Number of Pages: 24 Number of Sheets: 12

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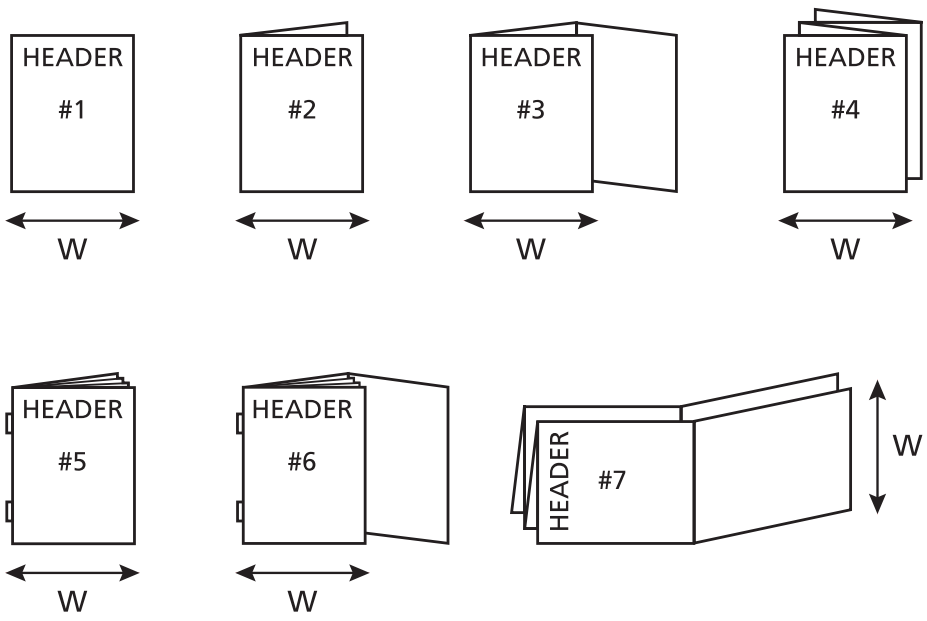

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BD FocalPoint™ Slide Profiler Product Insert

(For Export Only – For Use Outside the US)

CE IVD

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2018-04

BD FocalPoint™ Slide Profiler

REF **491464**

BD FocalPoint™ GS Review Station

REF **490189**

INTENDED USE

The **BD FocalPoint**™ Slide Profiler (formerly the AutoPap® System) is an automated cervical cytology screening device intended for use in initial screening of cervical cytology slides. The **BD FocalPoint** Slide Profiler identifies up to 25% of successfully processed slides as requiring no further review. The **BD FocalPoint** Slide Profiler also identifies at least 15% of all successfully processed slides for a second manual review.

The device is intended to be used on both conventionally-prepared and **BD SurePath**™ (formerly AutoCyte® PREP) cervical cytology slides. For both preparation methods, the device is intended to detect slides with evidence of squamous carcinoma and adenocarcinoma and their usual precursor conditions; it is not intended to be used on slides designated by the laboratory as *high-risk*.

Intended users are trained cytology laboratory personnel operating under the direct supervision of a qualified cytology supervisor or laboratory manager/director.

LIMITATIONS

The **BD FocalPoint** Slide Profiler analysis of cervical cytology slides is not intended to replace laboratory slide review processes for *high-risk* slides. Such *high-risk* slides are those where a primary health care provider has requested special handling of a case for a specified concern, or where the clinical laboratory, through its own procedures, has identified a need for an additional screening of the case.

The **BD FocalPoint** Slide Profiler classifies up to 25% of the slides as **No Further Review**. This **No Further Review** population of slides may contain abnormal or unsatisfactory slides. In addition, slides with infections present may be classified as **No Further Review**.

The performance characteristics of the **BD FocalPoint** Slide Profiler have not been established for the detection of the following diagnostic categories of The Bethesda System:

- Endometrial cells, cytologically benign, in a post-menopausal woman.
- Reactive changes associated with radiation and atrophy with inflammation.
- Rare malignant neoplasms, such as extrauterine and metastatic carcinomas, and sarcomas.

The **BD FocalPoint** Slide Profiler is intended to process conventional and **BD SurePath** cervical cytology slides that meet the slide, coverslip, and staining characteristics stated in the Operator's Manual.

Although the **BD FocalPoint** Slide Profiler is compatible with a wide range of staining procedures currently implemented in clinical laboratories, the device is not compatible with all staining methods currently in use. BD Life Sciences can assist the laboratory in ensuring that the staining method is compatible with the device.

All personnel who use the **BD FocalPoint** Slide Profiler should be trained in the use of the device. BD Life Sciences will train laboratory-designated personnel in the use of the device.

Although the **BD FocalPoint** Slide Profiler has demonstrated its effectiveness in processing conventional and **BD SurePath** slides, performance may vary from laboratory to laboratory.

SUMMARY AND EXPLANATION OF THE BD FOCALPOINT SLIDE PROFILER

The **BD FocalPoint** Slide Profiler is an automated cytology screening device that classifies slides using a high speed video microscope, image interpretation software, and morphology computers to image and analyze the complex images on a cervical cytology slide.

The device is intended to detect slides with evidence of squamous carcinoma and adenocarcinoma and their usual precursor conditions. These abnormalities fall within the following diagnostic categories of The Bethesda System:

Epithelial Cell Abnormalities

Squamous Cell

- Atypical squamous cells of undetermined significance (ASCUS)
- Low-grade squamous intraepithelial lesions (LSIL)
- High-grade squamous intraepithelial lesions (HSIL)
- Squamous cell carcinoma

Glandular Cell

- Atypical glandular cells of undetermined significance (AGCUS), including Adenocarcinoma in situ (AIS)
- Endocervical adenocarcinoma
- Endometrial adenocarcinoma

The **BD FocalPoint** Slide Profiler consists of two main components: the workstation (user interface) and the instrument (slide processor). The workstation components include a computer, monitor, keyboard, mouse, modem, and printer. The instrument is a floor standing unit designed to be placed out of the walkway. The instrument and workstation are inter-connected by an Ethernet local area network.

BD FOCALPOINT SLIDE PROFILER PROCESSING

Each prepared cervical cytology slide is affixed with a slide barcode label and loaded into a **BD FocalPoint** Slide Profiler slide tray, which holds up to eight slides. The trays (up to 36) are placed into the **BD FocalPoint** Slide Profiler instrument, which then automatically analyzes the slides.

After slide trays are loaded into the **BD FocalPoint** Slide Profiler instrument, they are moved automatically from the input hopper to the microscope stage. For each slide in the tray, the device checks the slide for physical integrity, reads the slide barcode label, scans and analyzes the slide at low power, and then scans and analyzes prioritized high-power fields.

Before the first tray and after each tray is processed, a comprehensive system integrity assessment of the instrument is performed automatically for quality assurance to ensure that all data collection and image analysis mechanisms are operating within specified limits. The results of all these tests are compared to specific performance limits to validate the processing result for each slide in the tray.

A slide is completely processed if the slide is checked for physical integrity, scanned and evaluated, and further qualified by system integrity checking. If slide processing is interrupted (for example, by power failure), partial, non-qualified results for slides will be stored by the device. These slides are termed incompletely processed and will not be validated or given slide processing results. The laboratory may print a report indicating the barcodes of these slides, which should be rerun on the instrument.

Results for completely and incompletely processed slides are validated and summarized into slide processing results. As slide processing results are computed, they may be printed in slide processing reports from the workstation.

BD FOCALPOINT SLIDE PROFILER SLIDE CLASSIFICATION

The **BD FocalPoint** Slide Profiler algorithms are trained to detect evidence of morphologic changes associated with epithelial abnormalities, specimen adequacy, and benign cellular changes and infections. For each processed slide, the **BD FocalPoint** Slide Profiler uses this morphological information to classify slides as **No Further Review**, **Review**, or **QC Review**.

Each slide is processed only once on the **BD FocalPoint** Slide Profiler. Each successfully processed slide is assigned a score, which the device uses to rank slides according to likelihood that a slide contains abnormalities, unsatisfactory conditions, or benign cellular changes. Some slides may not be suitable for processing on the device due to problems with the slide, the coverslip, or the preparation of the specimen; these slides require manual screening.

Classification of No Further Review Slides

The **BD FocalPoint** Slide Profiler classifies up to, but no more than, 25% of all successfully processed slides as **No Further Review.**

The **No Further Review** slides have the highest probability of being normal and may be archived by the laboratory as within normal limits (WNL).

Classification of Review Slides

The remaining slide population, at least 75%, is likely to contain the abnormal or unsatisfactory slides. These slides are classified as **Review** by the **BD FocalPoint** Slide Profiler and require manual review. All **Review** slides that are classified as WNL by the cytotechnologist are eligible for rescreening.

Classification of QC Review (Rescreen) Slides

The **BD FocalPoint** Slide Profiler also classifies at least 15% of *all* successfully processed slides as eligible for rescreening. The slides in this enriched group have the highest likelihood of being abnormal. This enriched population of slides may be used as a substitute for the 10% random selection of slides that constitutes laboratory quality control review.

BD FOCALPOINT SLIDE PROFILER REPORTS

The **BD FocalPoint** Slide Profiler reports including the Archive Report, Ranked Review Report, and Quality Control (QC) Ranked Review Report, provide the following information.

Ranking Information

To assist the cytotechnologist during manual review, the device ranks the slides for probable abnormality. Each slide is individually ranked from 1 to n, where a rank of 1 indicates a slide most likely to contain abnormality and n is the slide least likely to contain abnormality (n is the number of slides in a print set). Additionally, each slide is assigned a group ranking, ranging from 1 to 5, where a rank of 1 indicates the group most likely to contain abnormalities.

The **BD FocalPoint** Slide Profiler Archive Report for **No Further Review** slides does not provide slide ranks for probable abnormality or a slide adequacy evaluation of unsatisfactory because these slides are classified as WNL and archived.

Evaluation of Slide Adequacy

The device evaluates slide adequacy according to The Bethesda System slide adequacy criteria. For conventional and **BD SurePath** slides, the device reports three adequacy parameters: squamous component (detected, not detected), endocervical component (detected, not detected), and inflammation/obscuration (a percentage of the specimen area). Cytotechnologists may use these parameters as indicators of slide adequacy during manual review. Cytotechnologists should review the **BD FocalPoint** Slide Profiler Archive Report in depth to determine if any less-than- satisfactory slides are present in the **No Further Review** population.

Processing Information

The device confirms that the slide was completely and successfully processed.

INSTRUCTIONS AND INSTRUMENTATION

Slide Preparation

Conventional and **BD SurePath** cervical cytology slides processed on the **BD FocalPoint** Slide Profiler generally do not require special preparation by the laboratory. Refer to the Operator's Manual for slide labeling and loading instructions.

The compatibility of a laboratory's staining process will be assessed by BD Life Sciences prior to clinical use of the device by the laboratory as described in the Operator's Manual.

Materials Provided

The **BD FocalPoint** Slide Profiler consists of the following components:

- **BD FocalPoint** Slide Profiler instrument
- Slide trays
- **BD FocalPoint** Slide Profiler workstation
- Electronic interface cables
- Power cords

Additional Items Supplied (some items are optional, at additional cost):

- Printer paper (starter package)
- Head cleaning tape
- Slide barcode labels (starter package)
- Backup tapes (starter set)
- Switch slides for processing different slide preparation types (**BD SurePath** or conventional) and/or coverslip types (glass or plastic) on the same instrument.

Materials Required but Not Provided

- Instrument: see Operator's Manual for power specifications.
- Workstation: see Operator's Manual for power specifications.
- Dedicated analog telephone line
- Dustproof storage
- 70% Isopropyl Alcohol
- Cotton swabs
- Lint-free cloths
- Glass cleaning solution

WARNINGS

Broken Glass Hazard when Handling Slides

Do not drop or break slides during slide preparation and when loading and unloading slides into trays. If slides are broken, injuries may occur.

Moving Parts Hazard when Loading/ Unloading Trays

Remove all potentially obstructive jewelry and clothing before loading or unloading trays. After opening a hopper door, be sure all moving parts in the hopper have stopped before inserting or removing a tray. If trays are inserted before all moving parts have stopped, injuries may occur or the device may jam.

Shock Potential when Cleaning the Monitor

Failure to remove power to the monitor before performing the procedure could result in an electric shock. See the Operator's Manual.

Shock Potential when Power Applied Improperly

The symbol next to the power connector indicates potential shock hazard. Ensure that the system is connected to a power receptacle that provides voltage and current within the specified rating for the system. Use of an incompatible power receptacle may produce electrical shock and fire hazards.

Shock Potential when Improperly Grounded

Never use a two-prong plug adapter to connect primary power to the system. Use of a two-prong adapter disconnects the utility ground, creating a potential shock hazard. Always connect the system power cord directly to an appropriate receptacle with a functional ground.

Shock Potential when Cleaning with Power Applied

Always turn off the power switch and unplug the power cord before cleaning the outer surfaces or internal components of the device to avoid a potential shock hazard.

Shock Potential from Spilled Liquids

Do not place containers with liquids on the device or the workstation cart. Do not spill liquids on the system; fluid seepage into internal components creates a potential shock hazard. Shut down the device, disconnect from the power source and wipe up all spills immediately. Do not operate the system if internal components have been exposed to fluid.

Electromagnetic Fields

This is a Class A product. In a domestic environment, this product may cause radio interference with other electronic devices, such as telephones and other medical equipment, in which case the user may be required to take measures to reduce such interference.

PRECAUTIONS

Slide and Coverslip Requirements

This device cannot be recommended for use with slides and coverslips that do not comply with the specifications provided in the Operator's Manual, particularly broken slides, dirty or marked slides, and non-standard slide or coverslip sizes.

Staining Procedures

Staining procedures should be conducted carefully so that as many slides as possible may be processed on the device. See the Operator's Manual for additional information.

Backup Procedures

When performing the backup procedures, BD Life Sciences recommends that two tapes be used in rotation; each tape would be used every other day. This will ensure minimum loss of data in the unlikely event of a workstation failure.

Shutdown Procedures

Except in an emergency situation, such as those described in the Warnings section, shutting down the **BD FocalPoint** Slide Profiler should only be performed as described in the Operator's Manual to avoid loss of data. If no emergency situation exists, consult the Operator's Manual for the appropriate procedures or contact BD Life Sciences, or its designated representative to shut down the device.

Power Down Procedures

It is important to shut down the system components in the proper order. See the Operator's Manual for additional information.

Installation and Service

The device should be installed only by company authorized personnel. Only technically qualified personnel, trained by BD Life Sciences, should perform troubleshooting and service procedures on internal components.

REPORTS OF CLINICAL STUDIES

A prospective, intended use study was conducted at five cytology laboratories to evaluate the effectiveness of the **BD FocalPoint** Slide Profiler in detecting abnormal and normal conventional Pap smears when the device was used as a combined primary screener and quality control rescreener.

An additional, intended use study was conducted at three cytology laboratories to evaluate the **BD FocalPoint** Slide Profiler effectiveness in screening **BD SurePath** slides.

Conventional Slides: Prospective, Intended Use Study

Of the 31,507 Pap smear slides in the study, 25,124 were evaluated in a two-arm study comparing Current Practice with a **BD FocalPoint** Assisted Practice. These two study arms were defined as follows:

- Current Practice consisted of 100% manual initial screening and 10% random rescreening (designated as quality control)
- **BD FocalPoint** Assisted Practice consisted of 100% **BD FocalPoint** Slide Profiler initial screening, at least 75% **BD FocalPoint** Slide Profiler assisted manual screening, and 15% **BD FocalPoint** Slide Profiler assisted manual rescreening

Slides not meeting the inclusion criteria for the study, such as *high-risk* slides, were excluded from the analysis. The **BD FocalPoint** Slide Profiler is not intended to replace individual laboratory processes for screening *high-risk* slides.

The goal of the clinical study was to demonstrate that, compared to Current Practice, the **BD FocalPoint** Slide Profiler detected more slides with epithelial abnormality in the following diagnostic categories:

ASCUS+ (All abnormal slides combined): Atypical squamous cells of undetermined significance and above; additionally includes the categories AGUS, LSIL, HSIL, AIS, and cancer

LSIL: Low-grade squamous intraepithelial lesion

LSIL+: In addition to LSIL, includes the categories HSIL, AIS, and cancer

An additional goal was to demonstrate that, compared to Current Practice, the device detected an equivalent number of satisfactory but limited by (SBLB) and unsatisfactory slides.

Slide Accountability

As shown in Table 1, the clinical study analyzed a total of 25,124 slides.

Table 1 Conventional Slide Accountability

Number of slides in study	**31,507**
Excluded *(High-risk)*	–3,200
Excluded (Device exclusions)*	–1,132
Excluded (Lab exclusions)†	–1,004
Entered in study	26,171
Failed processing on **BD FocalPoint** Slide Profiler	–963
Processed on **BD FocalPoint** Slide Profiler	25,208
Excluded from analysis (no truth determination)‡	–84
Total Slides Analyzed	**25,124**

* Broken slides, slides with plastic coverslips, etc.
† Multiple slides from one patient, dotted slides, etc.
‡ Slides not available from labs for truth determination

Study Truth (Truth Determination Process)

Study truth was determined by cytologic confirmation, not by histologic biopsy. The true diagnosis for the slides analyzed during the clinical trial was determined as follows:

- When the cytotechnologists' screening diagnoses from the **BD FocalPoint** Assisted Practice and Current Practice agreed, this diagnosis was considered to be the true cytological diagnosis for the slide, or truth.
- When the cytotechnologists' screening diagnoses from the **BD FocalPoint** Assisted Practice and Current Practice disagreed, an External Discrepancy Panel (EDP) was convened. An EDP consisted of a group of three cytopathologists who independently diagnosed a slide. If two out of three agreed, a diagnosis was determined; otherwise, the slide was reviewed at a multi-head microscope until a consensus diagnosis was achieved. A total of 24 cytopathologists, or 8 groups of 3, participated in this process.
- When adequacy determinations between the two study arms agreed, this was also considered to be truth.
- When adequacy determinations between the two study arms disagreed, a single, independent senior cytotechnologist reviewed the slide to determine truth.

Definition of High Risk

During the study, each laboratory applied its own definition of *high-risk*. A *high-risk* definition consisted of one or more of the reasons listed below:

Physician-designated *high-risk* patients; prior abnormal gynecological history; postmenopausal or abnormal vaginal bleeding; DES patients; previous breast cancer or history of malignancy; previous tissue or Pap diagnosis of HPV, dysplasia, or HIV infection; multiple sex partners; visible lesion; early age of sexual intercourse; smoker.

All known *high-risk* slides were excluded from the study at all sites. Table 2 shows the percentage of slides excluded for *high-risk* reasons at each site.

Table 2 High Risk Exclusion Rates by Site

Site	High Risk Exclusion%
1	5.7%
2	6.1%
3	7.1%
4	11.8%
5	14.3%

Clinical Study Results

In this clinical study, 25,124 slides were analyzed in a comparison of two study arms: the **BD FocalPoint** Assisted Practice and Current Practice. The slides were submitted to the truth determination process described previously so that each slide had a final cytologic diagnosis (study truth). The cytotechnologist diagnoses from one study arm could be compared to the other study arm as well as to study truth. The distribution of these 25,124 slides is shown in tables 3 and 4:

Table 3 Distribution of Conventional Study Slides

Diagnosis	Number of Slides
Unsatisfactory	171
WNL	23,556
All Abnormals	1,397
Total	**25,124**

Table 4 Distribution of Conventional Abnormal Slides

Diagnosis	Number of Slides
ASCUS	998
AGUS	51
LSIL	278
HSIL	67
AIS	1
Cancer	2
Total	**1,397**

SUMMARY OF THE ANALYSES OF DIAGNOSTIC CATEGORIES

In this study, the **BD FocalPoint** Slide Profiler was used to detect abnormal and normal Pap smears, whereby up to 25% of the slides could be classified as **No Further Review** and archived by the laboratory.

The results of this study showed that the **BD FocalPoint** Assisted Practice improved the laboratories' ability to detect abnormal cervical cells and precursors, while also effectively assessing specimen adequacy. The **BD FocalPoint** Slide Profiler improved sensitivity by increasing the detection of abnormalities in the **Review** population and by enhancing the recovery of abnormalities that may have been missed during initial manual screening in the rescreen population (termed **QC Review**), without decreasing specificity.

Table 5 compares the **BD FocalPoint** Assisted Practice to Current Practice for all diagnostic categories. The shaded diagonal values show where the two study arms agreed on the diagnosis. The off-diagonals show where the study arms disagreed. These discordances were used to compare the diagnostic performance between the two study arms.

The *total* columns in the table show the number of abnormal slides for each diagnostic category that were correctly classified by each study arm. The values shown in parenthesis are the total number of slides in each diagnostic category as determined by truth.

Table 5 **BD FocalPoint** Assisted Practice Diagnosis vs. Current Practice Diagnosis: (N) = Total Number of Conventional Slides in the Diagnostic Category as Determined by Truth

		Current Practice Diagnosis								
		Unsat (171)	**WNL (23,566)**	**ASCUS (998)**	**AGUS (51)**	**LSIL (278)**	**HSIL (67)**	**AIS (1)**	**Cancer (2)**	**Total**
BD FocalPoint Assisted Practice Diagnosis	**Unsat (171)**	99	38	0	0	0	0	0	0	137
	WNL (23,566)	34	23,556	163	8	25	1	1	0	23,788
	ASCUS (998)	0	232	603	0	0	0	0	0	835
	AGUS (51)	0	9	0	34	0	0	0	0	43
	LSIL (278)	0	45	0	0	208	0	0	0	253
	HSIL (67)	0	3	0	0	0	63	0	0	66
	AIS (1)	0	0	0	0	0	0	0	0	0
	Cancer (2)	0	2	0	0	0	0	0	0	2
	Total	133	23,885	766	42	233	64	1	0	25,124

Epithelial Abnormalities

This section provides the results for the epithelial abnormality categories of ASCUS+, ASCUS/AGUS, LSIL, LSIL+, and HSIL+. To determine whether a statistically significant greater number of slides in these categories were detected by the cytotechnologists in the **BD FocalPoint** Assisted Practice arm, a one-sided exact conditional binomial test was used.

Note: *The lower right cells in the following 2x2 tables are blank because only abnormal slides are considered for the analysis of performance.*

ASCUS+

Table 6 shows the results for conventional slides identified by the truth determination process to be ASCUS+ (includes ASCUS, AGUS, LSIL, HSIL, AIS, and cancer). The laboratories detected a statistically significant greater number of ASCUS+ slides in the **BD FocalPoint** Assisted Practice compared to Current Practice.

Table 6 Classification of Conventional ASCUS+ Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	908	291	1,199
	WNL (-)	198		198
		1,106	291	1,397

ASCUS/AGUS

Tables 7 and 8 show the results for conventional slides identified by the truth determination process to be ASCUS and AGUS, respectively. When ASCUS and AGUS are combined for analysis, the laboratories detected a statistically significant greater number of ASCUS/AGUS slides in the **BD FocalPoint** Assisted Practice arm compared to the Current Practice arm.

Table 7 Classification of Conventional ASCUS Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	603	232	835
	WNL (-)	163		163
		766	232	998

Table 8 Classification of Conventional AGUS Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	34	9	43
	WNL (-)	8		8
		42	9	51

LSIL

Table 9 shows the results for conventional slides identified by the truth determination process to be LSIL. The laboratories detected a statistically significant greater number of LSIL slides in the **BD FocalPoint** Assisted Practice compared to Current Practice.

Table 9 Classification of Conventional LSIL Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	208	45	253
	WNL (-)	25		25
		233	45	278

LSIL+

Table 10 shows the results for conventional slides identified by the truth determination process to be LSIL+, which includes the categories LSIL, HSIL, AIS, and cancer. The laboratories detected a statistically significant greater number of LSIL+ slides in the **BD FocalPoint** Assisted Practice compared to Current Practice.

Table 10 Classification of Conventional LSIL+ Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	271	50	321
	WNL (-)	27		27
		298	50	348

HSIL+

In the prospective study of over 25,100 conventional slides, only 70 HSIL+ slides were available for analysis. HSIL+ includes the categories HSIL, AIS, and cancer. Table 11 shows that the laboratories detected more HSIL+ slides in the **BD FocalPoint** Assisted Practice as compared to Current Practice. The 70 HSIL+ sample size was insufficient to determine whether this increased detection was statistically significant.

Table 11 Classification of Conventional HSIL+ Slides

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	63	5	68
	WNL (-)	2		2
		65	5	70

Specimen Adequacy

This section provides the results for the specimen adequacy categories of satisfactory but limited by (SBLB) and unsatisfactory. The **BD FocalPoint** Slide Profiler evaluates slide adequacy according to The Bethesda System criteria. The device reports three adequacy parameters: squamous component (detected, not detected), endocervical component (detected, not detected), and inflammation/obscuration (a percentage of the coverslip area).

Satisfactory But Limited By (SBLB)

Out of 5,873 conventional slides identified by the truth determination process to be SBLB, the laboratories detected 5,059 slides in the **BD FocalPoint** Assisted Practice compared to 4,728 detected by Current Practice. The **BD FocalPoint** Assisted Practice is equivalent to Current Practice in identifying SBLB slides.

Unsatisfactory (Unsat)

Out of 171 conventional slides identified by the truth determination process to be unsatisfactory, the laboratories detected 137 slides in the **BD FocalPoint** Assisted Practice compared to 133 detected by Current Practice. The **BD FocalPoint** Assisted Practice is equivalent to Current Practice in identifying unsatisfactory slides.

Benign Cellular Changes (BCC)

The cytotechnologists on each arm of the study assessed the slides for evidence of epithelial abnormality and the presence or absence of benign cellular changes.

The results were compared to study truth for the slides and showed that the detection of BCC, reactive changes, and infection was equivalent in the **BD FocalPoint** Assisted Practice and Current Practice arms of the study. Out of 5,156 conventional slides identified by the truth determination process to be BCC, the **BD FocalPoint** Assisted Practice detected 3,276 compared to 3,431 detected by Current Practice.

Reactive Changes

The WNL slide population was evaluated for the presence of reactive changes. Of the 23,556 WNL conventional slides, 3,037 were noted for reactive changes by the cytotechnologists on either arm of the study. Of the 3,037 slides with reactive changes, 2,978 were noted for inflammation (without atrophy).

Infections

In the study, cytotechnologists on both study arms examined slides for the presence of infections, including actinomyces, herpes, coccobacilli, trichomonas, and candida. If a cytotechnologist on either or both study arms detected the presence of infection on a Pap smear, this was considered truth for the slide. Table 12 provides a breakdown by infection subcategories of the 2,925 conventional slides noted for infections.

Table 12 Detection of Infections: (N) = Total number of conventional slides noted for each infection category

Infections	BD FocalPoint Assisted Practice	Current Practice
All infections (2,925)	1,985	2,141
Actinomyces (17)	12	8
Candida (1,282)	865	983
Coccobacilli (1,375)	869	897
Herpes (14)	11	9
Trichomonas (343)	275	293

SITE-SPECIFIC COMPARISON OF SENSITIVITY PERFORMANCE

This section compares the sensitivity results by diagnostic category for each arm of the study. These results are provided for each site. The sensitivity is calculated as:

$$\frac{\text{All slides called abnormal by the cytotechnologist}}{\text{All study truth abnormal slides}}$$

In this study, the sensitivity for all abnormals, ASCUS+, (includes the categories ASCUS, AGUS, LSIL, HSIL, AIS, and cancer) for each study arm was:

BD FocalPoint Assisted Practice: $1{,}199 / 1{,}397 = 85.8\%$

Current Practice: $1{,}106 / 1{,}397 = 79.2\%$

Table 13 shows the site-specific sensitivity results for the categories of ASCUS+, ASCUS/AGUS, LSIL, LSIL+, and HSIL+. The **BD FocalPoint** Assisted Practice sensitivities are greater than those for Current Practice at all sites for all diagnostic categories except for HSIL+ at site 5.

Table 13 Site-Specific Sensitivity Results (Sensitivity%, [N])

		Site 1	Site 2	Site 3	Site 4	Site 5	Total
ASCUS+ (all abnormals)	**BD FocalPoint Assisted Practice**	90.6% (163/180)	81.3% (169/208)	90.3% (93/103)	83.5% (406/486)	87.6% (368/420)	85.8% (1,199/1,397)
	Current Practice	80.0% (144/180)	76.4% (159/208)	67.0% (69/103)	80.7% (392/486)	81.4% (342/420)	79.2% (1,106/1,397)
ASCUS/ AGUS	**BD FocalPoint Assisted Practice**	88.4% (114/129)	78.1% (114/146)	85.1% (57/67)	81.9% (307/375)	86.1% (286/332)	83.7% (878/1,049)
	Current Practice	77.5% (100/129)	76.7% (112/146)	58.2% (39/67)	78.7% (295/375)	78.9% (262/332)	77.0% (808/1,049)
LSIL	**BD FocalPoint Assisted Practice**	95.7% (45/47)	87.0% (47/54)	100% (30/30)	86.5% (77/89)	93.1% (54/58)	91.0% (253/278)
	Current Practice	85.1% (40/47)	75.9% (41/54)	86.7% (26/30)	85.4% (76/89)	86.2% (50/58)	83.8% (233/278)
LSIL+	**BD FocalPoint Assisted Practice**	96.1% (49/51)	88.7% (55/62)	100% (36/36)	89.2% (99/111)	93.2% (82/88)	92.2% (321/348)
	Current Practice	86.3% (44/51)	75.8% (47/62)	83.3% (30/36)	87.4% (97/111)	90.9% (80/88)	85.6% (298/348)
HSIL+	**BD FocalPoint Assisted Practice**	100% (4/4)	100% (8/8)	100% (6/6)	100% (22/22)	93.3% (28/30)	97.1% (68/70)
	Current Practice	100% (4/4)	75% (6/8)	66.7% (4/6)	95.5% (21/22)	100% (30/30)	92.8% (65/70)

COMPARISON OF FALSE NEGATIVE PERFORMANCE

The **BD FocalPoint** Slide Profiler classified 5,109 slides as **No Further Review**. Of these, 21 had unresolved diagnostic or adequacy truth (1 and 20 slides, respectively), leaving 5,088 slides. Table 14 shows the false negatives (FNs) in this population as determined by truth.

Within the population of 5,036 WNL slides, 4,800 slides were classified as WNL by the cytotechnologists in the Current Practice arm and as **No Further Review** by the **BD FocalPoint** Slide Profiler. After the study was completed, these slides were subjected to further rescreening by a senior cytotechnologist. If the senior cytotechnologist determined that a slide was not WNL, the slide was sent for pathologist confirmation.

The results of this rescreening and confirmation showed that an additional 11 unsatisfactory, 10 ASCUS, 1 AGUS, and 3 LSIL slides were detected in the **No Further Review** population. There were no HSIL, AIS, or cancer slides found by the senior cytotechnologist.

Table 14 False Negative Performance in the **No Further Review** Population (As Determined by Study Truth)

Diagnosis	No Further Review FNs
Unsat	9
WNL	5,036
ASCUS	31
AGUS	1
LSIL	11
HSIL	0
AIS	0
Cancer	0
Total	**5,088**

Table 15 compares the false negative performance of the **BD FocalPoint** Assisted Practice with Current Practice. The table shows the total number of false negative slides for each study arm. In all diagnostic categories (except AIS) the **BD FocalPoint** Assisted Practice had fewer false negatives; that is, the **BD FocalPoint** Assisted Practice detected more abnormal slides.

Table 15 Comparison of False Negative Performance for the 25,124 Study Slides

Diagnosis	BD FocalPoint Assisted Practice FNs*	Current Practice FNs
Unsat	34	38
ASCUS	163	232
AGUS	8	9
LSIL	25	45
HSIL	1	3
AIS	1	0
Cancer	0	2
Total	**232**	**329**

* Includes the **No Further Review** FNs shown in Table 14

SITE-SPECIFIC COMPARISON OF SPECIFICITY PERFORMANCE

In this study, specificity was defined as the percentage of WNL slides determined to be normal and adequate according to the truth determination process, defined as:

$$\frac{\text{All slides called WNL by cytotech \& confirmed as WNL by truth}}{\text{All Study truth WNL slides}}$$

Therefore, the specificity change is defined as:

$$\frac{\left(\text{\% Specificity of the } \textbf{BD FocalPoint} \text{ Assisted Practice}\right) - \left(\text{\% Specificity of the Current Practice}\right)}{\text{\% Specificity of Current Practice}}$$

In the clinical study, 23,556 slides were diagnosed as WNL according to study truth. Table 16 compares the specificity results for each arm of the study. A positive percent change in specificity indicates improved specificity for the **BD FocalPoint** Assisted Practice arm; a negative percent change indicates improved specificity for the Current Practice arm.

Table 16 Site-Specific Specificity Comparison

	BD FocalPoint Assisted Practice Specificity%	Current Practice Specificity%	% Change in Specificity
Site 1	96.1 (3,544/3,689)	97.1 (3,583/3,689)	-1.1
Site 2	97.8 (3,862/3,950)	98.0 (3,870/3,950)	-0.2
Site 3	96.0 (3,652/3,803)	97.9 (3,725/3,803)	-1.9
Site 4	94.9 (5,459/5,751)	93.7 (5,387/5,751)	+1.3
Site 5	93.1 (5,926/6,363)	89.1 (5,669/6,363)	+4.5
Total	95.3 (22,443/23,556)	94.4 (22,233/23,556)	+1.0

Using the data in Table 16, the combined percent change in specificity for all sites is:

$$\frac{95.3 - 94.4}{94.4} \times 100 = +1.0\%$$

These data indicate that, for all study sites combined, the **BD FocalPoint** Assisted Practice improved the specificity by 1.0%.

SITE-SPECIFIC COMPARISON OF FALSE POSITIVE PERFORMANCE

In this study, a false positive was defined as a WNL slide that the cytotechnologist incorrectly classified as abnormal and referred to a cytopathologist, defined as:

$$\frac{\text{All slides called abnormal by cytotech \& confirmed as WNL by truth}}{\text{All study truth WNL slides}}$$

Therefore, the false positive value change is defined as:

$$\frac{\left(\text{False Positive Value for Current Practice}\right) - \left(\text{False Positive Value for } \textbf{BD FocalPoint} \text{ Assisted Practice}\right)}{\text{False Positive Value for Current Practice}}$$

A total of 23,556 slides were diagnosed as WNL according to study truth. Table 17 compares the false positive results for each arm of the study. A positive percent change in the false positive value indicates a reduction of false positives in the **BD FocalPoint** Assisted Practice arm; a negative percent change indicates a reduction of false positives in the Current Practice arm.

Table 17 Site-Specific False Positive Value Comparison

	BD FocalPoint Assisted Practice False Positive Value%	Current Practice False Positive Value%	% Change in False Positive Value
Site 1	3.9 (145/3,689)	2.9 (106/3,689)	-36.9
Site 2	2.2 (88/3,950)	2.0 (80/3,950)	-9.8
Site 3	4.0 (151/3,803)	2.1 (78/3,803)	-91.8
Site 4	5.1 (292/5,751)	6.3 (364/5,751)	+19.7
Site 5	6.9 (437/6,363)	10.9 (694/6,363)	+37.0
Total	4.7 (1,113/23,556)	5.6 (1,323/23,556)	+16.0

Using the data in Table 17, the combined false positive value change for all sites is:

$$\frac{5.6 - 4.7}{5.6} \times 100 = +16\%$$

These data indicate that, for all study sites combined, the **BD FocalPoint** Assisted Practice reduced the false positive slides by 16%.

RANKED REVIEW REPORT ANALYSIS

Table 18 shows the distribution of the study truth abnormal slides with their associated group ranks. As shown in the table, the **BD FocalPoint** Slide Profiler placed the highest proportion of slides in the top ranks for all diagnostic categories. For example, 54 of the 70 HSIL+ slides were placed in the top rank.

Table 18 EDP Confirmed and Concordant Abnormal Slides by Rank

Group Rank	ASCUS	AGUS	LSIL	HSIL+
1	465	20	153	54
2	169	8	48	8
3	139	8	31	3
4	88	5	16	3
5	106	9	19	2
Total	**967**	**50**	**267**	**70**

These data demonstrate that the **BD FocalPoint** Slide Profiler was effective in ranking conventional slides according to the potential for abnormality. It is important to note that all slides designated as **Review** by the device require screening since the potential for abnormality exists across all group ranks.

BD SurePath Slides: BD FocalPoint Slide Profiler Performance

A clinical study was conducted to evaluate **BD FocalPoint** Slide Profiler performance in classifying **BD SurePath** slides as **Review**, **QC Review**, and **No Further Review**. A total of 3,638 **BD SurePath** slides were selected from the **BD FocalPoint** Slide Profiler clinical study of **BD SurePath** slides, and a new intended use study was conducted at three clinical laboratories to compare manual screening with the **BD FocalPoint** Assisted Practice. Of the 3,638 **BD SurePath** slides enrolled in the study, 3,621 were evaluated in a two-arm study design. These two study arms were defined as follows:

BD SurePath Practice: 100% manual screening of **BD SurePath** slides in standard laboratory practice to arrive at site diagnoses for the slides. These site diagnoses were taken from the PMA application for the **BD PrepStain** System, the device that processes and produces **BD SurePath** slides.

BD FocalPoint Assisted Practice: The **BD FocalPoint** Slide Profiler used in the standard workflow of the laboratory to arrive at site diagnoses for the slides. The intended use includes 100% initial screening of slides by the **BD FocalPoint** Slide Profiler, at least 75% **BD FocalPoint** Slide Profiler assisted manual screening of slides, and 15% **BD FocalPoint** Slide Profiler assisted manual rescreening.

The purpose of the study was to compare the diagnostic performance of the **BD FocalPoint** Assisted Practice and the **BD SurePath** Practice. The original PMA studies of the **BD PrepStain** System did not distinguish *high-risk* slides from non-*high-risk* slides. These slides were processed on the **BD FocalPoint** Slide Profiler during clinical studies. The performance of the device was evaluated by comparing the percentage of slides in each study arm in which the diagnoses agreed. In addition, the reliability of WNL diagnoses obtained through the **BD FocalPoint** Assisted Practice was evaluated by adjudicating a random sample of a subset of the slides classified as WNL by both study arms.

Slide Accountability

As shown in Table 19, this study analyzed a total of 3,621 **BD SurePath** slides.

Table 19 Slide Accountability

	Slides
Total number enrolled in study	**3,638**
Total number excluded from analysis	**–17**
No truth diagnosis*	–1
Missing Slides	–10
Incomplete Screening	–4
Broken Slide	–1
Bubbles under coverslip	–1
Total number included in analysis	**3,621**

* Excluded because the slide was discrepant between the two study arms and did not receive a truth diagnosis from the EDP

Study Adjudication Process

The study adjudication process compared the diagnoses of the slides between the two study arms. When the sites' screening diagnoses from the two study arms agreed, this diagnosis was considered the final diagnosis. When they disagreed, the slides were sent to an External Discrepancy Panel (EDP) for diagnostic adjudication. The EDP consisted of a total of nine cytopathologists screening in groups of three.

The EDP also adjudicated a random sample of a subset of the slides classified as WNL by both study arms. When adequacy determinations between the two study arms agreed, this was considered to be the final adequacy assessment. When they disagreed, a single senior cytotechnologist determined the adequacy of the slide.

Clinical Study Results

In this study, 3,621 slides were analyzed in a comparison of two study arms: the **BD FocalPoint** Assisted Practice and the **BD SurePath** Practice. The site diagnoses from the **BD FocalPoint** Assisted Practice study arm were compared to the site diagnoses from the **BD SurePath** Practice. Also, each study arm was compared to the final diagnoses established by the study adjudication process. These results are described in the following sections for each of the three clinical study sites.

COMPARISON OF STUDY ARMS FOR DIAGNOSTIC CATEGORIES

Tables 20–22 compare the **BD SurePath** Practice with the **BD FocalPoint** Assisted Practice for The Bethesda System categories of Unsatisfactory (Unsat), WNL, ASCUS, AGUS, LSIL, HSIL, AIS, and cancer (CA). These results are shown for each of the three study sites.

The diagonal values (shaded) in the tables show where there was agreement on the diagnosis between the **BD FocalPoint** Assisted Practice and **BD SurePath** Practice study arms. The values in the off-diagonals represent differing diagnoses between the two study arms.

Table 20 BD FocalPoint Assisted Practice vs. **BD SurePath** Practice—Site 801

		BD SurePath Practice Diagnosis								
		Unsat	**WNL**	**ASCUS**	**AGUS**	**LSIL**	**HSIL**	**AIS**	**Cancer**	**Total**
BD FocalPoint Assisted Practice Diagnosis	**Unsat**	9	5	0	0	0	0	0	1	15
	WNL	1	802	68	15	21	2	0	0	909
	ASCUS	0	63	33	3	9	2	0	0	110
	AGUS	0	3	3	2	1	0	0	1	10
	LSIL	0	23	12	0	49	8	0	0	92
	HSIL	0	5	5	2	20	27	0	4	63
	AIS	0	2	0	1	1	0	0	3	7
	Cancer	0	0	0	0	1	3	0	11	15
	Total	10	903	121	23	102	42	0	20	1,221

Table 21 BD FocalPoint Assisted Practice vs. **BD SurePath** Practice — Site 802

		BD SurePath Practice Diagnosis								
		Unsat	**WNL**	**ASCUS**	**AGUS**	**LSIL**	**HSIL**	**AIS**	**Cancer**	**Total**
BD FocalPoint Assisted Practice Diagnosis	**Unsat**	3	25	0	0	0	0	0	0	28
	WNL	0	765	35	2	10	1	0	0	813
	ASCUS	0	116	31	1	3	1	0	0	152
	AGUS	0	1	0	0	0	0	0	0	1
	LSIL	0	35	33	1	62	2	0	0	133
	HSIL	0	6	12	0	19	39	0	0	76
	AIS	0	0	1	0	0	1	0	0	2
	Cancer	0	0	0	0	0	0	0	2	2
	Total	3	948	112	4	94	44	0	2	1,207

Table 22 BD FocalPoint Assisted Practice vs. **BD SurePath** Practice — Site 803

		BD SurePath Practice Diagnosis								
		Unsat	**WNL**	**ASCUS**	**AGUS**	**LSIL**	**HSIL**	**AIS**	**Cancer**	**Total**
BD FocalPoint Assisted Practice Diagnosis	**Unsat**	4	75	11	1	1	0	0	0	92
	WNL	0	616	157	5	23	3	0	0	804
	ASCUS	0	74	42	1	24	6	0	0	147
	AGUS	0	3	2	0	0	0	0	0	5
	LSIL	0	19	13	0	54	5	0	0	91
	HSIL	0	5	8	1	12	25	0	1	52
	AIS	0	0	0	0	0	0	0	0	0
	Cancer	0	0	0	0	0	2	0	0	2
	Total	4	792	233	8	114	41	0	1	1,193

COMPARISON OF STUDY ARMS TO ADJUDICATED RESULTS FOR DIAGNOSTIC CATEGORIES

This section provides results for **BD SurePath** slides that the study adjudication process identified as ASCUS+, LSIL+, or HSIL+ according to the adjudication process described previously. These adjudicated results cannot be directly correlated with the slide results shown in tables 20–22, which compare the two study arms without slide adjudication.

The study adjudication process identified slides as ASCUS+, LSIL+, or HSIL+. ASCUS+ is defined as ASCUS and above and additionally includes the categories AGUS, LSIL, HSIL, AIS and cancer. LSIL+ is defined as *low-grade squamous intraepithelial lesion* and above and additionally includes the categories HSIL, AIS, and cancer. HSIL+ is defined as *high-grade squamous intraepithelial lesion* and above and additionally includes the categories AIS and cancer.

For sites 801, 802, and 803, respectively, the study adjudication process determined 248, 216, and 229 ASCUS+ slides; 178, 144, and 139 LSIL+ slides; and 81, 63, and 44 HSIL+ slides. Out of these totals, the EDP adjudicated all slides with differing diagnoses between the two study arms. Slides with the same diagnoses for both study arms were not adjudicated.

Each study arm was compared to the EDP adjudicated results for ASCUS+, LSIL+, and HSIL+ at each site. The **BD FocalPoint** Assisted Practice detected numerically more HSIL+ slides at all three sites, and numerically more LSIL+ and ASCUS+ slides at two of the three sites:

ASCUS+

Out of 123 (site 801), 82 (site 802), and 108 (site 803) **BD SurePath** slides identified by the EDP to be ASCUS+, the **BD FocalPoint** Assisted Practice detected 109, 74, and 81, respectively. The **BD SurePath** Practice detected 81, 57, and 83, respectively.

LSIL+

Out of 88 (site 801), 41 (site 802), and 60 (site 803) **BD SurePath** slides identified by the EDP to be LSIL+, the **BD FocalPoint** Assisted Practice detected 65, 37, and 33, respectively. The **BD SurePath** Practice detected 44, 22, and 34, respectively.

HSIL+

Out of 40 (site 801), 22 (site 802), and 19 (site 803) **BD SurePath** slides identified by the EDP to be HSIL+, the **BD FocalPoint** Assisted Practice detected 30, 19, and 12, respectively. The **BD SurePath** Practice detected 10, 2, and 6, respectively.

COMPARISON OF STUDY ARMS FOR ADEQUACY CATEGORIES OF UNSATISFACTORY AND SBLB

For each of the three study sites, the following tables compare the **BD SurePath** Practice with the **BD FocalPoint** Assisted Practice for the specimen adequacy categories of Unsatisfactory and SBLB.

Table 23 Classification of **BD SurePath** Unsatisfactory Slides — Site 801

		BD SurePath Practice		
		Unsat	Not Unsat	
BD FocalPoint Assisted Practice	Unsat	9	6	15
	Not Unsat	1	1,205	1,206
		10	1,211	1,221

Table 24 Classification of **BD SurePath** Unsatisfactory Slides — Site 802

		BD SurePath Practice		
		Unsat	Not Unsat	
BD FocalPoint Assisted Practice	Unsat	3	25	28
	Not Unsat	0	1,179	1,179
		3	1,204	1,207

Table 25 Classification of **BD SurePath** Unsatisfactory Slides — Site 803

		BD SurePath Practice		
		Unsat	Not Unsat	
BD FocalPoint Assisted Practice	Unsat	4	88	92
	Not Unsat	0	1,101	1,101
		4	1,189	1,193

Table 26 Classification of **BD SurePath** SBLB Slides — Site 801

		BD SurePath Practice		
		SBLB	Not SBLB	
BD FocalPoint Assisted Practice	SBLB	61	43	104
	Not SBLB	35	0	35
		96	43	139

Table 27 Classification of **BD SurePath** SBLB Slides — Site 802

		BD SurePath Practice		
		SBLB	Not SBLB	
BD FocalPoint Assisted Practice	SBLB	82	124	206
	Not SBLB	21	8	29
		103	132	235

Table 28 Classification of **BD SurePath** SBLB Slides — Site 803

		BD SurePath Practice		
		SBLB	Not SBLB	
BD FocalPoint Assisted Practice	SBLB	68	17	85
	Not SBLB	48	2	50
		116	19	135

WNL RELIABILITY ANALYSIS

To evaluate the reliability of WNL diagnoses in the clinical study, 299 slides diagnosed as WNL by both study arms (approximately 5%) were randomly chosen and seeded into the slide population sent to the EDP for diagnosis. Table 29 shows the results of their determinations.

Table 29 Reliability of WNL Diagnoses

	Truth			
Unsat	**WNL**	**ASCUS**	**HSIL**	**Total**
3	287	8	1	299

The reliability of WNL diagnoses may be estimated as follows:

$$100 \times \frac{287}{299} = 95.98\% = 96.0\%$$

These data demonstrate that, for all sites combined, the reliability of the **BD FocalPoint** Assisted Practice in detecting WNL slides was 96.0%. The 95% exact confidence interval was 93.2% to 97.9%.

BD FOCALPOINT SLIDE PROFILER SLIDE RANKING ANALYSIS

The **BD FocalPoint** Slide Profiler Ranked Review Report contains a quintile rank for every **Review** slide that corresponds to the slide's likelihood of abnormality. The quintile rank is expressed as a number between 1 and 5, where quintile 1 indicates that the slide is ranked in the highest scoring 20% of the **Review** slides. The lower the quintile rank, the higher the likelihood the slide is abnormal.

Table 30 shows the number of abnormal slides, as determined by the study adjudication process, with their associated ranks. These data demonstrate that, with increasing severity of disease, the proportion of abnormal slides in the lower ranks (higher potential of abnormality) increases: 51.2% (350/683) of abnormal slides were placed in rank quintile 1. Therefore, the **BD FocalPoint** Slide Profiler is effective in ranking **BD SurePath** slides in accordance with the likelihood of abnormality.

Table 30 Abnormal **Review** Slides by Rank

Group Rank	ASCUS	AGUS	LSIL	HSIL	AIS	CA*	Total
1	93	1	137	104	0	15	350
2	56	0	58	27	1	6	148
3	32	2	33	11	0	1	79
4	18	1	25	11	0	0	55
5	23	1	16	10	0	1	51
Total	222	5	269	163	1	23	683

* CA = Cancer

FALSE NEGATIVE PERFORMANCE

The **BD FocalPoint** Slide Profiler classified 1,184 slides as **No Further Review.** Of the 1,184 slides, two were excluded due to slide physical characteristics. Table 31 shows the classification in the **BD FocalPoint** Assisted Practice of the remaining 1,182 slides:

Table 31 BD FocalPoint Assisted Practice Performance in the **No Further Review** Population

Study Diagnosis	No Further Review
Unsat	3
WNL	1,169
ASCUS	5
AGUS	0
LSIL	4
HSIL	1
AIS	0
Cancer	0
Total	**1,182**

The **BD FocalPoint** Slide Profiler classified 10 abnormal slides (5 ASCUS, 4 LSIL, and 1 HSIL) as **No Further Review**. The total number of abnormal **BD SurePath** slides was 693 (683 slides from Table 30 + 10 slides in **No Further Review**). Therefore, the false negative fraction was 10/693, or 1.4%. For Unsatisfactory **BD SurePath** slides, the **BD FocalPoint** Slide Profiler classified 3 as **No Further Review** for a false negative fraction 3/106, or 2.8%.

COMPARISON OF NO FURTHER REVIEW RATES

The **BD FocalPoint** Slide Profiler is intended to be used at a **Review/No Further Review** rate of 75% / 25% with at least a 15% quality control rescreen (QC) of all successfully processed slides. The data in the following tables show the clinical performance of the **BD FocalPoint** Slide Profiler at **Review/No Further Review** rates of up to 50% / 50%. With QC rescreening, these data show that the **BD FocalPoint** Slide Profiler performance is numerically and statistically equivalent to Current Practice. A laboratory that elects not to conduct quality control rescreening with the **BD FocalPoint** Slide Profiler may not achieve the performance shown.

Tables 32–36 compare the **BD FocalPoint** Assisted Practice with Current Practice when using various **No Further Review** rates. This information was obtained from an additional analysis performed on the data from the Prospective, Intended Use Study. In the tables, *nominal 25%* represents the demonstrated performance of the **BD FocalPoint** Slide Profiler in the clinical study when the **No Further Review** rate was set to 25% and the **QC Review** rate was set to 15%. The other rates, 30% to 50%, represent a model of device performance at higher **No Further Review** rates.

Table 32 BD FocalPoint Assisted Practice with QC Compared to Current Practice with QC for LSIL+*

No Further Review Rate	Total Abnormals	BD FocalPoint Assisted Practice Detected Abnormals	Current Practice Detected Abnormals	Additional Abnormals Detected with BD FocalPoint
Nominal 25%	348	321	298	23
30%	348	308	298	10
35%	348	305	298	7
40%	348	303	298	5
45%	348	299	298	1
50%	348	298	298	0

* LSIL+ includes the Bethesda diagnostic categories of LSIL (low-grade squamous intraepithelial lesion), HSIL (high-grade intraepithelial lesion), AIS (adenocarcinoma in-situ), and cancer. The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses (Springer-Verlag New York, Inc. 1994.)

Note: *The figures in tables 32–36 are estimates of performance characteristics and have not been independently confirmed. Results may vary between laboratories.*

Table 32, above, shows the **No Further Review** rates for the diagnostic category of LSIL+ when a quality control review is performed as part of the laboratory's current practice. The number of abnormals detected by the **BD FocalPoint** Assisted Practice at the nominal 25% rate, 321, is derived from Table 10 as is the number of abnormal detected for Current Practice, 298.

Table 33 shows the number of slides picked up, or gained, by each arm of the study. In this table and in Table 23, **BD FocalPoint** Assisted Practice Gain means those slides correctly classified by the **BD FocalPoint** Assisted Practice as abnormal and incorrectly classified by Current Practice as WNL.

Similarly, Current Practice Gain means those slides correctly classified by Current Practice as abnormal and incorrectly classified by the **BD FocalPoint** Assisted Practice as WNL. The *nominal 25%* gains are actual numbers derived from Table 10 (e.g., the gain of 50 is shown in the upper right hand corner of the 2x2 array and 27 in the lower left hand). As previously stated, the other figures for 30% to 50% represent a model of device performance.

Table 33 Gain Comparison Between the **BD FocalPoint** Assisted Practice with QC and Current Practice with QC

	LSIL+	
No Further Review Rate	**BD FocalPoint Assisted Practice Gain**	**Current Practice Gain**
Nominal 25%	50	27
30%	43	33
35%	43	36
40%	43	38
45%	41	40
50%	41	41

The **BD FocalPoint** Assisted Practice at a 25% **No Further Review** rate and a 15% **QC Review** rate can also be compared to Current Practice *without* quality control rescreening of WNL slides. Table 34 shows the results of this comparison for slides identified by the truth determination process to be LSIL+. Table 34 is identical to Table 10, with the following exception: one slide was not detected by Current Practice during primary screening, but was detected during quality control rescreening. Thus, the total number of abnormals detected by Current Practice is reduced from 298 to 297. Correspondingly, the **BD FocalPoint** Assisted Practice is credited with one additional, detected abnormal (increasing from 50 to 51). A statistically significant greater number of LSIL+ slides was detected in the **BD FocalPoint** Assisted Practice with QC as compared to the Current Practice without QC.

Table 34 Classification of LSIL+ Slides Comparing the **BD FocalPoint** Assisted Practice with QC and Current Practice without QC

		Current Practice		
		Abnormal (+)	WNL (-)	
BD FocalPoint Assisted Practice	Abnormal (+)	270	51	321
	WNL (-)	27		27
		297	51	348

Table 35 shows the performance at various **No Further Review** rates for the diagnostic category of LSIL+ when quality control review of WNL slides is not performed as part of the laboratory's Current Practice.

In the same manner as shown in Table 33, Table 36 shows the number of slides picked up, or gained, in each arm of the study for the assumption of Current Practice *without* QC rescreening. Because of the single slide difference discussed above, the **BD FocalPoint** Assisted Practice is credited with an additional gain of one detected abnormal over the entire range of **No Further Review** rates.

Table 35 BD FocalPoint Assisted Practice with QC Compared to Current Practice without QC for LSIL+

No Further Review Rate	**Total Abnormals**	**BD FocalPoint Assisted Practice Detected Abnormals**	**Current Practice Detected Abnormals**	**Additional Abnormals Detected with BD FocalPoint**
Nominal 25%	348	321	297	24
30%	348	308	297	11
35%	348	305	297	8
40%	348	303	297	6
45%	348	299	297	2
50%	348	298	297	1

Table 36 Gain Comparison Between the **BD FocalPoint** Assisted Practice with QC and Current Practice without QC

	LSIL+	
No Further Review Rate	**BD FocalPoint Assisted Practice Gain**	**Current Practice Gain**
Nominal 25%	51	27
30%	44	33
35%	44	36
40%	44	38
45%	42	40
50%	42	41

BD FOCALPOINT GS IMAGING SYSTEM PERFORMANCE

BD Life Sciences conducted nonclinical validation studies to evaluate the performance of the **BD FocalPoint** Slide Profiler when used in combined primary screening and guided screening.

The **BD FocalPoint** GS Imaging System identifies up to 25% of successfully processed slides as requiring **No Further Review** while also providing the electronic capability of locating diagnostically relevant locations on the slides classified as **Review**. During slide processing, the **BD FocalPoint** GS Imaging System detects potentially abnormal cells and stores the corresponding slide locations (fields of view, or FOVs). For each slide classified as **Review**, the **BD FocalPoint** GS Imaging System provides up to 15 FOVs, which a cytotechnologist reviews to determine whether a slide is normal or abnormal. If all of the FOVs are determined to be normal, the slide diagnosis is within normal limits (WNL). If any of the FOVs are determined to be potentially abnormal or inadequate, the cytotechnologist reviews the entire slide.

A cytotechnologist accesses the FOV locations in one of two ways:

- PapMaps – Printouts showing the exact dimensions of the slide coverslip edges and the circled locations of the FOVs selected by the **BD FocalPoint** GS Imaging System. The slide is placed over the PapMap printout, and the FOVs are traced onto the slide coverslip for review.
- Workstation and motorized microscope stage (**BD FocalPoint** GS Review Station) — Microscope stage moves automatically to the x,y coordinates of each FOV. The image of the cellular material within the FOV can be viewed on the workstation to confirm the location.

BD FOCALPOINT GS IMAGING SYSTEM PERFORMANCE ON CONVENTIONAL SLIDES

The **BD FocalPoint** GS Imaging System was evaluated at three cytology laboratories in the United Kingdom. Approximately 6,000 conventionally-prepared Pap smear slides were enrolled in a prospective, two-arm study comparing current cytological practice with a **BD FocalPoint** GS Assisted Practice. The study objectives were as follows:

- The **BD FocalPoint** GS Assisted Practice is equivalent to the Current Practice when detecting all abnormal slides combined (Borderline+). Borderline+ is defined as nuclear changes bordering on dyskaryosis and above, and includes the categories Borderline squamous and glandular; mild, moderate, and severe dyskaryosis; AIS; and cancer.
- The **BD FocalPoint** GS Assisted Practice is equivalent to Current Practice when detecting slides determined to be inadequate for evaluation.

  Note: *Borderline is equivalent to The Bethesda System category of ASCUS. Dyskaryosis is synonymous with dysplasia. Mild and Moderate dyskaryosis are equivalent to The Bethesda System categories of LSIL and HSIL, respectively.*

In the **BD FocalPoint** GS Assisted Practice, slides that classified as **Review** were screened using the PapMap Reports. Laboratory personnel traced the PapMap FOVs onto the corresponding study slides. Cytotechnologists reviewed all FOVs on each **Review** slide to determine if the slide required a full-slide review.

A full-slide review was required if the cytotechnologist noted atypical cells within one or more of the FOVs. The cytotechnologist also reviewed the entire slide if there was inadequate cellular material within the FOVs to determine slide adequacy.

Slides having abnormal diagnoses that did not agree between the two arms were subjected to an External Discrepancy Review for a reference, or final truth, diagnosis. Slides with an adequacy interpretation that did not agree between the two study arms were subjected to an Internal Adequacy Review for a final adequacy determination.

Slide Accountability

In this study, 5,531 slides completed both study arms. The slides were submitted to the truth determination process so each slide had a final cytologic diagnosis (study truth). The distribution of these slides by diagnosis and the reasons for exclusion from the study are shown in tables 37 and 38, respectively.

Table 37 Distribution of Study Slides

Diagnosis	Total
Inadequate	6.7% (370/5531)
Negative	85.9% (4753/5531)
Abnormal	7.4% (408/5531)

Table 38 Total Slides Analyzed

Slides enrolled in study	**6070**
Excluded (unable to read barcode)	40
Excluded (incomplete data)	12
Excluded (Process Review)	482
Excluded (Lab related problems)	5
Total slides excluded	**539**
Total slides Analyzed	**5,531**

DIAGNOSTIC PERFORMANCE RESULTS

This section provides the results for Borderline+, Mild Dyskaryosis+, Moderate Dyskaryosis+, and Inadequate. The data analysis was performed using a conditional binomial test to determine the statistical significance of the differences between the two study arms in detecting abnormal and inadequate slides.[1] The conditional binomial test was the McNemar's exact test to test the quality of discrepant proportions in the matched pairs study design.[2]

Borderline+

Table 39 shows the results for slides determined by the truth determination process to be Borderline+. These data demonstrate that the **BD FocalPoint** GS Imaging System detected a statistically equivalent number Borderline+ slides when compared to Current Practice (p-value = 0.0047).

Table 39 Classification of Borderline+ Slides

		Current Practice			
		Abnormal	Inadequate	Negative	Total
BD FocalPoint GS Assisted Practice	Abnormal	248	6	66	320
	Inadequate	10	–	0	10
	Negative	78	0	–	78
		336	6	66	408

Mild Dyskaryosis+

Table 40 shows the results for slides determined by the truth determination process to be Mild Dyskaryosis+. These data demonstrate that the **BD FocalPoint** GS Imaging System detected a statistically equivalent number of Mild Dyskaryosis+ slides when compared to Current Practice (p-value = 0.0014).

Table 40 Classification of Mild Dyskaryosis+ Slides

		Current Practice			
		Abnormal	Inadequate	Negative	Total
BD FocalPoint GS Assisted Practice	Abnormal	153	2	45	200
	Inadequate	2	–	0	2
	Negative	43	0	–	43
		198	2	45	245

Moderate Dyskaryosis+

Table 41 shows the results for slides determined by the truth determination process to be Moderate Dyskaryosis+. These data demonstrate that the **BD FocalPoint** GS Imaging System detected a statistically equivalent number of Moderate Dyskaryosis+ slides when compared to Current Practice (p-value = 0.0124).

Table 41 Classification of Moderate Dyskaryosis+ Slides

		Current Practice			
		Abnormal	Inadequate	Negative	Total
BD FocalPoint GS Assisted Practice	Abnormal	71	1	10	82
	Inadequate	2	–	0	2
	Negative	5	0	–	5
		78	1	10	89

Specimen Adequacy

The secondary objective evaluated whether the **BD FocalPoint** GS Assisted Practice was equivalent to Current Practice when detecting inadequate slides. The slides were identified as inadequate according to a combination of three reasons noted by the cytotechnologists:

- Scant cellularity
- Inflammation or obscuration
- Insufficient evidence of cells from the transformation zone

1. Breslow, N.E., and N.E. Day. *The Analysis of Case-Control Studies Statistical Methods in Cancer Research. Volume 1,* International Agency for Research on Cancer. Lyon: (1980): 167.
2. Fleiss, Joseph L. *Statistical Methods for Rates and Proportions*. 2nd Ed. New York: John Wiley and Sons, 1981.

The following tables show the performance of the study arms when each adequacy reason is evaluated separately. Overall, 370 slides were determined by truth to be inadequate. Of these, 254 were inadequate in part, or entirely, due to scant cellularity; 297 were inadequate in part, or entirely, due to inflammation/obscuration, and 70 were inadequate in part, or entirely, due to lack of transformation zone cells.

Table 42 Inadequate for Scant Cellularity

		Current Practice		
		Scant Cellularity	Adequate Cellularity	Total
BD FocalPoint GS Assisted Practice	Scant Cellularity	71	83	154
	Adequate Cellularity	65	35	100
		136	118	254

Table 43 Inadequate for Inflammation/Obscuration

		Current Practice		
		Infl/Obsc	No Infl/ Obsc	Total
BD FocalPoint GS Assisted Practice	Infl/Obsc	42	130	172
	No Infl/Obsc	56	69	125
		98	199	297

Table 44 Inadequate for Lack of Transformation Zone (TZ) Cells

		Current Practice		
		Inadequate TZ	Adequate TZ	Total
BD FocalPoint GS Assisted Practice	Inadequate TZ	70	0	70
	Adequate TZ	0	0	0
		70	0	70

Note: A total of 21 slides that were inadequate for lack of transformation zone cells were classified as **No Further Review** by the **BD FocalPoint** Slide Profiler. Of these slides, 8 were identified as not having sufficient endocervical component by the device.

BD FOCALPOINT GS IMAGING SYSTEM PERFORMANCE ON BD SUREPATH™ SLIDES

An internal, nonclinical validation study was conducted to estimate the expected sensitivity and specificity of the **BD FocalPoint** GS Imaging System on **BD SurePath** slides. A total of 1,665 study slides were processed on the **BD FocalPoint** GS Imaging System to identify fields of view (FOVs) for cytotechnologist review. The FOVs were assessed for their diagnostic and adequacy content using the **BD FocalPoint** GS Review Station.

In the **BD FocalPoint** GS Imaging System practice, the **BD SurePath** slides were processed on the **BD FocalPoint** Slide Profiler and up to 15 FOVs were archived for each slide classified as **Review**. The FOV coordinates and images for each slide were transferred from the **BD FocalPoint** Slide Profiler to the **BD FocalPoint** GS Review Station. Cytotechnologists used the **BD FocalPoint** GS Review Station motorized stage to move to, review, and electronically label each identified FOV. A full slide review was required if the cytotechnologist labeled one or more of the FOVs abnormal, inadequate, or reactive. Otherwise, the slide was considered WNL.

The final diagnosis, or truth, for each slide was determined from prior characterizations of the slides by separate panels of BD Life Sciences cytotechnologists. A concordant diagnosis between the panels was considered the truth diagnosis. If the diagnoses were discordant, then an independent pathologist reviewed the slide to determine truth.

Slide Distribution

Table 45 shows the distribution of the 1,665 study slides by **BD FocalPoint** GS Imaging System classification and final slide diagnosis.

Table 45 Slide Distribution

	WNL	ASCUS	AGUS	LSIL	HSIL	Cancer	Total
Process Review	84	37	2	11	6	1	141
Review	813	334	15	76	74	1	1,313
No Further Review	183	18	3	6	1	0	211
Total	1,080	389	20	93	81	2	1,665

Sensitivity Results

Table 46 shows the sensitivity, and the corresponding 95% confidence intervals, of the **BD FocalPoint** GS Imaging System to the diagnostic categories of ASCUS+ (includes ASCUS, AGUS, LSIL, HSIL, and cancer), LSIL+ (includes LSIL, HSIL, and cancer), and HSIL+ (includes HSIL, and cancer).

Table 46 BD FocalPoint GS Imaging System Sensitivity

Diagnosis	Sensitivity
ASCUS+	72.2 381/528 (68.2, 75.9)
LSIL+	94.3 149/158 (89.4, 97.1)
HSIL+	98.7 75/76 (93.0, 99.9)

Adequacy Results

The slide adequacy analysis evaluated **BD FocalPoint** GS Imaging System performance on Satisfactory with endocervical component slides. Other specimen adequacy characteristics such as inflammation obscuration were not considered.

The study population included 996 WNL slides of which 16 were atrophic, 2 were without endocervical component and 978 were Satisfactory with endocervical component. Of these, the **BD FocalPoint** GS Imaging System detected 751 for a sensitivity of 76.8% (751/978). The 95% confidence interval was 74.0–79.4.

Storage and Operation

Do not expose the system to direct sunlight or temperature extremes (i.e., airflow from heating or cooling systems). The operating temperature range is 18–30 °C, 64–86 °F.

Technical Service and Product Information

For technical service and assistance related to use of the **BD FocalPoint** Slide Profiler, contact BD Life Sciences.

Technical Information: In the United States contact BD Technical Service and Support at 1.800.638.8663 or www.bd.com.

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AAAA-MM-JJ / AAAA-MM (MM = fin du mois)
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Positive control / Положителен контрол / Pozitivní kontrola / Positiv kontrol / Positive Kontrolle / Θετικός μάρτυρας / Control positivo / Positiivne kontroll / Contrôle positif / Pozitivna kontrola / Pozitív kontroll / Controllo positivo / Оң бақылау / 양성 컨트롤 / Teigiama kontrolė / Pozitīvā kontrole / Positieve controle / Kontrola dodatnia / Controlo positivo / Control pozitiv / Положительный контроль / Pozitif kontrol / Позитивний контроль / 阳性对照试剂

CONTROL –

Negative control / Отрицателен контрол / Negativní kontrola / Negativ kontrol / Negative Kontrolle / Αρνητικός μάρτυρας / Control negativo / Negatiivne kontroll / Contrôle négatif / Negativna kontrola / Negatív kontroll / Controllo negativo / Неративтік бақылау / 음성 컨트롤 / Neigiama kontrolė / Negatīvā kontrole / Negatieve controle / Kontrola ujemna / Controlo negativo / Control negativ / Отрицательный контроль / Negatif kontrol / Неративний контроль / 阴性对照试剂

STERILE EO

Method of sterilization: ethylene oxide / Метод на стерилизация: етиленов оксид / Způsob sterilizace: etylenoxid / Steriliseringsmetode: ethylenoxid / Sterilisationsmethode: Ethylenoxid / Μέθοδος αποστείρωσης: αιθυλενοξείδιο / Método de esterilización: óxido de etileno / Steriliseerimismeetod: etüleenoksiid / Méthode de stérilisation : oxyde d'éthylène / Metoda sterilizacije: etilen oksid / Sterilizálás módszere: etilén-oxid / Metodo di sterilizzazione: ossido di etilene / Стерилизация әдісі – этилен тотығы / 소독 방법: 에틸렌옥사이드 / Sterilizavimo būdas: etileno oksidas / Sterilizēšanas metode: etilēnoksīds / Gesteriliseerd met behulp van ethyleenoxide / Steriliseringsmetode: etylenoksid / Metoda sterylizacji: tlenek etylu / Método de esterilização: óxido de etileno / Metodă de sterilizare: oxid de etilenă / Метод стерилизации: этиленоксид / Metóda sterilizácie: etylénoxid / Metoda sterilizacije: etilen oksid / Steriliseringsmetod: etenoxid / Sterilizasyon yöntemi: etilen oksit / Метод стерилізації: етиленоксидом / 灭菌方法：环氧乙烷

STERILE R

Method of sterilization: irradiation / Метод на стерилизация: ирадиация / Způsob sterilizace: záření / Steriliseringsmetode: bestråling / Sterilisationsmethode: Bestrahlung / Μέθοδος αποστείρωσης: ακτινοβολία / Método de esterilización: irradiación / Steriliseerimismeetod: kiirgus / Méthode de stérilisation : irradiation / Metoda sterilizacije: zračenje / Sterilizálás módszere: besugárzás / Metodo di sterilizzazione: irradiazione / Стерилизация әдісі – сәуле түсіру / 소독 방법: 방사 / Sterilizavimo būdas: radiacija / Sterilizēšanas metode: apstarošana / Gesteriliseerd met behulp van bestraling / Steriliseringsmetode: bestråling / Metoda sterylizacji: napromienianie / Método de esterilização: irradiação / Metodă de sterilizare: iradiere / Метод стерилизации: облучение / Metóda sterilizácie: ožiarenie / Metoda sterilizacije: ozračavanje / Steriliseringsmetod: strålning / Sterilizasyon yöntemi: irradyasyon / Метод стерилізації: опроміненням / 灭菌方法：辐射

Biological Risks / Биологични рискове / Biologická rizika / Biologisk fare / Biogefährdung / Βιολογικοί κίνδυνοι / Riesgos biológicos / Bioloogilised riskid / Risques biologiques / Bioloških rizik / Biológiailag veszélyes / Rischio biologico / Биологиялық тәуекелдер / 생물학적 위험 / Biologinis pavojus / Bioloģiskie riski / Biologisch risico / Biologisk risiko / Zagrożenia biologiczne / Perigo biológico / Riscuri biologice / Биологическая опасность / Biologické riziko / Biološki rizici / Biologisk risk / Biyolojik Riskler / Біологічна небезпека / 生物学风险

Caution, consult accompanying documents / Внимание, направете справка в придружаващите документи / Pozor! Prostudujte si přiloženou dokumentaci! / Forsigtig, se ledsagende dokumenter / Achtung, Begleitdokumente beachten / Προσοχή, συμβουλευτείτε τα συνοδευτικά έγγραφα / Precaución, consultar la documentación adjunta / Ettevaatust! Lugeda kaasnevat dokumentatsiooni / Attention, consulter les documents joints / Upozorenje, koristi prateču dokumentaciju / Figyelem! Olvassa el a mellékelt tájékoztatót / Attenzione: consultare la documentazione allegata / Абайлаңыз, тиісті құжаттармен танысыңыз / 주의, 동봉된 설명서 참조 / Dėmesio, žiūrėkite pridedamus dokumentus / Piesardzība, skatīt pavaddokumentus / Voorzichtig, raadpleeg bijgevoegde documenten / Forsiktig, se vedlagt dokumentasjon / Należy zapoznać się z dołączonymi dokumentami / Cuidado, consulte a documentação fornecida / Atenţie, consultaţi documentele însoţitoare / Внимание: см. прилагаемую документацию / Výstraha, pozri sprievodné dokumenty / Pažnja! Pogledajte priloženа dokumenta / Obs! Se medföljande dokumentation / Dikkat, birlikte verilen belgelere başvurun / Увага: див. супутню документацію / 小心，请参阅附带文档。

Upper limit of temperature / Горен лимит на температурата / Horní hranice teploty / Øvre temperaturgrænse / Temperaturobergrenze / Ανώτερο όριο θερμοκρασίας / Límite superior de temperatura / Ülemine temperatuuripiir / Limite supérieure de température / Gornja dozvoljena temperatura / Felső hőmérsékleti határ / Limite superiore di temperatura / Температураның рұқсат етілген жоғарғы шеri / 상한 온도 / Aukščiausia laikymo temperatūra / Augšējā temperatūras robeža / Hoogste temperatuurlimiet / Øvre temperaturgrense / Górna granica temperatury / Limite máximo de temperatura / Limită maximă de temperatură / Верхний предел температуры / Horná hranica teploty / Gornja granica temperature / Övre temperaturgräns / Sıcaklık üst sınırı / Максимальна температура / 温度上限

Keep dry / Пазете сухо / Skladujte v suchém prostředí / Opbevares tørt / Trocklagern / Φυλάξτε το στεγνό / Mantener seco / Hoida kuivas / Conserver au sec / Držati na suhom / Száraz helyen tartandó / Tenere all'asciutto / Құрғақ күйінде ұста / 건조 상태 유지 / Laikykite sausai / Uzglabāt sausu / Droog houden / Holdes tørt / Przechowywać w stanie suchym / Manter seco / A se feri de umezeală / Не допускать попадания влаги / Uchovávajte v suchu / Držite na suvom mestu / Förvaras torrt / Kuru bir şekilde muhafaza edin / Берегти від вологи / 请保持干燥

Collection time / Време на събиране / Čas odběru / Opsamlingstidspunkt / Entnahmeuhrzeit / Ώρα συλλογής / Hora de recogida / Kogumisaeg / Heure de prélèvement / Sati prikupljanja / Mintavétel időpontja / Ora di raccolta / Жинау уақыты / 수집 시간 / Paėmimo laikas / Savākšanas laiks / Verzameltijd / Tid prøvetaking / Godzina pobrania / Hora de colheita / Ora colectării / Время сбора / Doba odberu / Vreme prikupljanja / Uppsamlingstid / Toplama zamanı / Час забору / 采集时间

Peel / Обелете / Otevřete zde / Åbn / Abziehen / Αποκολλήστε / Desprender / Koorida / Décoller / Otvoriti skini / Húzza le / Staccare / Ұстіңгі қабатын алып таста / 벗기기 / Plėšti čia / Atlīmēt / Schillen / Trekk av / Oderwać / Destacar / Se dezlipeşte / Отклеить / Odtrhnite / Oljuštiti / Dra isär / Ayırma / Відклеїти / 撕下

Perforation / Перфорация / Perforace / Perforering / Διάτρηση / Perforación / Perforatsioon / Perforacija / Perforálás / Perforazione / Тесік тесу / 절취선 / Perforacija / Perforācija / Perforatie / Perforacja / Perfuração / Perforare / Перфорация / Perforácia / Perforasyon / Перфорація / 穿孔

Do not use if package damaged / Не използвайте, ако опаковката е повредена / Nepoužívejte, je-li obal poškozený / Må ikke anvendes hvis emballagen er beskadiget / Inhal beschädigter Packungnicht verwenden / Μη χρησιμοποιείτε εάν η συσκευασία έχει υποστεί ζημιά. / No usar si el paquete está dañado / Mitte kasutada, kui pakend on kahjustatud / Ne pas l'utiliser si l'emballage est endommagé / Ne koristiti ako je oštećeno pakiranje / Ne használja, ha a csomagolás sérült / Non usare se la confezione è danneggiata / Егер пакет бұзылған болса, пайдаланба / 패키지가 손상된 경우 사용 금지 / Jei pakuotė pažeista, nenaudoti / Nelietot, ja iepakojums bojāts / Niet gebruiken indien de verpakking beschadigd is / Må ikke brukes hvis pakke er skadet / Nie używać, jeśli opakowanie jest uszkodzone / Não usar se a embalagem estiver danificada / A nu se folosi dacă pachetul este deteriorat / Не использовать при повреждении упаковки / Nepoužívajte, ak je obal poškodený / Ne koristite ako je pakovanje oštećeno / Använd ej om förpackningen är skadad / Ambalaj hasar görmüşse kullanmayın / Не використовувати за пошкодженої упаковки / 如果包装破损，请勿使用

Keep away from heat / Пазете от топлина / Nevystavujte přílišnému teplu / Må ikke udsættes for varme / Vor Wärme schützen / Κρατήστε το μακριά από τη θερμότητα / Mantener alejado de fuentes de calor / Hoida eemal valgusest / Protéger de la chaleur / Držati dalje od izvora topline / Óvja a melegtől / Tenere lontano dal calore / Салқын жерде сақта / 열을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no karstuma / Beschermen tegen warmte / Må ikke utsettes for varme / Przechowywać z dala od źródeł ciepła / Manter ao abrigo do calor / A se feri de căldură / Не нагревать / Uchovávajte mimo zdroja tepla / Držite dalje od toplote / Får ej utsättas för värme / Isıdan uzak tutun / Берегти від дії тепла / 请远离热源

Cut / Срежете / Odstřihněte / Klip / Schneiden / Κόψτε / Cortar / Lõigata / Découper / Reži / Vágja ki / Tagliare / Кесіңіз / 잘라내기 / Kirpti / Nogriezt / Knippen / Kutt / Odciąć / Cortar / Decupaţi / Отрезать / Odstrihnite / Iseći / Klipp / Kesme / Розрізати / 剪下

Collection date / Дата на събиране / Datum odběru / Opsamlingsdato / Entnahmedatum / Ημερομηνία συλλογής / Fecha de recogida / Kogumiskuupäev / Date de prélèvement / Dani prikupljanja / Mintavétel dátuma / Data di raccolta / Жинаған тізбекүні / 수집 날짜 / Paėmimo data / Savākšanas datums / Verzameldatum / Dato prøvetaking / Data pobrania / Data de colheita / Data colectării / Дата сбора / Dátum odberu / Datum prikupljanja / Uppsamlingsdatum / Toplama tarihi / Дата забору / 采集日期

µL/test / µL/тест / µL/Test / µL/εξέτασηη / µL/prueba / µL/teszt / µL/테스트 / мкл/тест / µL/tyrimas / µL/pārbaude / µL/teste / мкл/аналіз / µL/检测

Keep away from light / Пазете от светлина / Nevystavujte světlu / Må ikke udsættes for lys / Vor Licht schützen / Κρατήστε το μακριά από το φως / Mantener alejado de la luz / Hoida eemal valgusest / Conserver à l'abri de la lumière / Držati dalje od svjetla / Fény nem érheti / Tenere al riparo dalla luce / Қараңғыланған жерде ұста / 빛을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no gaismas / Niet blootstellen aan zonlicht / Må ikke utsettes for lys / Przechowywać z dala od źródeł światła / Manter ao abrigo da luz / Feriți de lumină / Хранить в темноте / Uchovávajte mimo dosahu svetla / Držite dalje od svetlosti / Får ej utsättas för ljus / Işıktan uzak tutun / Берегти від дії світла / 请远离光线

Hydrogen gas generated / Образуван е водород газ / Možnost úniku plynného vodíku / Frembringer hydrogengas / Wasserstoffgas erzeugt / Δημιουργία αερίου υδρογόνου / Producción de gas de hidrógeno / Vesinikgaasi tekitatud / Produit de l'hydrogène gazeux / Sadrži hydrogen vodik / Hidrogén gázt fejleszt / Produzione di gas idrogeno / Газтектес сутеги пайда болды / 수소 가스 생성됨 / Išskiria vandenilio dujas / Rodas ūdeņradis / Waterstofgas gegenereerd / Hydrogengass generert / Powoduje powstawanie wodoru / Produção de gás de hidrogénio / Generare gaz de hidrogen / Выделение водорода / Vyrobené použitím vodíka / Oslobađa se vodonik / Genererad vätgas / Açığa çıkan hidrojen gazı / Реакція з виділенням водню / 会产生氢气

Patient ID number / ИД номер на пациента / ID pacienta / Patientens ID-nummer / Patienten-ID / Αριθμός αναγνώρισης ασθενούς / Número de ID del paciente / Patsiendi ID / No d'identification du patient / Identifikacijski broj pacijenta / Beteg azonosító száma / Numero ID paziente / Пациенттің идентификациялық нөмірі / 환자 ID 번호 / Paciento identifikavimo numeris / Pacienta ID numurs / Identificatienummer van de patiënt / Pasientens ID-nummer / Numer ID pacjenta / Número da ID do doente / Număr ID pacient / Идентификационный номер пациента / Identifikačné číslo pacienta / ID broj pacijenta / Patientnummer / Hasta kimlik numarası / Ідентифікатор пацієнта / 患者标识号

Fragile, Handle with Care / Чупливо, Работете с необходимото внимание. / Křehké. Při manipulaci postupujte opatrně. / Forsigtig, kan gå i stykker. / Zerbrechlich, vorsichtig handhaben. / Εύθραυστο. Χειριστείτε το με προσοχή. / Frágil. Manipular con cuidado. / Õrn, käsitsege ettevaatlikult. / Fragile. Manipuler avec précaution. / Lomljivo, rukujte pažljivo. / Törékeny! Óvatosan kezelendő. / Fragile, maneggiare con cura. / Сынғыш, абайлап пайдаланыңыз. / 조심 깨지기 쉬운 처리 / Trapu, elkitės atsargiai. / Trausls; rīkoties uzmanīgi / Breekbaar, voorzichtig behandelen. / Ømtålig, håndter forsiktig. / Krucha zawartość, przenosić ostrożnie. / Frágil, Manuseie com Cuidado. / Fragil, manipulați cu atenție. / Хрупкое! Обращаться с осторожностью. / Krehké, vyžaduje sa opatrná manipulácia. / Lomljivo - rukujte pažljivo. / Bräckligt. Hantera försiktigt. / Kolay Kırılır, Dikkatli Taşıyın. / Тендітна, звертатися з обережністю / 易碎，小心轻放

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