510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K100818

B. Purpose for Submission:

To obtain substantial equivalence for the Illumigene *C. difficile* assay

C. Measurand:

C. difficile toxin A gene

D. Type of Test:

Loop mediated isothermal amplification

E. Applicant:

Meridian Bioscience Inc.

F. Proprietary and Established Names:

Illumigene *C. difficile* Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2660 – Microorganism differentiation and identification device

2. Classification:

   Class 1

3. Product code:

   OMN – *C. difficile* nucleic acids

4. Panel:

   83 - Microbiology

H. Intended Use:

1. Intended use:

   The illumigene *C. difficile* DNA amplification assay, performed on the *illumipro-10,* is a qualitative *in vitro* diagnostic test for the direct detection of toxigenic *C. difficile* in human stool specimens from patients suspected of having *Clostridium difficile*-associated disease (CDAD).

   The illumigene *C. difficile assay* utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect the pathogenicity locus (PaLoc) of toxigenic *Clostridium difficile.* The *Clostridium difficile* PaLoc is a gene segment present in all known toxigenic *C. difficile* strains. The *C. difficile* PaLoc codes for both the Toxin A gene (tcdA) and the Toxin B gene (tcdB), has conserved border regions, and is found at the same site on the *C. difficile* genome for all toxigenic strains. The illumigene *C. difficile* assay detects the PaLoc by targeting a partial DNA fragment on the Toxin A gene. The tcdA target region was selected as an intact region remaining in all known A+/B+ and A-/B+ toxinotypes.

   illumigene *C. difficile* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

2. Indication(s) for use:

   The illumigene *C. difficile* DNA amplification assay, performed on the *illumipro-10,* is a qualitative *in vitro* diagnostic test for the direct detection of toxigenic *C. difficile* in human stool specimens from patients suspected of having *Clostridium difficile*-associated disease (CDAD).

   The illumigene *C. difficile* assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the pathogenicity locus (PaLoc) of toxigenic *Clostridium difficile.* The *Clostridium difficile* PaLoc is a gene segment present in all known toxigenic *C. difficile* strains. The *C. difficile* PaLoc codes for both the Toxin A gene (tcdA) and the Toxin B gene (tcdB), has conserved border regions, and is found at the same site on the *C. difficile* genome for all toxigenic strains. The illumigene *C. difficile* assay detects the PaLoc by targeting a partial DNA fragment on the Toxin A gene. The tcdA target region was selected as an intact region remaining in all known A+/B+ and A-/B+ toxinotypes.

   illumigene *C. difficile* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

3. Special conditions for use statement:

   For professional use

4. Special instrument requirements:

   Illumipro -10 Automated Isothermal Amplification and Detection System

I. Device Description:

The ***illumi****gene* Molecular Diagnostic Test System is comprised of the ***illumi****gene C. difficile* DNA Amplification Test Kit, the ***illumi****gene C. difficile* External Control Kit and the ***illumi****pro-10* Automated Isothermal Amplification and Detection System. Additional specialized laboratory equipment is not required for execution of ***illumi****gene* Molecular Diagnostic Test System assays.

The ***illumi****gene C. difficile* DNA amplification assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the presence of toxigenic *C. difficile* in patients suspected of having *C. difficile* associated disease (CDAD). Each ***illumi****gene C. difficile* assay is completed using materials provided: ***illumi****gene* Sample Preparation Apparatus, ***illumi****gene* Reaction Buffer, ***illumi****gene C. difficile* Test Device, Sample Collection Brush, and ***illumi*** *gene* Extraction Tube. Samples are prepared using the Sample Collection Brush and the ***illumi****gene* Sample Collection Apparatus, target DNA is heat extracted in the Extraction Tube and DNA amplification occurs in the ***illumi****gene C. difficile* Test Device.

The ***illumi****pro-10* heats each ***illumi*** *gene C. difficile* Test Device containing prepared samples, facilitating amplification of target DNA. When toxigenic *C. difficile* is present in the patient sample, a cytotoxin specific sequence is amplified and magnesium pyrophosphate is formed. As the LAMP reaction progresses, magnesium pyrophosphate forms a precipitate in the reaction mixture. The optics system of the ***illumi****pro-10* detects the change in light transmission through the reaction mixture created by the precipitating Magnesium pyrophosphate. Sample results are reported as Positive or Negative based on the detected change in transmission.

The ***illumi****gene C. difficile* External Control Kit consists of a Positive Control Reagent and a Negative Control Reagent. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. The ***illumi****gene C. difficile* External Control Kit is required for routine Quality Control.

Final Component Summary

illumi*gene C. difficile DNA* Amplification Assay

·***illumi****gene* ***C. difficile*** **Sample Preparation Apparatus:** Sampling unit consisting of sample preparation chamber, dropper tip, cap and Sample Dilution Buffer (Phosphate Buffered Saline and formalin treated *Staphylococcus aureus* , with sodium azide (0.09%) as a preservative)
·***illumi****gene* **Reaction Buffer:** Tris-buffered solution containing sodium azide (0.09%)as a preservative
·***illumi****gene* ***C. difficile*** **Test Device:** Two separate chambers containing dry reagent lyospheres comprised of DNA polymerase, Deoxyribonucleoside Triphsophate (dNTPs), and either *C. difficile* specific primers (TEST Chamber) or *S. aureus* primers (CONTROL Chamber). The Control lyosphere contains quinoline yellow dye to differentiate it from the Test lyosphere
·**Sample Collection Brushes:** Tube cap fitted with stainless steel rod and nylon bristles
·***illumi****gene* **Extraction Tubes:** 1.5 mL polypropylene microcentrifuge tubes with caps; RNase, DNase and pyrogen-free
illumi*gene C. difficile* External Control Kit
·***illumi****gene* **Positive Control:** Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus* and *C. difficile inserts)* with azide (0.09%) as a preservative
·***illumi****gene* **Negative Control:** Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus insert)* with azide (0.09%) as a preservative

J. Substantial Equivalence Information:

1. Predicate device name:
   Cepheid Xpert C.difficile

2. Predicate 510(k) number:
   K091109

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Sample matrix	Uniformed unpreserved stool samples	Same
Assay type	DNA amplification	Same

Differences		
Item	Device	Predicate
Intended Use	Assay targets a conserved DNA fragment on the toxin A (tcdA) gene in the pathogenicity locus of toxigenic *C. difficile.*	Assay targets the toxin B (tcdB) gene
Instrument	Assay uses the Illumipro-10 instrument	Assay uses the Cepheid GeneXpert Dx System

Differences		
Item	Device	Predicate
Detection method	Assay uses loop mediated isothermal amplification (LAMP) technology and detects changes in turbidity by visible light transmission	Assay uses automated real time polymerase chain reaction (PCR) and detects fluorescence
Transport media	Sample in Cary Blair media is acceptable	Not for use with Cary Blair media
Extraction method	Manual	Self contained, automated

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

User Protocol for Evaluation of Qualitative Test Performance (EP 12-A2)
User Verification of Performance for Precision and Trueness (IVD) (EP 15-A2)
Guidance for Industry and FDA Staff: Class II Special Controls Guidance Document: Nucleic Acid Amplification Assay for the Detection of Enterovirus RNA
Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff
Draft Guidance for Industry and FDA Staff: Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Influenza Viruses
General Principles of Software Validation; Final Guidance for Industry and FDA Staff

L. Test Principle:

The ***illumi****gene C. difficile* Assay is based on loop-mediated isothermal amplification technology (LAMP). Loop-mediated amplification is accomplished by the use of specially designed primers that provide specific and continuous isothermal DNA amplification. Magnesium-pyrophosphate is produced as a by-product of LAMP amplification. The magnesium-pyrophosphate forms a white precipitate in the reaction solution, giving the reaction solution a turbid appearance. The presence of turbidity signifies a positive reaction while the absence of turbidity represents a negative reaction.

The Toxigenic *C. difficile* Pathogen Locus (PaLoc) and *illumigene C. difficile* Primer Regions:

The ***illumi****gene C. difficile* assay contains primers that specifically amplify an ~204 base pair (bp) sequence within the 5' region of the toxin A (*tcd*A) gene that is part of the cytotoxin pathogen locus found in toxigenic *C. difficile*. This region is found in all cytotoxin positive (A+/B+ and A-/B+) strains characterized and is not present in cytotoxin negative strains (A-/B-).

The ***illumi****gene C. difficile* assay detects the presence of toxigenic *C. difficile* in stool samples from patients suspected of having *Clostridium difficile* associated disease in the following manner:

Patient stool sample is collected using the sample brush portion of the ***illumi****gene* Sample Collection Apparatus. The sample is added to the Sample Collection Apparatus containing Sample Dilution Buffer and formalin treated *Staphylococcus aureus*. *S. aureus* serves as an internal control for inhibition and system suitability.

The diluted sample is mixed, filtered through the Sample Collection Apparatus and dispensed drop-wise into an ***illumi*** *gene* Extraction Tube. The Extraction Tube is heated to facilitate DNA extraction of the sample and the internal control material.

Extracted DNA is added to an ***illumi****gene* Reaction Buffer tube, mixed and added to the ***illumi****gene C. difficile* Test Device. The ***illumi*** *gene* Test Device consists of two chambers, one for the sample (TEST) and one for the internal assay control (CONTROL). The TEST chamber contains a lyosphere comprised of DisplaceAce™ DNA polymerase, dNTPs, Bovine Serum Albumin, and ***illumi****gene C. difficile* primers. The CONTROL chamber contains a lyosphere comprised of DisplaceAce™ DNA polymerase, dNTPs, Bovine Serum Albumin, yellow dye and ***illumi****gene Staphylococcus aureus* internal control primers.

The Test Device is placed in the ***illumi****pro-10*™ for amplification and detection. Amplification occurs when the ***illumi****gene C. difficile* Test Device is incubated at 63 C. When toxigenic *C. difficile* is present in the patient sample, the cytotoxin specific sequence is amplified. Magnesium pyrophosphate, a by-product of DNA amplification, will reach saturation and precipitate producing a turbid solution in the TEST chamber of the Test Device. When sample preparation and the assay procedure have has been performed successfully and inhibition has not occurred, DNA from the internal control will amplify. Magnesium pyrophosphate will precipitate and form a turbid solution in the CONTROL chamber of the test device. Assay reactions take place in approximately 40 minutes.

Light transmission (650 ± 20 nm) through the TEST and CONTROL solutions is measured by the ***illumi****pro-10* at the on-set of the assay run and at completion. The ***illumi****pro-10* calculates the ratio between the initial absorbance reading and the final absorbance reading and compares the ratio to an established cut-off value. Valid test results will be reported for a change in absorbance above 90% in the CONTROL chamber. Positive test results will be reported for a change in absorbance above 90% in the TEST chamber and the CONTROL

chamber.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility studies were performed by three clinical sites using coded panels. The panels consisted of moderately positive (n=2), low positive (n=3), high negative (n=3) and negative (n=2) samples. The moderately positive and low positive samples were contrived from negative specimens spiked with toxinogenic *C. difficile* VPI 10463 to just above the LoD for the strain (weak positive) or below the limit of blank (high negative sample), as determined by replicate testing during manufacture of the samples. Negative samples were natural samples. Three lots of ***illumi****gene C. difficile* and nine ***illumi*** *pro-10* instruments were used in reproducibility studies. Positive and Negative Controls were tested with each panel. Each clinical site tested two panels each day for five days. At least two operators each day at each facility performed the testing to demonstrate reproducibility. Reproducibility of the assay is 100% for moderate positive, low positive and negative samples. Reproducibility is 91% for high negative samples.

Positive samples were contrived from negative specimens. The moderately positive and low positive samples were contrived from negative specimens spiked with toxinogenic C. difficile VPI 10463 to just above the LoD for the strain (weak positive) or below the limit of blank (high negative sample), as determined by replicate testing during manufacture of the samples. Negative samples were natural samples. **Final concentrations of C. difficile in reproducibility panel samples were as follows:** Moderate Positive: 200 CFU/test (Positive) Low Positive: 64 CFU/test (Positive) High Negative: 0.5 CFU/test (Negative)

The sources of variability examined in the study included operators (minimum 2 at each site), laboratories (3 sites), runs (Panels tested twice per day), test date (panels tested for five days), and ***illumi*** pro-10 instruments (9 instruments).

Precision (within-run and within-laboratory) was calculated following CLSI EP 15-A2. 95% confidence intervals were calculated using the Wilson method.

Reproducibility of the assay is 100% for moderate positive, low positive and negative samples. Reproducibility is 91% for high negative samples. Sample type and replicate data is as follows: Percent Agreement Positive Samples: 60/60 Replicates or 100% Percent Agreement Low Positive: 90/90 Replicates or 100% Percent Agreement High Negative: 82/90 Replicates or 91% Percent Agreement Negative: 59/59 Replicates or 100% *(One negative sample produced an invalid result during testing. This value was not included in the calculations.)*

b. Linearity/assay reportable range:

N/A

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

Internal control is provided in the Sample Preparation Apparatus and the Assay Device. The Sample Preparation Apparatus contains Sample Dilution Buffer with formalin treated *Staphylococcus aureus*. The CONTROL Chamber of the Assay Device contains a lyosphere with *S. aureus* primers. The internal control has the same reactants to that of the test chamber except for the primer composition and a yellow dye. Internal Control components are intended to monitor sample preparation, polymerase inhibition, system suitability and reagent integrity.

illumi*gene* External Control Reagents will be sold separately as adjunct reagents to the ***illumi****gene C. difficile* Assay. Each External Control kit contains a Negative Control reagent and a Positive Control reagent. External Controls aid the user in detection of reagent deterioration, adverse environmental or test conditions or variance in operator performance that can cause test errors. External Controls are required for routine Quality Control.

Positive Control: Tris-buffered solution containing non-infectious Plasmid DNA (S. aureus and C. difficile inserts) at 200.0 fg/µL with sodium azide (0.09%) as a preservative.

Negative Control: Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus insert)* at 200.0 fg/µL with sodium azide (0.09%) as a preservative.

d. Detection limit:

Sensitivity studies were designed to determine, within 95% confidence intervals, the analytical limit of detection (LoD) of *C. difficile* diluted in a human stool matrix. The LoD is the lowest number of colony-forming units (CFUs) per test aliquot that can be distinguished from Native samples with a high degree of probability.

Seven different strains representing five toxinotypes of *C. difficile* were evaluated. Each bacterial strain was spiked into negative stool and then diluted serially. Twenty replicates of each dilution were individually processed and tested to give a stated probability of 95% for the LoD dilution. The results obtained with each individual strain are given in Tables 2 – 5 on the following pages. The LoD point estimates and 95% upper and lower confidence intervals for each toxinotype are summarized in Table 1 below.

Table 1. 95% confidence intervals for *illumigene C. difficile* analytical LoD.

Strain ID	Toxinotype	Phenotype	LoD/Test	Lower Limit (95% CI)	Upper Limit (95% CI)
VPI 10463	0	A+/B+	4 CFU/test	83.9%	100%
2007431	III (NAP1)	A+/B+	32 CFU/test	83.9%	100%
BI8	III	A+/B+	64 CFU/test	76.4%	99.1%
2006240	V (NAP7)	A+/B+	32 CFU/test	83.9%	100%
CF1	VIII	A-/B+	64 CFU/test	83.9%	100%
2007858	IX/XXIII	A+/B+	32 CFU/test	83.9%	100%
8864	X	A-/B+	64 CFU/test	83.9%	100%

e. Analytical specificity:

Interference Studies:

Potentially interfering substances were added to a natural negative and a contrived positive sample at final concentrations of 5% v/v or greater. The contrived positive samples were prepared from a pool of donor stools that were confirmed negative by toxinogenic culture. The sample was inoculated with *C. difficile* VPI 10463 to just above the limit of detection (18 CFU/test) for this organism.

Potentially interfering substances were added at final concentrations of 5% V/V or greater. Dilution Controls for each sample were prepared by adding a phosphate-buffered saline solution in place of the potentially interfering substance. Each sample was tested in triplicate. The following substances, at the specified saturated solvent/diluents concentrations, were included in the study: Barium sulfate (5 mg/mL), fecal fat (equivalent to 2.65 mg stearic plus 1.3 mg palmitic acids per mL), hemoglobin (as methemoglobin) (3.2 mg/mL), IgA (5 mg/mL), Imodium AD® (0.00667 mg/mL), Kaopectate® (0.87 mg/mL), Metronidazole (12.5 mg/mL), mucin (3.33 mg/mL) Mylanta® (4.2 mg/mL), Pepto-Bismol® (0.87 mg/mL), Prilosec® (0.5 mg/mL), Tagamet® (0.5 mg/mL), TUMS® (0.5 mg/mL), Vancomycin (12.5 mg/mL), white blood cells (5%V/V), whole blood (5% V/V).

Crossreactivity Studies:

Potentially crossreactive or interfering microorganisms were added to a natural negative and a contrived positive sample at concentrations of 1.2×10^8/mL (bacteria and fungi) or at a minimum of $1 \times 10^{5.06}$ $TCID_{50}$/mL (viruses). The contrived positive sample was prepared from a pool of donor stools that were confirmed negative by toxinogenic culture. The sample was inoculated with toxinogenic *C. difficile* VPI 10463 to just above the limit of detection (18 CFU/test) for this strain.

Potentially cross-reactive microorganisms were added at concentrations of 1.2 x 10^8/mL (bacteria and fungi) or at a minimum of 1 x $10^{5.06}$ /mL $TCID_{50}$/mL (viruses). Dilution Controls for each sample were prepared by adding a phosphate-buffered saline solution in place of the potentially cross-reactive microorganisms. Each potential cross-reactive microorganism was tested in replicates of three. The following microorganisms were included in the study: *Aeromonas hydrophila, Bacteroides fragilis, Campylobacter coli, Campylobacter fetus, Campylobacter jejuni, Candida albicans, Citrobacter freundii, Clostridium sordellii, Clostridium perfringens, Enterobacter cloacae, Enterococcus faecalis, Escherichia coli, Escherichia coli O157:H7, Escherichia fergusonii, Escherichia hermannii, Helicobacter pylori, Klebsiella pneumoniae, Lactococcus lactis, Listeria monocytogenes, Peptostreptococcus anaerobius, Plesiomonas shigelloides, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Salmonella* Groups B-E, *Serratia liquefaciens, Serratia marcescens, Shigella boydii, Shigella flexneri, Shigella sonnei, Staphylococcus aureus, Staphylococcus epidermidis, Vibrio parahaemolyticus, Yersinia enterocolitica,* Adenovirus Types 40 and 41, Coxsackievirus, Echovirus, Rotavirus.

Strain Reactivity Studies:

Aliquots from culture filtrates of each organism were first adjusted to MacFarland Standard 4 (approximately 1.2 X 10^9), then spiked into a natural negative stool matrix to a final concentration of (1) 64 CFU/test (the LoD at 95% confidence as determined in the LoD study, and (2) at 100 times the LoD (to represent heavily infected samples).

Strain reactivity studies were performed by testing *C. difficile* stock cultures from different sources at 64 CFU/test and 640 CFU/test with ***illumi****gene C. difficile.* Each sample was testing in triplicate. Strains and toxinotypes tested were as follows: **Type 0 Strains:** 10463, 2004111, 2004205, 2005070, 2005257, 2008029, 2008162, 2008341, 2008351, 2009066, 2009099, B1, G1, J7, K12, Y1; **Type III Strains:** 2004052, 2004118, 2007431, BI17, BI8; **Type V Strains:** 2005325, 2006240, 2008188, 2009018, 2009065, BK6; **Type VIII Strains:** 43598, 2008016, CF1; **Type X Strains:** 8864; **Type XII Strains:** 2007435; **Type IX/XXIII Strains:** 2007858; **Unknown Strains:** 2009132, 2009155, 2009277.

f. Assay cut-off:

The assay has a fixed cut-off based on the measured change in light transmission at the assay endpoint. There are no range values for the cut-off. The ***illumi****pro-10* measures the transmission of light through the Test Solution and the Control Solution at the start of the Assay Run and at the end point of the Assay Run, approximately 40 minutes for the ***illumi****gene C. difficile* assay. The ***illumi****pro-10* calculates the ratio of the Run End (Signal final or S_f) reads with the Run Start (Signal Initial or S_i) reads. Calculated S_f : S_i ratios less than 90% are reported as positive; Calculated S_f : S_i ratios greater than or equal to 90% are reported as negative. Fixed cut-off values

were based on well characterized clinical specimens.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Only discrepant samples were tested with the predicate device, Cepheid® Xpert® *C. difficile,* and TECHLAB® C. DIFF CHEK™ - 60.

      Of 5 false-negative samples, 2 were negative by an FDA-cleared molecular assay.

      Of 27 false-positive samples, 15 were positive by an FDA-cleared molecular assay

      Of the 12 remaining false-positive samples, 8 were positive by an FDA-cleared assay for C. difficile Common Antigen.

   b. *Matrix comparison:*

      N/A

3. Clinical studies:

   a. *Clinical Sensitivity:*

      Samples utilized in this study were stool specimens from patients suspected of having C. *difficile* associated disease. No restrictions with regard to age, gender or geographical location were included. All samples were left-over samples. The consistency of each sample was categorized as solid, semisolid, bloody, and watery with no solids or in transport medium. A total of 697 qualified patient samples were used in the study. One sample was obtained per patient. Two tests were performed with each sample (cytotoxic bacterial culture and illumigene C. difficile assay). Performance characteristics of the illumigene C. difficile assay were determined by comparison to cytotoxic bacterial culture. Four independent clinical test sites located in the Midwestern and Southern regions of the United States and the manufacturer evaluated a total of 697 qualified patient samples. Samples were collected from 274 (39.3%) males and 419 (60.1%) females. In the case of 4 (0.6%) of the patients, sex was not known. The age groups of patients range from 2 years of age to 96 years. No differences in test performance were observed based on patient age, sex, or geographical location.

      Overall sensitivity was determined to be 95.2% (95% CI: 89.2% - 97.9%); overall specificity was determined to be 95.3% (95% CI: 93.2% - 96.7%).

Overall performance data

Cytotoxic bacterial culture		*illumigene C. difficile*	
	Positive	**Negative**	**Total**
Positive	99	5	104
Negative	27	546	573
Total	126	551	677
			95% CI
Sensitivity	99/104	**95.2%**	89.2 - 97.9%
Specificity	546/573	**95.3%**	93.2 - 96.7%
Correlation	645/677	**95.3%**	93.4 - 96.6%

*b. Clinical specificity**:***

See 3(a) above

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

N/A

4. Clinical cut-off**:**

N/A

5. Expected values/Reference range:

Samples used in this study were left-over samples for which a physician had ordered *C. difficile* testing. Observed *C. difficile* prevalence rate was approximately 15%.

N. Instrument Name:

The ***illumipro***-10

O. System Descriptions:

1. Modes of Operation:
The ***illumi****pro-10* is a menu driven laboratory instrument with two independent sample processing blocks: Block A and Block B. Each ***illumi****pro-10* Block is capable of batch processing up to five closed ***illumi****gene* test devices.
The ***illumi****pro*-10 operates in four basic modes: ASSAY, RESULTS, SERVICE, and SYSTEM. Assay Selection and Sample Amplification occur in the ASSAY mode; Test Results are managed in the RESULTS mode; Basic instrument set-up is performed in the SYSTEM mode; and Optical performance verification is completed in the SERVICE

mode.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

3. Specimen Identification:

   Samples are identified by position. Default Sample Identification is based on Block and Well position (e.g. Block A, Well 1). The user may input Sample Identification information using the keypad, the barcode scanner or the optional external keyboard.

4. Specimen Sampling and Handling:

   Specimen Sampling and Handling is performed external to the ***illumi*** *pro-10*. Prepared Samples in closed ***illumi****gene* Test Devices are placed in the ***illumi****pro-10* for amplification and detection. The ***illumi****pro-10* has no direct contact with samples. Closed ***illumi****gene* Test Devices are discarded at the end of the assay to reduce the likelihood of contamination of the ***illumi****pro-10* or the workspace.

5. Calibration:

   The ***illumi****pro-10* was designed to be a self-monitoring instrument. Calibration by the end user is not required.

6. Quality Control:

   Quality Control requirements for the ***illumi****pro-10* are limited to verification of optical performance and routine surface cleaning/decontamination. Optics system verification is performed by the user at installation and at 30 day intervals thereafter. Optics Verification Standards consist of ten red acrylic pieces molded and polished to replicate the dimensions of each ***illumi****gene* Test Device chamber. The verification standards act like a high pass optical filter with the pass wavelength of 650 nm extending into the infrared range. Light transmission through the verification standard is used to confirm proper performance of the optics system. Failed optics verification testing for an instrument block will disable the block until the error is resolved. The ***illumi****pro-10* completes a Power-On Self Test (POST) at each power-on. POST testing confirms that the Hardware and Software elements of the system are performing as expected. The ***illumi****pro-10* reports an error if POST failures are obtained; the instrument is disabled until the error is resolved.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

N/A

Q. Proposed Labeling:

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

R. Conclusion:

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