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

A. 510(k) Number:

K173250

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Solana GBS Assay

C. Measurand:

Conserved region of the *Streptococcus agalactiae* (Group B *Streptococcus*) *atoB* gene

D. Type of Test:

Qualitative real-time DNA amplification and detection assay

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Solana GBS Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3740: *Streptococcus* serological reagents

2. Classification:

   Class I (non-exempt)

3. Product code:

   NJR: Nucleic acid amplification assay system, Group B *Streptococcus*, direct specimen test

4. Panel:

   83-Microbiology

H. Intended Use:

1. Intended use(s):

   The Solana GBS Assay is a qualitative *in vitro* diagnostic test for detection of Group B *Streptococcus* from either Lim or Carrot enrichment broth cultures of vaginal/rectal swabs from antepartum women following 18 to 24 hours of incubation.

   The Solana GBS Assay utilizes helicase-dependent amplification (HDA) of the thiolase (*atoB*) gene sequence. The Solana GBS Assay is intended for use only with the Solana Instrument.

   The Solana GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

2. Indication(s) for use:

   Same as Intended Use.

3. Special conditions for use statement(s):

   For in vitro diagnostic use.

   For prescription use only.

4. Special instrument requirements:

   The Solana GBS Assay is for use only with the Solana instrument.

I. Device Description:

The Solana GBS Assay is an *in vitro* diagnostic, real-time DNA amplification test for the direct, qualitative detection of Group A *Streptococcus* DNA in vaginal/rectal swab specimens that have been incubated for 18-24 hours in enrichment broth.

The assay kit comprises pre-filled tubes containing Process Buffer that are used for specimen processing, and separate Reaction Tubes that contain lyophilized reagents for Helicase-Dependent Amplification and fluorescence-based detection of the target nucleic acid and a Process Control.

After incubation of a vaginal/rectal swab specimen in Lim or Carrot broth, a portion of the

culture medium is transferred to a Process Buffer tube that is heated at 95°C for 5 minutes to lyse the target organisms (if present). An aliquot of the lysate is then used to rehydrate the contents of a Reaction Tube which is placed in the Solana instrument for nucleic acid amplification, detection and automated result interpretation.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   AmpliVue GBS Assay

2. Predicate 510(k) number(s):

   K133503

3. Comparison with predicate:

Similarities		
Item	**Device (K173250) Solana GBS Assay**	**Predicate (K133503) AmpliVue GBS Assay**
Regulation	21 CFR 866.3740: *Streptococcus* serological reagents	Same
Product Code	NJR: Nucleic acid amplification assay system, Group B *Streptococcus*, direct specimen test	Same
Classification	Class II	Same
Intended Use	The Solana GBS Assay is a qualitative *in vitro* diagnostic test for detection of Group B *Streptococcus* from either Lim or Carrot enrichment broth cultures of vaginal/rectal swabs from antepartum women following 18 to 24 hours of incubation. The Solana GBS Assay utilizes helicase-dependent amplification (HDA) of the Thiolase (*atoB*) gene sequence. The Solana GBS Assay is intended for use	The AmpliVue GBS Assay is a qualitative *in vitro* diagnostic test for the rapid detection of Group B *Streptococcus* from vaginal/rectal swabs from antepartum women following 18 to 24 hours of incubation in an [*sic*] Lim enrichment broth culture. The AmpliVue GBS Assay utilizes helicase-dependent amplification (HDA) of the Thiolase (*atoB*) gene sequence and a self-contained disposable amplification detection

Similarities		
Item	**Device (K173250) Solana GBS Assay**	**Predicate (K133503) AmpliVue GBS Assay**
	only with the Solana Instrument. The Solana GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.	device that allows for manual evaluation of assay results. Results can be used as an aid in determining the colonization status of antepartum women. The AmpliVue GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended far penicillin-allergic women. The AmpliVue GBS Assay is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.
Specimen Type	Vaginal/rectal swab specimen following enrichment broth culture	Same
Measurand	Conserved region of the *S. agalactiae atoB* gene	Same
DNA Amplification Technology	Helicase-Dependent Amplification	Same

Differences		
Item	**Device (K173250) Solana GBS Assay**	**Predicate (K133503) AmpliVue GBS Assay**
Enrichment Broth	Lim or Carrot Broth	Lim Broth
Nucleic Acid Detection	Cleavage of fluorescently-labeled probes; automated interpretation of fluorescence values	Lateral flow sandwich assay; visual interpretation of lines on the detection strip
Instrument	Solana	None
Time-to-result (post enrichment)	38-42 minutes	75-90 minutes

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

Not applicable

L. Test Principle:

The Solana GBS Assay uses Helicase-Dependent Amplification with fluorescently-labeled probes to detect a conserved region of the *S. agalactiae* thiolase *atoB* gene in culture medium from vaginal/rectal swabs that are obtained from pregnant women.

Vaginal/rectal swab specimens are cultured for 18-24 hours in either Lim or Carrot broth, after which a sample of the culture medium is transferred to a tube containing Process Buffer. The tube is heated at 95°C for 5 minutes to lyse the target organisms, and an aliquot of the lysate is used to rehydrate Reaction Tubes that contain reagents for the amplification and detection of *S. agalactiae* target DNA and an internal Process Control. After rehydration, the test operator loads the Reaction Tubes into the Solana instrument for automated incubation, fluorescence detection and result interpretation. Results are reported on the instrument screen as "GBS Positive," "GBS Negative" or "Invalid" (due to Process Control failure) and may be printed.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Analytical studies to characterize the performance of the Solana GBS Assay were conducted using Lim or Carrot broth that was inoculated with clinical vaginal/rectal swab matrix, incubated for 18-24 hours at 37°C, screened as GBS-negative using the Solana GBS Assay, pooled and stored frozen at ≤-20°C. Samples for testing were prepared by mixing an aliquot of the vaginal/rectal swab culture medium with enumerated stock suspensions of *S. agalactiae*, Solana GBS Assay Process Buffer and other components appropriate to the conditions under investigation.

a. Precision/Reproducibility:

Reproducibility
The reproducibility of the Solana GBS Assay between laboratories was evaluated in a study performed by two operators at each of three sites over a period of five non-consecutive days. The Solana GBS Assay exhibited similar analytical sensitivity with Lim and Carrot broth samples and therefore the Reproducibility Study was performed with a panel of contrived positive and negative Lim broth samples as the representative sample type (refer to **Sections M(1)(d)** and **M(2)(b)**). The positive samples were prepared using two strains of GBS at three different target levels based on the limit of detection of the assay. On each day, each operator tested three negative samples and one or two replicates of each *S. agalactiae* positive panel member (3 sites x 2 operators x 5 days x 2-4 samples per target level per day = 90 replicates per target level). The results of the study are summarized in **Table 1**.

Table 1. Summary of results from the Solana GBS Assay Reproducibility Study

Target Level	Strain of GBS	CFU/mL	Positive/Number Tested (%)				
			Site 1	Site 2	Site 3	All Sites	Overall
Moderate Positive (3X LoD)	SS617	2.4×10^6	16/16 (100)	16/16 (100)	16/16 (100)	48/48 (100)	90/90 (100)
	SS618	2.1×10^6	14/14 (100)	14/14 (100)	14/14 (100)	42/42 (100)	
Low Positive (1X LoD)	SS617	8.0×10^5	16/16 (100)	16/16 (100)	16/16 (100)	48/48 (100)	90/90 (100)
	SS618	7.1×10^5	14/14 (100)	14/14 (100)	14/14 (100)	42/42 (100)	
High Negative (0.01X LoD)	SS617	8.0×10^3	5/16 (31.3)	7/16 (43.8)	8/16 (50.0)	20/48 (41.7)	50/90 (55.6)
	SS618	7.1×10^3	12/14 (85.7)	8/14 (57.1)	10/14 (71.4)	30/42 (71.4)	
Negative	NA	0	0/30 (0.0)	0/30 (0.0)	0/30 (0.0)	0/90 (0.0)	

NA: Not applicable; LoD: Limit of Detection

In addition to testing the reproducibility panel members, on each day of the study, the operators each tested three Positive and three Negative External Controls (3 sites x 2 operators x 3 replicates x 5 days = 90 replicates per control). The controls were prepared using the Quidel Molecular GBS Control Set. In all cases the Positive and Negative External Controls produced the expected results (90/90 = 100%).

The results of this study demonstrated acceptable reproducibility from site-to-site at target levels close to the limit of detection (LoD) of the Solana GBS assay.

Repeatability

The within-laboratory repeatability of the Solana GBS Assay was evaluated by testing a panel of contrived positive and negative Lim broth samples over a period of 15 non-consecutive days. The positive samples were prepared using two strains of GBS at three different target levels. On each day, six negative samples and either two or four replicates of each positive panel member were tested (15 days x 2 strains x 2-4 replicates per panel member = 90 replicates per target level). The results of the study are summarized in **Table 2**.

Table 2. Summary of results from the Solana GBS Assay Repeatability Study

Target Level	Strain of GBS	CFU/mL	Positive/Number Tested (%)	
			By Strain	Overall
Moderate Positive (3X LoD)	SS617	2.4×10^6	48/48 (100)	90/90 (100)
	SS618	2.1×10^6	42/42 (100)	
Low Positive (1X LoD)	SS617	8.0×10^5	48/48 (100)	90/90 (100)
	SS618	7.1×10^5	42/42 (100)	
High Negative (0.01X LoD)	SS617	8.0×10^3	22/48 (45.8)	50/90 (55.6)
	SS618	7.1×10^3	29/42 (69.0)	
Negative	NA	0	0/90 (0.0)	

NA: Not applicable; LoD: Limit of Detection

In addition to testing the panel members, on each day of the Repeatability Study, six Positive and six Negative External Controls were also tested (6 replicates x 15 days = 90 replicates per control). The controls were prepared using the Quidel Molecular GBS Control Set. In all cases the Positive and Negative Controls produced the expected results (90/90 = 100%).

The Solana GBS Assay demonstrated acceptable repeatability between days.

b. Linearity/assay reportable range:

Not applicable.

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

Sample Stability
Studies were conducted to evaluate the stability of samples of vaginal/rectal swab culture matrix prior to addition to the Process Buffer. Testing was performed using Lim and Carrot broth vaginal/rectal swab culture matrix that was seeded with *S. agalactiae* strain ATCC BAA-611 at 2X LoD (**Section M(1)(d)**). Enrichment cultures in both Lim and Carrot broth were shown to be stable for up to 48 hours at 20-25°C or 7 days at 2-8°C. Following addition to Process Buffer, samples stored at 2-8°C were found to be stable for up to 72 hours prior to or after heat lysis.

Process Control
The Solana GBS Assay Process Buffer Tube contains a Process Control that is designed to monitor sample processing and the presence of substances that are inhibitory to DNA amplification, as well as reagent or instrument failure. Specimens that are negative for *S. agalactiae* by the Solana GBS Assay and in which the Process Control is also not detected are reported as "Invalid" and should be retested from the processed sample. If an Invalid result is obtained upon retesting, another aliquot of

the same broth culture should be processed or a new enrichment culture should be prepared.

External Controls
External Controls should be tested according to guidelines or requirements of local, provincial and/or federal regulations or accreditation organizations. External Positive and Negative Controls should be processed in the same manner as patient specimens to monitor for substantial reagent or instrument failure.

Positive and Negative External Controls from the Quidel Molecular GBS Control Set were tested on each day that patient specimens were evaluated during the prospective Clinical Study described in **Section M(3)(a)**. A total of 52 pairs of Positive and Negative Controls were tested during the study, all of which (100%) produced the expected results.

Additional Positive and Negative External Controls were also tested during the Reproducibility and Repeatability Studies and in all cases produced the expected results (refer to **Section M(1)(a)**).

d. Detection Limit:

Limit of Detection
The LoD of the Solana GBS Assay was determined for six strains of *S. agalactiae* using contrived Lim broth-enriched vaginal/rectal samples that were seeded with *S. agalactiae* cells at different concentrations. Initial testing was performed with a single lot of Solana GBS Assay reagents. The preliminary LoD for each strain was defined as the lowest concentration at which ≥19/20 replicates produced a positive result. The preliminary LoD was confirmed by testing two additional lots of Solana GBS Assay reagents at the estimated LoD target level. For the LoD for each strain to be confirmed ≥19/20 replicates with each reagent lot had to produce positive results. The results of the study are summarized in **Table 3**.

The highest LoD among the six strains of *S. agalactiae* tested was for strain ATCC 12403 at 2.6 x 10^6 CFU/mL. The LoD for this strain was shown to be the same in the presence of contrived Lim and Carrot broth-enriched vaginal/rectal swab matrices, demonstrating that the analytical sensitivity of the Solana GBS Assay is independent of the type of broth culture medium used.

Table 3. Limits of Detection for the Solana GBS Assay

Culture Medium	Strain	Serotype	Confirmed LoD	
			CFU/mL [1]	CFU/Assay [2]
Lim Broth	ATCC BAA-611	V	5.9×10^5	1.4×10^3
	SS617	Ia	8.0×10^5	1.9×10^3
	SS618	Ib	7.1×10^5	1.7×10^3
	SS619	II	7.6×10^5	1.8×10^3
	ATCC 12403	III	2.6×10^6	6.3×10^3
	SS700	Ic	4.9×10^5	1.2×10^3
Carrot Broth	ATCC 12403	III	2.6×10^6	6.3×10^3

ATCC: American Type Culture Collection
[1] CFU/mL of vaginal/rectal swab culture medium
[2] Number of CFU per amplification reaction

Inclusivity (Analytical Reactivity)
The inclusivity of the Solana GBS Assay was evaluated by testing 14 different strains of *S. agalactiae* in addition to those included in the LoD Study (**Table 4**). Each strain was tested in triplicate in Lim broth cultured vaginal/rectal swab matrix at the claimed LoD target level (2.6×10^6 CFU/mL of culture medium). All the replicates of each of strain produced positive results. These results are acceptable.

Table 4. Strains of *S. agalactiae* evaluated in the Inclusivity Study for the Solana GBS Assay

Strain	Serotype	Strain	Serotype
ATCC 12973	II	ATCC 4768	Not typed
CCUG 28551	IV	ATCC 7077	
CCUG 29785	VI	ATCC 9925	
CNCTC 6609	VII	ATCC 12927	
ATCC BAA-2669	VIII	ATCC 27956	
ATCC BAA-2668	IX	ATCC 55191	
ATCC 49449	X	ATCC 55194	

ATCC: American Type Culture Collection

Bioinformatic Analysis
The inclusivity of the Solana GBS Assay primers and probes for the detection of GBS was analyzed *in silico* using the Basic Local Alignment Search Tool (BLAST). Overall, the region was shown to be highly conserved. One strain of *S. agalactiae* was found to have a single mismatch near the middle of the reverse primer, although this is not predicted to have an adverse effect of amplification/detection. These results are acceptable.

e. *Analytical specificity:*

Cross-reactivity Study
The analytical specificity of the Solana GBS Assay was evaluated by testing a panel of 97 organisms and viruses that may be found in vaginal/rectal specimens, as well as human DNA (**Table 5**). Three replicates of each potentially cross-reactive organism

or virus were prepared using Lim broth vaginal/rectal swab culture matrix. Bacteria and yeast species were tested at 10^6 CFU/mL of vaginal/rectal swab culture medium, while viruses were tested at 10^5 $TCID_{50}$/mL. No false positive or Invalid results were obtained. These results are acceptable.

Table 5. Organisms and viruses evaluated for potential cross-reaction and/or interference in the Solana GBS Assay

Gram Negative (43)	**Gram Positive (36)**
Acinetobacter baumanii	*Abiotrophia defectiva*
Aeromonas hydrophila (2 strains)	*Bacillus cereus*
Alcaligenes faecalis subsp. *faecalis*	*Bacillus subtilis* (2 strains)
Bacteroides fragilis (2 strains)	*Bifidobacterium adolescentis* (2 strains)
Campylobacter fetus	*Clostridium bifermentans*
Campylobacter hyointestinalis	*Clostridium butyricum*
Campylobacter jejuni (2 strains)	*Clostridium difficile*
Citrobacter freundii	*Clostridium haemolyticum*
Edwardsiella tarda	*Clostridium novyi*
Enterobacter aerogenes	*Clostridium orbiscindens*
Enterobacter cloacae	*Clostridium perfringens*
Escherichia coli	*Clostridium septicum*
Escherichia fergusonii	*Clostridium sordellii*
Helicobacter pylori	*Clostridium sporogenes*
Klebsiella oxytoca	*Enterococcus faecalis*
Klebsiella pneumoniae	*Enterococcus faecium*
Legionella pneumophila	*Lactobacillus acidophilus*
Mobiluncus mulieris	*Listeria monocytogenes*
Moraxella cartarrhalis	*Peptostreptococcus anaerobius*
Morganella morganii	*Staphylococcus aureus*
Neisseria gonorrhoeae	*Staphylococcus epidermidis*
Pleisiomonas shigelloides	*Streptococcus* Group C
Porphyromonas asaccharolytica	*Streptococcus mutans*
Prevotella melaninogenica	*Streptococcus pyogenes*
Proteus mirabilis	*Streptococcus bovis*
Providencia alcalifaciens	*Streptococcus dysgalactiae*
Pseudomonas aeruginosa	*Streptococcus gordonii*
Pseudomonas fluorescens	*Streptococcus intermedius*
Salmonella choleraesius (typhimurium)	*Streptococcus mitis*
Salmonella enterica arizonae	*Streptococcus oralis*
Salmonella enterica enterica serovar *typhimurium*	*Streptococcus pneumoniae*
Salmonella enterica indica	*Streptococcus salivarius*
Serratia liquefaciens	*Streptococcus suis*
Serratia marcescens	*Streptococcus uberis*
Shigella boydii	

Gram Negative (43)	Gram Positive (36)
Shigella flexneri	
Shigella sonnei	
Stenotrophomonas maltophilia	
Vibrio parahaemolyticus	
Yersinia enterocolitica	
Other (8)	
Candida albicans	*Gardnerella vaginalis*
Candida glabrata	*Trichomonas vaginalis* [2]
Candida parapsilosis	*Ureaplasma urealyticum* [3]
Chlamydia trachomatis [1]	Human Genomic DNA [3]
Viruses (11)	
Adenovirus	Herpes Simplex Virus 1 (Macintyre)
Cytomegalovirus	Herpes Simplex Virus 2 (G)
Coxsackie virus	Norovirus
Echovirus	Rotavirus
Enterovirus	Varicella Zoster Virus
Human Papillomavirus 16 [4]	

[1] Tested at 10^6 IFU (Inclusion Forming Units)/mL
[2] Tested at 10^6 trichomonads/mL
[3] Tested at 10^6 copies/mL
[4] Tested at 10^5 copies/mL

Bioinformatic Analysis
In silico analysis using the Basic Local Alignment Search Tool (BLAST) was performed to evaluate the potential for cross-reaction of the Solana GBS Assay primers and probes with non-target organisms. No significant similarity was observed between the Solana *atoB* amplicon, primers or probes and sequences from other species. These results are acceptable.

Contamination Study
The potential for false-positive results with the Solana GBS Assay due to within run or between run cross-contamination was evaluated by testing an alternating series of *S. agalactiae* "high positive" and negative samples in successive instrument runs, in addition to Positive and Negative External Controls. The high positive samples contained *S. agalactiae* at a concentration of 1.8×10^8 CFU/mL of Lim broth vaginal/rectal matrix. Negative samples comprised simulated throat swab matrix alone. The expected results were obtained for all *S. agalactiae* positive and negative samples (50/50 each). Each of the Positive and Negative External Controls also produced the expected results (10/10 each). These results are acceptable.

f. Assay cut-off:

The algorithm parameters for the Solana GBS Assay were established through analysis of fluorescence amplification curves obtained from testing known GBS positive and negative samples on the Solana Instrument. The cut-offs were chosen to

optimize sensitivity for detection of GBS and minimize Invalid test results due to failure of the Process Control.

g. *Assay interference:*

Potentially Interfering Substances
The potential for interference with the Solana GBS Assay was evaluated with endogenous and exogenous substances that may be present in vaginal/rectal swab specimens (**Table 6**). Each substance was tested in triplicate in the presence and absence of *S. agalactiae* at 2X LoD (5.2×10^6 CFU/mL) using samples prepared with Lim broth-enriched vaginal/rectal matrix. No false positive, false negative or Invalid test results were observed under any of the conditions tested. These results are acceptable.

Table 6. Substances evaluated for potential interference with the Solana GBS Assay

Substance	Test Concentration [1]
Amniotic Fluid	2% (v/v)
Baby Powder	0.1% (w/v)/µL [2]
Barium sulfate	0.1 mg/mL
Benzalkonium Chloride Towelettes	0.002% (v/v)
Body Powder	0.1% (w/v)/µL [2]
Cortizone 10 (Hydrocortisone)	0.1% (w/w)/µL [2]
Desitin (Zinc Oxide)	0.1% (w/w)/µL [2]
Ethanol	0.2% (v/v)
Fecal Fat - Palmitic acid	0.026 mg/mL
Fecal Fat - Stearic Acid	0.52 mg/mL
Fecal Sugar - Dextrose	0.02 mg/mL
Fleet Mineral Oil Enema	0.2% (v/v)
Gynol II Vaginal Contraceptive (Nonoxynol-9)	0.1% (w/w)/µL [2]
Hemoglobin	0.064 mg/mL
Hemorrhoidal Cream	0.1% (w/v)/µL [2]
Human Serum Albumin	0.2 mg/mL
Imodium AD (Loperamide)	0.02 mg/mL
KY Jelly	0.1% (w/v)/µL [2]
Meconium	0.1% (w/v)/µL [2]
Miconazole Nitrate Salt	0.04% (w/v)
Mucin	0.06 mg/mL
Mylanta ($Al(OH)_3$, $Mg(OH)_3$)	0.002 mg/mL
Nystatin	200 U/mL
Pepto Bismol (Bismuth subsalicylate)	0.017 mg/mL
Petroleum Jelly	0.1% (w/v)/µL [2]
Preparation H (Phenylephrine)	0.04% (w/v)
Prilosec (Esomeprazole magnesium hydrate)	0.01 mg/mL
Stool	0.1% (w/v)/µL [2]
Tagamet (Cimetidine)	0.01 mg/mL
Triclosan	0.002% (w/v)
Tucks Personal Cleaning Pads (Witch-hazel)	2% (v/v)
Tums (Calcium carbonate)	0.01 mg/mL
Urine	2% (v/v)
Whole Blood	2% (v/v)

[1] Concentration in the cultured vaginal/rectal swab Lim broth matrix
[2] 0.1% of the quantity adsorbed on the collection swab/µL of matrix

Microbial Interference

The potential for interference with the Solana GBS Assay by organisms and viruses that may be present in vaginal/rectal swab specimens was evaluated using the same list of species that were evaluated for potential cross-reactivity (**Section M(1)(e)**; **Table 5**). Testing was performed by mixing each potentially interfering organism or virus with *S. agalactiae* strain ATCC 12403 at a concentration of 2X LoD in Process Buffer containing Lim broth-enriched vaginal/rectal swab matrix. For bacteria and yeasts, the final concentrations were 10^6 CFU/mL, while viruses were tested at 10^5 $TCID_{50}$/mL (except as noted in **Table 5**). No false negative or Invalid results were obtained with any of the organisms or viruses tested. These results are acceptable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not applicable.

   b. *Matrix comparison:*

      The LoD of the Solana GBS Assay was initially established using samples prepared with matrix derived from Lim broth vaginal/rectal swab cultures. The claimed LoD was subsequently confirmed by testing samples prepared in matrix derived from Carrot broth vaginal/rectal swab cultures. Refer to **Section M(1)(d)**. Additional studies also demonstrated that equivalent Solana GBS Assay results are obtained with Lim and Carrot broth cultures that are incubated for 18 or 24 hours.

3. Clinical studies:

   a. *Clinical Sensitivity:*

      The performance of the Solana GBS Assay was evaluated in a prospective Clinical Study that was performed at four (4) sites in the U.S. Vaginal/rectal swab specimens were obtained from a total of 753 pregnant women at between 35 and 37 weeks of gestation. The age of the subjects ranged from 15 to 44 years old. The specimens were inoculated into either Lim broth (403) or Carrot broth (350) and incubated for between 18 and 24 hours at 35°C after which the cultures were tested using the Solana GBS Assay and the results were compared to those obtained from subculture of the broth to blood agar, followed by Gram staining of suspected colonies of *S. agalactiae*, catalase testing (*S. agalactiae* is catalase negative) and latex agglutination using GBS-specific reagents. The results of the study are summarized in **Table 7**. One specimen produced repeated Invalid results with the Solana assay and was excluded from the analysis of performance.

Table 7. Performance of the Solana GBS Assay with enriched vaginal/rectal swab cultures in comparison to conventional microbiological isolation and identification of *S. agalactiae*

Lim Broth		**Reference Method**		
		Positive	**Negative**	**Total**
Solana GBS Assay	**Positive**	88	13 [1]	**101**
	Negative	0	301	**301**
	Total	**88**	**314**	**402**
Sensitivity		88/88 = 100% (95% CI: 95.8-100%)		
Specificity		301/314 = 95.9% (95% CI: 93.0-97.6%)		
Positive Predictive Value		88/101 = 87.1% (95% CI: 79.2-92.3%)		
Negative Predictive Value		301/301 = 100% (95% CI: 98.7-100%)		
Carrot Broth		**Reference Method**		
		Positive	**Negative**	**Total**
Solana GBS Assay	**Positive**	97	10 [2]	**107**
	Negative	0	243	**243**
	Total	**97**	**253**	**350**
Sensitivity		97/97 = 100% (95% CI: 96.2-100%)		
Specificity		243/253 = 96.0% (95% CI: 92.9-97.8%)		
Positive Predictive Value		97/107 = 90.7% (95% CI: 83.6-94.8%)		
Negative Predictive Value		243/243 = 100% (95% CI: 98.4-100%)		
Lim & Carrot Broth Combined		**Reference Method**		
		Positive	**Negative**	**Total**
Solana GBS Assay	**Positive**	185	23 [3]	**208**
	Negative	0	544	**545**
	Total	**185**	**567**	**752**
Sensitivity		185/185 = 100% (95% CI: 98.0-100%)		
Specificity		544/567 = 95.9% (95% CI: 94.0-97.3%)		
Positive Predictive Value		185/208 = 88.9% (95% CI: 84.0-92.5%)		
Negative Predictive Value		301/301 = 100% (95% CI: 99.3-100%)		

[1] 12/13 (92.3%) cultures were positive by another FDA-cleared test method
[2] 7/10 (70.0%) cultures were positive by another FDA-cleared test method
[3] 19/23 (82.6%) cultures were positive by another FDA-cleared test method

The sensitivity and specificity of the Solana GBS Assay for the detection of *S. agalactiae* in Lim broth cultures compared to standard microbiological isolation and identification were 100% (95% Confidence Interval: 95.8-100%) and 95.9% (95% CI: 93.1-97.6%), respectively. Whereas with Carrot broth, the sensitivity and specificity

were 100% (95% CI: 96.2-100%) and 96.0% (95% CI: 92.9-97.8%), respectively. Overall, for both types of broth culture combined, the sensitivity and specificity were 100% (95% CI: 98.0-100%) and 95.9% (95% CI: 94.0-97.3%).

The performance of the Solana GBS Assay with each type of broth culture medium, stratified by clinical site is shown in **Table 8**. The point estimate for sensitivity relative to conventional culture was 100% at each site, irrespective of the type of enrichment broth, while the specificity of the Solana GBS Assay ranged from 93.4 to 100% with Lim broth, and 94.7 to 97.1% with Carrot broth.

Table 8. Performance of the Solana GBS Assay stratified by clinical site and culture medium

Culture Medium	Site Number	Culture Positive (%)	Solana GBS (%; 95% Score Confidence Interval)	
			Sensitivity	Specificity
Lim Broth	1	33/147 (22.4)	33/33 (100; 89.6-100)	114/114 (100; 96.7-100)
	3 [1]	42/181 (23.2)	42/42 (100; 91.6-100)	130/139 (93.5; 88.2-96.6)
	4	13/74 (17.6)	13/13 (100; 77.2-100)	57/61 (93.4; 84.3-97.4)
	Overall	**88/402 (21.9)**	**88/88 (100; 95.8-100)**	**301/314 (95.9; 93.0-97.6)**
Carrot Broth	2	44/183 (24.0)	44/44 (100; 92.0-100)	135/139 (97.1; 92.8-98.9)
	3 [1]	53/167 (31.7)	53/53 (100; 93.2-100)	108/114 (94.7; 90.0-97.6)
	Overall	**97/350 (27.7)**	**97/97 (100; 96.2-100)**	**243/253 (96.0; 92.9-97.8)**
Total		**185/752 (24.6)**	**185/185 (100; 98.0-100)**	**544/567 (95.9; 94.0-97.3)**

[1] At Site 3, testing with the Solana GBS Assay was performed sequentially using Lim and Carrot broth enrichment media; the first 181 contiguous specimens were inoculated into Lim broth and the next 167 were cultured in Carrot broth

The overall performance of the Solana GBS Assay in comparison to conventional microbiological identification of *S. agalactiae* in Lim and Carrot broth enrichment cultures of vaginal/rectal swabs is acceptable.

b. Clinical specificity:

Refer to **Section M(3)(a)**, above.

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

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The performance of the Solana GBS Assay was evaluated in a prospective Clinical Study of pregnant women conducted at four sites in the U.S. (**Section M(3)(a)**). Overall, the prevalence of GBS colonization as determined by the Solana GBS Assay was 27.7% (208/752) whereas by conventional culture it was 24.6% (185/752). In **Table 9**, the prevalence as determined by the Solana assay is shown stratified by clinical site and the type of broth culture used.

Table 9. Observed prevalence of GBS colonization in pregnant women as determined by the Solana GBS Assay, stratified by clinical site and culture medium

Culture Medium	Site	Number	Solana Positive	% Prevalence
Lim Broth	1	147	33	22.4
	3	181	51	28.2
	4	74	17	23.0
	Overall	**402**	**101**	**25.1**
Carrot Broth	2	183	48	26.2
	3	167	59	35.3
	Overall	**350**	**107**	**30.6**
Combined	**Overall**	**752**	**208**	**27.7**

[1] At Site 3, testing with the Solana GBS Assay was performed sequentially using Lim and Carrot broth enrichment media; the first 181 contiguous specimens were inoculated into Lim broth and the next 167 were cultured in Carrot broth

N. Instrument Name:

Solana Instrument

O. System Descriptions:

1. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes____X____ or No _____

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes _____ or No ____X____

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:

   Specimens are identified by scanning a barcode or by manual entry.

4. Specimen Sampling and Handling:

   Swab specimens are cultured in Lim or Carrot broth for 18-24 hours after which 50µL the medium is transferred to a tube containing Process Buffer which is then heated at 95±2°C for 5 min to lyse the target organisms. A 50µL aliquot of the lysate is then used to rehydrate Reaction Tubes that contain lyophilized reagents for amplification and detection of the target sequence (and Process Control). Refer to **Sections I** and **L** for additional details.

5. Calibration:

   The end user is not required to calibrate the instrument. Automated calibration happens by comparing between the measured magnitude of the optical signal of and an integrated calibration standard and the expected magnitude of the optical signal.

6. Quality Control:

   Refer to **Section M(1)(a)** and **Section M(1)(c)** for information on the internal and external controls associated with the Solana GBS Assay and their performance.

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

Not applicable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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