July 27, 2018

Diagenode
% Jinjie Hu
Principle Consultant
Axteria BioMed Consulting Inc.
8040 Cobble Creek Circle
Potomac, Maryland 20854

Re: K181156
Trade/Device Name: Panther Fusion GBS Assay
Regulation Number: 21 CFR 866.3740
Regulation Name: *Streptococcus* spp. serological reagents
Regulatory Class: Class I
Product Code: NJR, OOI
Dated: May 1, 2018
Received: May 1, 2018

Dear Jinjie Hu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Noel J. Gerald -S
For

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K181156

Device Name
Panther Fusion GBS Assay

Indications for Use *(Describe)*
The Panther Fusion GBS assay is an automated qualitative in vitro diagnostic test utilizing real-time PCR for detection of Group B Streptococcus DNA from either Lim or Carrot enrichment broth cultures of vaginal/rectal swabs from antepartum women following 18-24 hours incubation.

This test is performed on the Hologic Panther Fusion system and is intended to aid in determining the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The Panther Fusion GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

A. GENERAL INFORMATION

SUBMITTER

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Belgium

Contact person: Jinjie Hu,
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Date prepared: July 9, 2018

Purpose of Submission: To obtain a substantial equivalence for the Panther Fusion GBS Assay

B. MEASURAND

SIP and Cfb genes of *Streptococcus agalactiae* (Group B *Streptococcus*, GBS)

C. DEVICE INFORMATION

Proprietary Name of the device:	Panther Fusion GBS Assay
Classification name:	Streptococcus spp. serological reagents and Real-time Nucleic Acid Amplification
Regulation number:	21 CFR 866.3740 and 862.2570
Classification Name and Reference:	Class 1 (Not exempt)
Device product Code	NJR and OOI
Panel:	83, Microbiology

D. INTENDED USE/INDICATIONS FOR USE

The Panther Fusion GBS assay is an automated qualitative *in vitro* diagnostic test utilizing real-time PCR for detection of Group B *Streptococcus* DNA from either Lim or Carrot enrichment broth cultures of vaginal/rectal swabs from antepartum women following 18-24 hours incubation.

This test is performed on the Hologic Panther Fusion system and is intended to aid in determining the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The Panther Fusion GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

E. DEVICE DESCRIPTION

The Panther Fusion GBS assay involves the following steps: Sample lysis, nucleic acid capture and elution, and multiplex RT-PCR where analytes (when present) are simultaneously amplified, detected and differentiated. Nucleic acid capture and elution takes place in a single tube on the Panther Fusion system. The eluate is transferred to the Panther Fusion system reaction tube containing the assay reagents. RT-PCR is then performed for the eluted nucleic acid on the Panther Fusion system.

Sample Collection and Enrichment: After collecting and transporting a swab sample to the laboratory, the swab is placed in Lim Broth or Carrot Broth for 18 to 24 hours of enrichment. Prior to testing on the Panther Fusion system, enriched specimens are then transferred to a tube containing specimen transport media (STM) that lyses the cells, releases target nucleic acid and protects them from degradation during storage.

Nucleic Acid Capture and Elution: Specimens are then first incubated in an alkaline reagent (FER-X) to enable cell lysis. The Internal Control (IC-X) is added to each test specimen and controls via the working Panther Fusion capture Reagent-X (wFCR-X). The IC-X monitors specimen processing, amplification and detection. Magnetic particles with covalently bound oligonucleotides, contained in Panther Fusion capture Reagent-X (FCR-X), mediate the nucleic acid capture by hybridizing to total nucleic acid in the test specimen. The capture nucleic acids are then separated from residual specimen matrix in a magnetic field by a series of wash steps with a mild detergent. The captured nucleic acid is then eluted from the magnetic particles with a reagent of low ionic strength (Panther Fusion Elution Buffer).

Elution transfer and PCR: During the elution transfer step, eluted nucleic acid is transferred to a Panther Fusion Reaction tube already containing oil and reconstituted mastermix. PCR-based target amplification subsequently occurs with target-specific forward and reverse primers, generating a fluorescence signal. The Panther Fusion GBS Software computes a cycle threshold result (Ct) to qualitatively determine the presence of the analyte. The analyte targets and corresponding fluorescent channels used in the Panther Fusion GBS Assay are summarized in the ***Table 1*** below.

Table 1: Analytes and Detection Channels

Analyte	Gene Targeted	Instrument Channel
GBS	SIP and Cfb	FAM
Internal Control	Not applicable	RED677

Assay Components

The reagents required to perform the Panther Fusion GBS assay are packed together in the Panther Fusion GBS assay box. A description of the components that are required to perform the Panther Fusion GBS assay are detailed in ***Table 2***.

Table 2: Reagents Required to Perform the Panther Fusion GBS Assay

Box	Components
1	Panther Fusion GBS Cartridges
2	Panther Fusion Extraction Reagent-X - Panther Fusion Capture Reagent-X - Panther Fusion Enhancer Reagent-X
3	Panther Fusion Internal Control-X
4	Panther Fusion Elution Buffer
5	Panther Fusion Reconstitution Buffer I
6	Panther Fusion Oil
7	Panther Fusion GBS Assay Controls - Panther Fusion GBS Assay Positive Control - Panther Fusion GBS Assay Negative Control

Instrumentation

The Panther Fusion GBS assay has been designated for and validated on the Panther Fusion system. The Panther Fusion system is an integrated hardware and software system that together with the Panther Fusion GBS assay automates all the steps necessary to perform the assay.

The Panther Fusion system integrates Hologic's commercialized Panther instrument system with an add-on sidecar, the Panther Fusion module, which extends the functionality of the Panther system by increasing the assay processing capabilities to include multiplex real-time RT-PCR. The Panther Fusion module includes instrument hardware and software and can be installed on existing Panther instruments or ordered with new Panther instruments.

The Panther Fusion system employs non-specific target capture (NSTC) for the purification of RNA and DNA from the sample, followed by nucleic acid amplification and real-time fluorescent detection. The process involves sample loading and preparation (i.e. nucleic acid extraction) on the Panther instrument using the same workflow and processing steps as for other commercialized Hologic Aptima Transcription Mediated Amplification (TMA) assays. The extracted nucleic acid for each sample is transferred to the Panther Fusion module where PCR amplification and detection occurs.

F. SUBSTANTIAL EQUIVALENCE INFORMATION

Predicate device
Cepheid Xpert® GBS LB (K121539).

Comparison with Predicate
A comparison of the Panther Fusion GBS assay to the predicate is summarized in ***Table 3*** (similarities) and ***Table 4*** (differences).

Table 3 : Similarities between Panther Fusion GBS Assay and Predicate Device

	Proposed Device: **Panther Fusion GBS assay**	**Predicate Device:** **Cepheid Xpert® GBS LB assay (K121539)**
Classification	Class I	Same
Technology Principle of Operation	Fully automated Real Time nucleic acid amplification, detection and result interpretation	Same
Analyte	Genomic DNA	Same
Organism Detected	Group B *Streptococcus*	Same
Patient Population	Antepartum women	Same
Specimen Types	From 18-24 hour enriched-media cultures of vaginal/rectal swab	Same
Intended Use	The Panther Fusion GBS assay is an automated qualitative *in vitro* diagnostic test utilizing real-time PCR for detection of Group B *Streptococcus* DNA from either Lim or Carrot enrichment broth cultures of vaginal/rectal swabs from antepartum women following 18-24 hours incubation. This test is performed on the Hologic Panther Fusion system and is intended to aid in determining the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The Panther Fusion GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.	The Cepheid Xpert GBS LB Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test designed to detect Group B *Streptococcus* (GBS) DNA from enriched vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS LB Assay testing is indicated as an aid in determining GBS colonization status in antepartum women. The Xpert GBS LB Assay is used for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18-24 hours of incubation. The Xpert GBS LB assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin allergic women.
Users	Professional use	Same

Table 4 : Differences between Panther Fusion GBS Assay and Predicate Device

	Proposed Device: **Panther Fusion GBS assay**	**Predicate Device:** **Cepheid Xpert® GBS LB assay (K121539)**
Platform	Panther Fusion System	GeneXpert® Dx System (Cepheid) GeneXpert® Infinity-48 System (Cepheid) GeneXpert ® Infinity-80 System (Cepheid)
Assay Format	**Extraction:** Hologic Non- Specific Target Capture **Amplification**: Real-time PCR **Detection**: Fluorogenic target-specific hybridization	**Extraction:** Solid Phase Capture **Amplification:** Real-time PCR **Detection:** Fluorogenic target-specific hybridization
DNA Target Sequence	SIP and cfb genes	3'untranslated region of the cfb gene
Specimen Enrichment	Lim Broth and Carrot Broth	Lim Broth
Time to Obtain Results	≤ 2.5 hours total after sample loading on the Panther Fusion system	≤ 55 minutes total after sample addition to the cartridge

G. PERFORMANCE CHARACTERISTICS DATA

The following performance data were provided to support the substantial equivalence determination.

Brief Description of Analytical (Non-Clinical) Studies

The following analytical studies (non-clinical) were conducted to support the clearance of the Panther Fusion GBS Assay on the Panther Fusion System.

Analytical Sensitivity and Limit of Detection (LoD) of GBS in Vaginal/Rectal Swab Specimens

The LoD of the Panther Fusion GBS assay was determined by testing serial dilutions of 11 GBS serotypes and one non-hemolytic (NH) isolate in Lim Broth clinical negative matrix. Thirty replicates were tested with each of the three reagent lots for a combined total of 90 replicates per dilution. Probit analysis was performed for each reagent lot with the reported 95% LoD based upon the worst estimate, as shown in ***Table 5***. Serotype specific LoD predictions were verified by testing an additional 20 replicates with one reagent lot.

Table 5 : GBS Limit of Detection (LoD)

GBS Serotype	95% LoD in CFU/mL (95% CI)
Ia	137.4 (103.7 – 209.7)
Ib	140.5 (100.6 – 234.7)
Ic	136.3 (99.2 – 220.5)
II	179.0 (135.1 – 276.2)
III	168.0 (125.2 – 261.5)
IV	84.0 (63.0 – 130.4)
V	122.3 (92.2 – 186.8)
VI	282.0 (201.9 – 475.8)
VII	250.8 (180.2 – 424.8)
VIII	231.3 (167.3 – 380.9)
IX	301.0 (202.0 – 567.7)
NH	300.2 (212.0 – 523.0)

CFU= colony forming units, CI= confidence interval,
NH= non-hemolytic

Interferences

Amniotic fluid, blood, urine, stool and other potentially interfering endogenous and exogenous substances that may be present in vaginal/rectal specimens were evaluated in the Panther Fusion GBS assay. Concentrations exceeding clinically relevant amounts of the potentially interfering substances were added to Lim Broth clinical negative matrix and tested un-spiked or spiked with GBS analyte at a 3X LoD concentration. The substances consisted of topical medications, lubricants, deodorants, laxatives and contraceptives as shown in ***Table 6***.

All of the substances tested were found to have no impact on the performance of the Panther Fusion GBS assay, at the concentrations tested.

Table 6 : Potentially Interfering Substances

Substance Name	Ingredient(s)	Concentration
Human Amniotic Fluid	N/A	4% v/v
Human Whole Blood EDTA	N/A	4% v/v
Human Whole Blood Na Citrate	N/A	4% v/v
Human Serum	N/A	4% v/v
Human Urine Sample	N/A	4% v/v
Human Fecal Sample	N/A	4% v/v
Topical Hemorrhoid Ointment (Preparation H Cream)	Mineral Oil, Petrolatum, Phenylephrine HCl	3.4% w/v
Anti-Diarrheal Medication (Pepto Bismol)	Bismuth subsalicylate	4% v/v
Personal Lubricant (K-Y Jelly Personal Lubricant)	Glycerine, Methylparaben, Propylparaben	2.2% w/v

Substance Name	Ingredient(s)	Concentration
Lubricating gel (Aquagel)	N/A	2.1% w/v
Vaginal Anti-itch Cream (OTC) (Vagisil)	Benzocaine, Resorcinol	3.9% w/v
Vaginal Anti-itch Cream (OTC) (Gyno-Daktarin)	Miconazole nitrate	3.8% w/v
Vaginal Antifungal Cream (OTC) (Monistat)	Miconazole nitrate	3.1% w/v
Vaginal Antifungal Gel	Candida albicans 27X HPUS, Candida parapsilosis 27X HPUS, Pulsatilla 27X HPUS	3.0% w/v
Anti-Diarrheal Caplet (Kaopectate)	Bismuth subsalicylate	1.1% w/v
Deodorant Powder (Vagisil)	Zea Mays Starch, Magnesium Stearate, Sodium Bicarbonate, Aloe Barbadensis Leaf extract, Tocopheryl Acetate, Tricalcium Phosphate, Mineral Oil, Polyoxymethylene Urea, Maltodextrin, Fragrance	1.1% w/v
Deodorant Suppositories (Norforms Suppositories)	PEG-20, PEG-32, PEG-20 Stearate, Benzethonium Chloride, Methylparaben, Lactic Acid, Fragrance, Neutresse (Odor synthesis)	2.1% w/v
Deodorant Spray (FDS)	Isopropyl Myristate, Zea Mays Strach, Magnesium Stearate, Fragrance, Zinc Ricinoleate, Laureth-3, Benzyl alcohol, Mineral Oil (Paraffinum Liquidum, Huile Minérale), Tetrahydroxypropyl Ethylenediamine, Sodium Bicarbonate, Citronellol, Linalool, Propylene Glycol, Butylphenyl Methylpropional, Lanolin Alcohol, Anise Alcohol, Oleyl Alcohol, Benzyl Benzoate, Chamomilla Recutita, Flower extract, Tocopheryl Acetate, Aloe Barbadensis Leaf extract	1.5% w/v
Body Powder (Gold Bond Powder)	Menthol	0.4% w/v
Body Oil	Isoppropyl Myristate, sesame seed oil, PEG-40, Sorbitan Peroleate, Propylparaben, BHT, Fragrance	4% v/v
Spermicidal Foam	Nonoxynol-9	2.1% w/v
Oral Laxative (Metamucil Fiber Supplement)	Psyllium husk	2.2% w/v
Grains de Vals (SennosideB)	Sennocide B	0.4% w/v
Oral Laxative (Phillips Mikl of Magnesia)	Magnesium hydroxide	7.3% w/v
Stool Softener	Bisacodyl	0.9% w/v
Astroglide Liquid personal lubricant	Glycerin, Propylene Glycol, Polyquaternium 15, Methylparaben, Propylparaben	2.7% w/v
Enema Solution (Fleet enema)	Dinatriumhydrogenphosphat-Dodecahydrat / Natriumhydrogenphosphat-Dihydrat	4% v/v

Analytical Specificity and Microbial Interference

The analytical specificity of the Panther Fusion GBS assay was evaluated by testing a panel of 110 microorganisms (as listed in ***Table 7***), consisting viral, bacterial, fungal, parasite, protozoan and yeast strains representing pathogens or flora commonly present in the vaginal/rectal tract or related to the GBS family. Bacteria and yeast were tested at 1 $x10^6$ CFU/mL, except where noted. Viruses, fungi, parasites and protozoan were tested at 1x 10^5 PFU/mL, except where noted. Organisms were tested both with and without GBS spiked at a concentration 3X the established LoD. All of the microorganisms tested were found to have no impact on the performance or analytical specificity of the Panther Fusion GBS assay.

Table 7 : Microorganisms and Evaluated Concentrations

Pathogen	Concentration* (CFU/mL or PFU/mL)	Pathogen	Concentration* (CFU/mL or PFU/mL)
Bacillus cereus	$1x10^6$	*Streptococcus anginosus*	$1x10^6$
Yersinia enterocolitica subsp. enterocolitica	$1x10^6$	*Prevotella oralis*	$1x10^6$
Anaerococcus prevotii	$1x10^6$	*Streptococcus canis*	$1x10^6$
Propionibacterium acnes	$1x10^6$	*Lactobacillus delbrueckii subsp. lactis*	$1x10^6$
Clostridium difficile	$1x10^6$	*Corynebacterium sp (genitalium)*	$1x10^6$
Fusobacterium nucleatum	$1x10^6$	*Neisseria gonorrhoeae*	$1x10^6$
Bifidobacterium adolescentis Reuter	$1x10^6$	*Streptococcus pneumoniae (oral group)*	$1x10^6$
Candida albicans (NIH 3147)	$1x10^6$	*Streptococcus mutans (oral group)*	$1x10^6$
Candida glabrata (CBS 138)	$1x10^6$	*Corynebacterium urealyticum*	$1x10^6$
Candida tropicalis	$1x10^6$	*Lactobacillus reuteri*	$1x10^6$
Cryptococcus neoformans	$1x10^5$*	*Lactobacillus sp.*	$1x10^6$
Klebsiella pneumoniae	$1x10^6$	*Lactobacillus casei*	$1x10^6$
Proteus mirabilis	$1x10^6$	*Lactobacillus acidophilus*	$1x10^6$
Alcaligenes faecalis	$1x10^6$	*Streptococcus gordonii (oral group)*	$1x10^6$
Enterobacter aerogenes	$1x10^6$	*Bulkholderia cepacia*	$1x10^6$
Stenotrophomonas maltophilia	$1x10^6$	*Aeromonas hydrophila*	$1x10^6$
Campylobacter jejuni	$1x10^6$	*Moraxella atlantae*	$1x10^6$
Providencia stuartii	$1x10^6$	*Prevotella bivia*	$1x10^6$
Micrococcus luteus	$1x10^6$	*Pasteurella aerogenes*	$1x10^6$
Staphylococcus haemolyticus	$1x10^6$	*Rhodococcus equi*	$1x10^6$
Enterococcus faecalis	$1x10^6$	*Listeria monocytogenes*	$1x10^6$
Pseudomonas fluorescens	$1x10^6$	*Lactobacillus gasseri*	$1x10^6$
Staphylococcus saprophyticus	$1x10^6$	*Peptoniphilus asaccharolyticus*	$1x10^6$
Proteus vulgaris	$1x10^6$	*Atopobium vaginae*	$1x10^6$
Toxoplasma gondii	$1x10^5$*	*Bifidobacterium brevis*	$1x10^6$
Enterococcus faecium	$1x10^6$	*Abiotropha defectiva*	$1x10^6$
Escherichia coli	$1x10^6$	*Anaerococcus tetradius*	$1x10^6$

Pathogen	Concentration* (CFU/mL or PFU/mL)	Pathogen	Concentration* (CFU/mL or PFU/mL)
Enterobacter cloacae	$1x10^6$	*Finegoldia magna*	$1x10^6$
Morganella morganii	$1x10^6$	*Peptostreptococcus anaerobius*	$1x10^6$
Shigella flexneri	$1x10^6$	*Anaerococcus lactolyticus*	$1x10^6$
Streptococcus pyogenes (group A)	$1x10^6$	Human herpesvirus 4 (EBV)	$1x10^5$*
Streptococcus ratti	$1x10^6$	*Bacteroides fragilis*	$1x10^6$
Staphylococcus lugdunensis	$1x10^6$	*Bordetella pertussis*	$1x10^6$
Acinetobacter baumannii	$1x10^6$	*Chlamydia trachomatis*	$1x10^6$
Staphylococcus aureus	$1x10^6$	Human herpesvirus 5 (CMV)	$1x10^5$*
Staphylococcus epidermidis	$1x10^6$	*Hafnia alvei*	$1x10^6$
Shigella sonnei	$1x10^6$	*Trichomonas vaginalis*	$1x10^5$*
Citrobacter freundii	$1x10^6$	Human immuno-deficiency virus-1 (HIV-1)	$1x10^5$*
Enterococcus gallinarum	$1x10^6$	*Moraxella catarrhalis*	$1x10^6$
Acinetobacter lwoffii	$1x10^6$	*Mycoplasma genitalium*	$1x10^6$
Pseudomonas aeruginosa	$1x10^6$	*Prevotella melaninogenica*	$1x10^6$
Streptococcus criceti	$1x10^6$	Rubella Virus	$1x10^5$*
Haemophilus influenzae	$1x10^6$	*Serratia marcescens*	$1x10^6$
Klebsiella oxytoca	$1x10^6$	*Streptococcus intermedius*	$1x10^6$
Streptococcus bovis (group D)	$1x10^6$	Human Papilloma Virus Type 16 (HPV16)	$1x10^5$*
Streptococcus parasanguinis	$1x10^6$	Hepatitis B Virus	$1x10^5$*
Streptococcus equi subsp. equi (group D)	$1x10^6$	Hepatitis C Virus	$1x10^5$*
Enterococcus durans	$1x10^6$	Herpes Simplex Virus-1 (HSV-1)	$1x10^5$*
Lactobacillus plantarum	$1x10^6$	Herpes Simplex Virus-2 (HSV-2)	$1x10^5$*
Streptococcus dysgalactiae	$1x10^6$	Human herpesvirus 3 (VZV)	$1x10^5$*
Streptococcus constellatus	$1x10^6$	*Arcanobacterium pyogenes*	$1x10^6$
Streptococcus oralis (oral group)	$1x10^6$	*Mobiluncus curtisii subsp. curtisii*	$1x10^6$
Bacillus coagulans	$1x10^6$	*Gardnerella vaginalis*	$1x10^6$
Streptococcus pseudoporcinus	$1x10^6$	*Salmonella enterica subsp. enterica ser. dublin (group D)*	$1x10^6$
Streptococcus mitis (oral group)	$1x10^6$	*Streptococcus acidominus*	$1x10^6$

*Microorganisms evaluated as extracted DNA were tested in Copies/mL

Carryover/Cross-Contamination

The carryover/cross-contamination study was performed with Lim Broth clinical negative samples alternately placed between high positive samples and tested. High positive samples were prepared by spiking GBS at > 1x 10^6 CFU/mL (> 5,000X LoD). A total of ten separate runs with negative samples and positive samples placed in a checkerboard pattern were tested in addition to four runs of negative specimens over two different instruments a combined total of 300 positive and 420 negative samples. There were no false positive results observed for a carry-over rate of 0.0%.

Assay Precision

Panther Fusion GBS Assay precision was evaluated with a 7-member panel. The panel was tested by three operators on five separate runs per day, using three reagent lots on one Panther Fusion systems over 12 non-consecutive days. The panel members are described in ***Table 8*** along with a summary of the agreement with expected results for each target.

Table 8 : Percent Agreement to the Expected Result

Panel Member	**% Positive (Pos n/valid n)**	**% Agreement (95% CI)**
GBS III Low Positive (1-2X LoD)	100% (180/180)	100% (97.9-100)
GBS III Moderate Positive (3X LoD)	100% (180/180)	100% (97.9-100)
GBS V Low Positive (1-2X LoD)	100% (180/180)	100% (97.9-100)
GBS V Moderate Positive (3X LoD)	100% (180/180)	100% (97.9-100)
GBS NH Low Positive (1-2X LoD)	100% (180/180)	100% (97.9-100)
GBS NH Moderate Positive (3X LoD)	100% (180/180)	100% (97.9-100)
Negative	0% (0/180)	100% (97.9-100)

CI= confidence interval, LoD= limit of detection, NH= non-hemolytic

Table 9 presents the mean and variability analysis between reagent lots, between operators, between days, between runs and within runs, and overall (total) for Ct.

Table 9 : Signal Variability

Panel Member	Mean Ct	Between Reagents Lots		Between Operators		Between Days		Between Runs		Within Runs		Total	
		SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
GBS III 1-2X LoD	36.3	0.06	0.16%	0.16	0.45%	0.11	0.31%	0.33	0.91%	0.43	1.18%	0.53	1.46%
GBS III 3X LoD	35.4	0.17	0.48%	0.12	0.35%	0.13	0.36%	0.34	0.95%	0.32	0.90%	0.43	1.22%
GBS V 1-2X LoD	36.4	0.13	0.37%	0.13	0.35%	0.17	0.46%	0.29	0.78%	0.50	1.36%	0.55	1.51%
GBS V 3X LoD	35.4	0.13	0.38%	0.11	0.31%	0.12	0.34%	0.28	0.79%	0.41	1.14%	0.46	1.31%
GBS NH 1-2X LoD	35.7	0.23	0.65%	0.12	0.35%	0.14	0.39%	0.31	0.86%	0.38	1.06%	0.46	1.28%
GBS NH 3X LoD	34.8	0.19	0.55%	0.04	0.12%	0.10	0.29%	0.28	0.81%	0.29	0.84%	0.40	1.14%
Negative	31.5	0.24	0.77%	0.08	0.24%	0.14	0.43%	0.32	1.03%	0.27	0.86%	0.41	1.32%

Ct= threshold cycle, CV= coefficient of variation, LoD= limit of detection, SD= standard deviation

Reproducibility

Panther Fusion GBS Assay reproducibility was evaluated at three US sites using a seven panel members. Testing was performed using one lot of assay reagents and six operators (two at each site). At each site, testing was performed two times per day during five non-consecutive days. Each run had three replicates of each panel member. A negative panel member was created using Lim Broth matrix. Positive panel members were created by spiking GBS at 1-2X LoD (low-positive) or 3X LoD (moderate-positive) concentrations of the target analyte into Lim Broth matrix. The agreement with expected results was 100% in the negative and moderate positive panel members and ≥98.9% in low-positive panel members for the three GBS strains evaluated (serotypes III, V and non-hemolytic isolate- NH), as shown in ***Table 10.***

Table 10 : Agreement of Panther Fusion GBS Assay Results with Expected Results

Panels			Expected Result	Agreement with Expected Result	
Description	Composition	Concentration (CFU/mL)	GBS	N	% (95% CI)
GBS III Low Positive	1-2X LoD	262	+	90/90	100% (95.9-100%)
GBS III Moderate Positive	3X LoD	504	+	90/90	100% (95.9-100%)
GBS V Low Positive	1-2X LoD	188	+	89/90	98.9% (94.0-99.8%)
GBS V Moderate Positive	3X LoD	367	+	90/90	100% (95.9-100%)
GBS NH Low Positive	1-2X LoD	523	+	90/90	100% (95.9-100%)
GBS NH Moderate Positive	3X LoD	900	+	90/90	100% (95.9-100%)
Nec.	Negative	N/A	-	90/90	100% (95.9-100%)

The total GBS signal variability measured as %CV ranged from 1.51% to 2.25% in low and moderate positive panel members. Across the sources of variation, excluding within run, %CV values were ≤ 1.33%, as shown in ***Table 11*****.**

Table 11 : Signal Variability of the Panther Fusion GBS Assay by Panel Member

Panel Description	N	Mean Ct	Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
GBS III Low Pos	90	37.1	0.49	1.33%	0.47	1.26%	0.18	0.48%	0.14	0.37%	0.55	1.47%	0.77	2.09%
GBS III Mod Pos	90	36.2	0.45	1.24%	0.41	1.12%	0.15	0.41%	0.05	0.14%	0.42	1.15%	0.66	1.81%
GBS V Low Pos	90	37.3	0.44	1.17%	0.41	1.09%	0.09	0.23%	0.11	0.31%	0.68	1.82%	0.84	2.25%
GBS V Mod Pos	90	36.3	0.31	0.84%	0.31	0.85%	0.26	0.72%	0.08	0.23%	0.48	1.33%	0.61	1.69%
GBS NH Low Pos	90	36.2	0.27	0.75%	0.27	0.74%	0.14	0.40%	0.10	0.28%	0.50	1.37%	0.58	1.61%
GBS NH Mod Pos	90	35.4	0.20	0.57%	0.20	0.55%	0.16	0.45%	0.03	0.08%	0.46	1.31%	0.53	1.51%
Negative (IC)	90	31.9	0.32	1.00%	0.30	0.95%	0.06	0.20%	0.16	0.50%	0.26	0.83%	0.56	1.77%

The signal variability as measured as % CV was ≤1.35% between sites/operators, between days/runs, or overall for the Panther Fusion GBS assay positive control and negative control, as shown in ***Table 12***.

Table 12 : Signal Variability of the Panther Fusion GBS Assay Controls

Control	N	Mean Ct	Between Sites/Operators		Between Days/ Runs		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)
Positive	15	31.9	0.17	0.53%	0.10	0.32%	0.22	0.70%
Negative	15	28.3	0.20	0.72%	0.27	0.94%	0.38	1.35%

Ct= threshold cycle, CV= coefficient of variation, SD= standard deviation

H. COMPARISON STUDIES

Method Comparison

Not applicable.

Matrix Comparison

GBS strains (serotypes III and V and non-hemolytic) were serially diluted in each negative clinical matrix (Lim Broth and Carrot Broth) to their respective concentrations at ½x, 2x, or 5x LoD. 30 replicates per strain per concentration and per broth were processed along with at least 5 replicates of negative clinical matrix for each type of broth. All positives and negative specimen were correctly identified by the Panther Fusion GBS Assay.

According to the acceptance criteria, the equivalence between Lim Broth and Carrot Broth was demonstrated at 2x and 5x LoD concentrations for the 3 tested GBS strains. Equivalence below the LoD level is not demonstrated for these enrichment broths. This concentration has been chosen as a most challenging scenario and is not clinically relevant considering that the Panther Fusion GBS Assay is intended to aid for GBS diagnosis after 24 hours enrichment. The concentration of GBS target in either broth is not expected to be below the LoD after enrichment.

I. CLINICAL STUDY

Prospective Clinical Study

This prospective study was performed at three sites using leftover enriched culture samples in Lim broth and Carrot broth from vaginal/rectal specimens collected from antepartum women during routine GBS screening. The leftover culture samples were selected according to the inclusion and exclusion criteria, patient information was de-identified and each specimen was given a unique ID number. All samples were tested with both the Panther Fusion GBS Assay and the reference culture method following CDC recommendations. Results obtained using the Panther Fusion GBS Assay were compared to those obtained with the reference method to calculate the clinical sensitivity and specificity of the Panther Fusion GBS Assay.

This study was performed from January 2018 to March 2018 at clinical evaluation at three geographically distinct sites in the United States in compliance with Good Clinical Practices (GCP). Among the three sites, two sites enrolled specimen enriched in Lim Broth and one site enrolled leftover specimen enriched in Carrot Broth. A total of 947 clinical leftover samples, meeting the inclusion criteria, were enrolled in the study with an average GBS prevalence of 24% (229 positive) in culture.

Results showed a clinical sensitivity of 100% in both matrices and a clinical specificity of 96.9% and 95.5% in Lim Broth and Carrot Broth respectively. Overall performance of the Panther Fusion Assay demonstrated a clinical sensitivity of 100% and a clinical specificity of 96.5%. Study results are summarized in ***Table 13***, ***Table 14*** *and* ***Table 15***.

Table 13 : Lim Broth Specimens

Lim Broth		Reference Method		
		Positive	**Negative**	**Total**
Panther Fusion GBS Assay	**Positive**	120	16*	**136**
	Negative	0	507	**507**
	Total	**120**	**523**	**643**
Sensitivity		120/120 = 100% (95% CI: 96.9% - 100%)		
Specificity		507/523 = 96.9% (95% CI: 95.1% - 98.1%)		
Positive Predictive Value		120/136 = 88.2% (95% CI: 81.7% - 92.6%)		
Negative Predictive Value		507/507 = 100% (95% CI: 99.3% - 100%)		

* Of 16 False Positives, 14 (87.5%) were positive on the Becton Dickinson BD MAX GBS Assay

Table 14 : Carrot Broth Specimens

Carrot Broth: Carolinas		Reference Method		
		Positive	**Negative**	**Total**
Panther Fusion GBS Assay	**Positive**	83	10*	**93**
	Negative	0	211	**211**
	Total	**83**	**221**	**304**
Sensitivity		83/83 = 100% (95% CI: 95.6% - 100%)		
Specificity		211/221 = 95.5% (95% CI: 91.9% - 97.5%)		
Positive Predictive Value		83/93 = 89.3% (95% CI: 81.3% - 94.1%)		
Negative Predictive Value		211/211 = 100% (95% CI: 98.2% - 100%)		

Table 15 : Combined Lim Broth and Carrot Broth Specimens

Lim & Carrot Broth Combined		Reference Method		
		Positive	**Negative**	**Total**
Panther Fusion GBS Assay	**Positive**	203	26	**229**
	Negative	0	718	**718**
	Total	**203**	**744**	**947**
Sensitivity		203/203 = 100% (95% CI: 98.1% - 100%)		
Specificity		718/744 = 96.5% (95% CI: 94.9% - 97.6%)		
Positive Predictive Value		203/229 = 88.7% (95% CI: 83.9% -92.1%)		
Negative Predictive Value		718/718 = 100% (95% CI: 99.5% - 100%)		

Expected Values/Reference Range

The performance of the Panther Fusion GBS assay was evaluated in a prospective Clinical Study on clinical vaginal specimen from antepartum women conducted at three sites in the U.S. Overall, the prevalence of GBS colonization as determined by the Panther Fusion GBS Assay was 24.2% (229/947) whereas by conventional culture it was 21.4% (203/947) as shown in ***Table 16.***

Table 16 : Panther Fusion GBS Assay and Culture Prevalence

Culture Medium	Clinical Site	N	Panther Fusion GBS Assay		Conventional Culture	
			N Positive	% Prevalence	N Positive	% Prevalence
Lim Broth	1	300	65	21.7%	60	20.0%
	2	343	71	20.7%	60	17.5%
	Overall	**643**	**136**	**21.2%**	**120**	**18.7%**
Carrot Broth	3	304	93	30.6%	83	27.3%
Combined	**Overall**	**947**	**229**	**24.2%**	**203**	**21.4%**

J. CONCLUSIONS

The analytical and the clinical study results demonstrate that the Panther Fusion GBS assay on the Panther Fusion system performs comparably to the predicate device that is currently marketed for the same intended use. Hardware and software verification and validation demonstrate that the Panther Fusion GBS Assay on the Panther Fusion system will perform as intended. The submitted information in this premarket notification support a substantial equivalence decision.