510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K163042

B. Purpose for Submission:

To obtain a substantial equivalence determination for chromID Strepto B agar for the qualitative detection of Group B Streptococcus (GBS)

C. Measurand:

Group B Streptococcus (GBS)

D. Type of Test:

Detection of GBS using a selective and differential chromogenic medium

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

chromID® Strepto B agar

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2360

2. Classification:

   Class I (non-exempt)

3. Product code:

   PQZ

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

   chromID® Strepto B agar is a selective chromogenic medium that is intended to aid in the qualitative determination of Group B Streptococcus (GBS) colonization in pregnant women. This medium supports the growth of, but does not differentiate between, hemolytic and non-hemolytic GBS strains. The test is performed on 18-24 hour LIM broth enrichments of vaginal/rectal swabs obtained from pregnant women. chromID® Strepto B agar results can be interpreted after 24 hours incubation with confirmation of characteristic GBS colonies from the media.

   chromID® Strepto B agar is not intended to diagnose infection nor to guide or monitor treatment for infections. chromID® Strepto B agar does not provide susceptibility results. Subculture to non-selective media should be performed as needed for susceptibility testing. chromID® Strepto B agar is intended for use by laboratory health practitioners in a clinical laboratory.

2. Indication(s) for use:

   Same as the Intended Use.

3. Special conditions for use statement(s):

   Presumptive GBS colonies (pale pink to red colonies) should be confirmed by a biochemical or laboratory test.

4. Special instrument requirements:

   Not Applicable

I. Device Description:

chromID Strepto B agar is a selective chromogenic medium used for the screening of *Streptococcus agalactiae* (*S. agalactiae*) carriage in pregnant women from LIM broth enrichments of vaginal/rectal swabs. The medium contains antibiotics and synthetic substrates that enable the screening of *S. agalactiae* by the appearance of pale pink to red colonies. Growth of microorganisms belonging to other species is either inhibited, or if there is growth, the colonies appear as different colored colonies.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Modified Selective Streptococcus Agar

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

   K881577

3. Comparison with predicate:

Similarities		
Item	chromID Strepto B Agar (K163042)	Acumedia Modified Selective Streptococcus Agar (K881577)
Intended Use	chromID® Strepto B agar is a selective chromogenic medium that is intended to aid in the qualitative determination of Group B Streptococcus (GBS) colonization in pregnant women. This medium supports the growth of, but does not differentiate between, hemolytic and non-hemolytic GBS strains. The test is performed on 18-24 hour LIM broth enrichments of vaginal/rectal swabs obtained from pregnant women. chromID® Strepto B agar results can be interpreted after 24 hours incubation with confirmation of characteristic GBS colonies from the media. chromID® Strepto B agar is not intended to diagnose infection nor to guide or monitor treatment for infections. chromID® Strepto B agar does not provide susceptibility results. Subculture to non-selective media should be performed as needed for susceptibility testing. chromID® Strepto B agar is intended for use by laboratory health practitioners in a clinical laboratory.	Selective agar medium for the isolation and detection of pathogenic *Streptococci*
Reading	Manual	Manual
Culture Media Type	Selective agar	Selective agar

Differences		
Item	chromID Strepto B Agar (K163042)	Acumedia Modified Selective Streptococcus Agar (K881577)
Organism(s) Detected	GBS	*Streptococcus* species
Growth Detection	Pale pink to red colonies after 24 hrs	Colonies with/without hemolysis (alpha-hemolysis or beta-hemolysis)
Starting Material	Enriched LIM broth culture of vaginal/rectal swabs	Direct Specimen
Culture Media Type	Chromogenic agar	No chromogenic substrates

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

L. Test Principle:

chromID Strepto B agar is a selective, differential medium for the detection of GBS. The ability to detect GBS is based on the presence of an antibiotic mixture that selectively suppresses growth of organisms other than GBS, and the presence of chromogenic substrates that allow the identification of presumptive GBS colonies. Vaginal/rectal swabs from antepartum women are enriched in LIM broth and inoculated directly onto chromID Strepto B agar plates and incubated aerobically at 35°-37°C for 24 hrs. The cultures are examined after 24 hrs incubation for the presence of light pink to red colonies, which are then confirmed by biochemical methods. No growth or colonies presenting as other than pale pink to red in appearance should be interpreted as a negative result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated at three sites using a blinded panel of eleven well-characterized strains, which included 10 *S. agalactiae* strains and one *Staphylococcus aureus* strain. Both hemolytic and non-hemolytic strains of GBS were tested. At each site, panel members were tested in triplicate at 1.5 $x10^3$ CFU/ml with three different lots of chromID Strepto B agar each day for five days. chromID Strepto B agar plates were observed for the growth of pale pink to red colonies at 24 hrs. All strains produced the expected results with the chromID Strepto B agar at 24 hrs (990/990). Isolates were also plated onto Tryptic Soy Agar with 5% sheep blood to ensure viability and purity of cultures.

b. Linearity/assay reportable range:

Not Applicable

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

Quality control (QC) testing was performed at each testing site for growth/color development on chromID Strepto B agar. Two quality control organisms (*Streptococcus agalactiae* ATCC 12386 and *Staphylococcus aureus* ATCC 6538) were tested at each study site on chromID Strepto B agar for each day of testing. The strains were also subcultured to Trypticase Soy Agar with 5% sheep blood to ensure viability of the organisms. The positive control was tested at a level of 1.5×10^3 CFU/ml, while the negative control was tested at a concentration of 1.5×10^6 CFU/ml. QC testing results provided expected reactions across each testing site (Table 1). The submitted QC data are acceptable.

Table 1. QC Data Summary

QC Strain	Expected Results after 24 hrs at 35-37°C	QC Results (all sites)
Staphylococcus aureus ATCC 6538	No growth	107/107
Streptococcus agalactiae ATCC 12386	Growth-pale pink to red colonies	107/107

d. *Detection limit:*

Recovery Study

A Recovery Study was performed with two GBS strains (ATCC 12386 and ATCC 13813). After preparing six serial dilutions per strain in saline and plating on chromID Strepto B agar, growth and colony color were evaluated after 18 hrs, 24 hrs, and 48 hrs of incubation at 35°C-37°C. The minimum concentration of GBS reliably detected by chromID Strepto B agar at 24 hrs was 10^3 CFU/ml. At 10^2 CFU/ml, growth of non-characteristic colonies (grey) was observed at 18 hrs incubation for one GBS Strain (ATCC 13813). The use of LIM broth in place of saline did not have an impact on the LoD.

Analytical Reactivity

A study was conducted to demonstrate the sensitivity of chromID Strepto B agar to detect various GBS strains at a concentration of 10^3 CFU/ml. The study included 20 GBS strains (15 hemolytic, 5 non-hemolytic) from bioMérieux stock and other commercial collection sites as shown in Table 2 below.

Table 2. GBS Panel for Inclusivity Testing

Panel Member	GBS Serotype	Collection	Strain ID	Hemolytic
1	Unknown	ATCC	BAA-2575	Yes
2	II	ATCC	12973	Yes
3	Unknown	ATCC	BAA-2576	Yes
4	Unknown	ATCC	12386	Yes

5	Ic	ATCC	27591	Yes
6	Unknown	ATCC	624	Yes
7	Ib	NCTC	8180	No
8	Ia	NCTC	9993	Yes
9	III	ATCC	BAA-1176	Yes
10	IV	ATCC	49446	Yes
11	V	ATCC	BAA-611	Yes
12	VI	ATCC	BAA-2671	Yes
13	VII	ATCC	BAA-2670	Yes
14	VIII	ATCC	BAA-2669	Yes
15	IX	ATCC	BAA-2668	Yes
16	III	ATCC	12403	Yes
17	Unknown	ATCC	13813	No
18	Unknown	bioMérieux	8602036	No
19	Unknown	bioMérieux	8706019	No
20	Unknown	bioMérieux	8709013	No

Results demonstrated that 17/20 GBS strains were detected with typical growth on chromID Strepto B agar plates at 24 hrs, while all 20 organisms were detected at 48 hrs. Table 3 below shows results from the Analytical Reactivity Study.

Table 3. Analytical Reactivity Study Results at 18, 24 and 48 hrs.

Organism	Number of Strains	18 hr Results		24 hr Results		48 hr Results	
		Growth with Pale Pink to Red Color	% Detected	Growth with Pale Pink to Red Color	% Detected	Growth with Pale Pink to Red Color	% Detected
GBS	20	12/20	60% (11-hemolytic) (1-non-hemolytic)	17/20	85% (13-hemolytic) (4-non-hemolytic)	20/20	100%

Incubation Study

An Incubation Study was performed to determine the effect of various incubation times on the performance of chromID Strepto B agar when tested with ten GBS strains (hemolytic and non-hemolytic) at 10^3 CFU/ml concentration. The growth of characteristic colonies was evaluated every hour from 18-28 hrs and every hour from 44-52 hrs. At the earliest time point (16 hrs), 5 of 10 GBS strains grew as characteristic colonies. By 24 hrs, 8 of 10 GBS strains were detected. All GBS strains were detected after 44 hrs.

e. Analytical specificity:

Cross-Reactivity Study

In order to evaluate the performance of chromID Strepto B agar with microorganisms potentially encountered in vaginal/rectal swabs, a Cross-Reactivity Study was completed with 88 strains (gram negative bacteria, gram positive bacteria, and yeast) at approximately10^6 CFU/ml. Results showed that 68 organisms from the cross-reactivity panel did not grow on chromID Strepto B agar at 24 hrs.

Table 4 below shows a list of organisms yielding pale pink to red colonies on chromID Strepto B agar after 24 hrs.

Table 4. Cross-Reactivity Study Results

Incubation Time	Total Strains Tested	# Strains Growing on chromID Strepto B agar	Strains with Pale Pink to Red Colonies	
			# Strains	Organism Name
24 hrs	88	20/88	3	• (1) *Streptococcus Group C* • (1) *Streptococcus mitis* • (1) *Klebsiella pneumoniae (KPC)*

Interference Study

The purpose of this study was to evaluate the impact of potentially interfering substances commonly found in vaginal/rectal swab specimens on the detection of two GBS strains (hemolytic and non-hemolytic) at approximately 10^3 CFU/ml. Growth of GBS with characteristic colors (pale pink to red) was evaluated in the presence of 15 interfering substances and 6 human samples.

Interfering substances were tested at physiologically or biologically relevant concentrations and mixed with bacterial suspensions. Naproxen sodium (27.5 mg/ml) or topical product (body powder at 0.125 g/ml) may demonstrate partial inhibition of growth on GBS with chromID Strepto B agar. Use of compounds containing the active ingredients below had an inhibitory effect on GBS growth that was unrelated to chromID Strepto B medium performance: nystatin (10^4 UI/ml), hydrocortisone (0.625 mg/ml), aluminum hydroxide (2.125 mg/ml)/magnesium hydroxide (2.250 mg/ml), mesalazine (5 mg/ml), barium sulfate (5 mg/ml), esomeprazole (1 mg/ml), loperamide (1 mg/ml), sennosides (40 mg/ml), metronidazole (25 mg/ml), lidocaine (2.5 mg/ml), econazole (7.2 mg/ml), naproxen sodium (27.5 mg/ml), nonoxynol-9 (one condom/50 ml sterile water; used at 1:1 dilution), benzalkonium chloride (1 wipe/100 ml sterile water; used at 1:1 dilution). Benzalkonium chloride had to be diluted (1/10, 1/100, and 1/1000) before growth was observed on both the control plates (Tryptic Soy Agar with 5% sheep blood) and chromID Strepto B agar plates.

Despite the reduction in growth, characteristic GBS colonies were recovered on chromID Strepto B agar plates in the presence all interfering substance panel members. GBS detection was not significantly affected by vaginal fluid, amniotic fluid, sperm, whole blood, concentrated buffy coat, or stool.

Mixed Infection Study

A Mixed Infection Study was conducted to demonstrate that high levels of non-target organism will not suppress growth of GBS. Table 5 below shows a list of non-target organisms included in the study.

Table 5. List of Non-Target Organisms Included in the Mixed Infection Study

• *Klebsiella pneumoniae* (ATCC BAA-1900, KPC) • *Staphylococcus aureus* (ATCC 43300, MRSA) • *Streptococcus* group C (NCTC 8546) • *Streptococcus pyogenes* (ATCC 19615) • *Streptococcus mitis* (ATCC 6249) • *Lactobacillus sakei* (0706001) • *Streptococcus anginosus* (9501029)

The panel of seven non-target organisms included strains capable of producing characteristic or non-characteristic colonies after 24 hrs growth on chromID Strepto B medium. Two GBS strains (one hemolytic and one non-hemolytic) were incubated at approximately 10^3 CFU/ml with each non-target organism. At 24 hrs, both GBS strains were detected in the presence of 10^8 CFU/ml of non-target strains in the Mixed Infection Study, except in the presence of *Streptococcus* Group C (NCTC 8546). Growth of the two GBS strains in the presence of the *Streptococcus* Group C strain (10^8 CFU/ml) produced purple colonies instead of the expected pale pink to red colonies. Upon decreasing the concentrations of non-target organisms (10^3-10^7 CFU/ml), both GBS strains grew as the characteristic colony color. At 10^8 CFU/ml, 5/7 non-target organisms gave characteristic colonies when grown on chromID Strepto B medium; however, at 10^5 CFU/ml, it was observed that non-target organisms either did not grow or grew as non-characteristic colonies on chromID Strepto B agar in the presence of both GBS strains at 24 hrs. For those non-target strains yielding pink to red colonies on chromID Strepto B agar, colony features were used to distinguish GBS from the non-target organisms. Results of the study revealed GBS was still detected on chromID Strepto B agar in the presence of high levels of non-target organisms.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not Applicable. Compared to Standard Reference Method

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

chromID Strepto B culture medium was evaluated at three clinical sites. A total of 681 enriched LIM broth cultures (18-24 hrs) of vaginal/rectal swab specimens from pregnant women were included in the performance calculations for chromID Strepto B agar. Five cultures and 60 isolates were excluded because sample acceptance criteria were not met or there were protocol deviations. One culture was excluded because *S. agalactiae* was not confirmed for one of two characteristic colonies recovered on chromID Strepto B medium from the same culture sample.

All enriched LIM broth cultures were inoculated onto the following media:

- chromID Strepto B agar
- Columbia blood agar with Colistin and Nalidixic Acid (CNA)

For the Reference Culture Method, turbid LIM broth cultures were subcultured to CNA plates, and all suspicious colonies were screened to confirm or rule-out the presence of GBS using established laboratory methods: gram stain, catalase, PYR testing, and latex agglutination. If LIM broth or CNA plates were negative after 24 hrs incubation, cultures were re-incubated an additional 24 hrs before calling samples negative by the Reference Culture Method.

After enrichment, an aliquot of culture was taken for inoculation onto chromID Strepto B agar. Plates were incubated at 35°C-37°C for 24 hrs under aerobic conditions with minimal light exposure. Pale pink to red colonies detected on chromID Strepto B agar plates after 24 hrs of incubation were suggestive of GBS. All colonies growing on chromID Strepto B medium were evaluated for the study and characterized using one or more of the following laboratory tests: gram stain, catalase, PYR testing, and latex agglutination. VITEK MS was used to identify all organisms growing on chromID Strepto B agar plates and GBS colonies by the Reference Method. Performance (sensitivity and specificity) of chromID Strepto B medium compared to the Reference Culture Method is presented in Table 6 below**.**

Table 6. Comparison between chromID Strepto B medium and Reference Culture Method

	Reference Culture Method		
chromID Strepto B (24 hr result)	Positive	Negative	Total
Positive[a]	172	40[c]	212
Negative[b]	4[d]	465	469
Total	176	505	681
	Sensitivity: 97.7%, 95%CI: 94.3%-99.1% Specificity: 92.1%, 95%CI: 89.4%-94.1%		

[a]Positive—pale pink to red colonies on chromID Strepto B agar

[b]Negative—colorless colonies or colony colors other than pale pink to red on chromID Strepto B agar

[c]40 discordant samples (FP) were observed. Of these 40 chromID Strep B pale pink to red colonies, four were confirmed as GBS by biochemical testing and VITEK MS identification. Thirty six samples grew pale pink to red colonies on chromID Strepto B plates that were not GBS. An additional eight FP samples were observed after 48 hrs of incubation on chromID Strepto B plates.

[d]4 discordant samples (FN) were observed. 3 of 4 samples that did not grow pale pink to red colonies after 24 hrs of incubation on chromID Strepto B plates grew colonies indicative of GBS at 48 hrs.

b. Clinical specificity:

See 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 overall prevalence of GBS by the Reference Culture Method was 25.8% (176/681).

N. Proposed Labeling:

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

O. Conclusion:

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