

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

A. 510(k) Number:

K091489

B. Purpose for Submission:

To determine substantial equivalence for the Clearview Advanced Strep A test

C. Measurand:

Group A Streptococcus antigen

D. Type of Test:

Lateral flow immunochromatographic assay

E. Applicant:

Binax Inc.

F. Proprietary and Established Names:

Clearview Advanced Strep A test

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3740 - Streptococcus spp. Serological Reagents

2. Classification:

Class I

3. Product code:

GTY – Antigens, All Groups, Streptococcus spp.

4. Panel:

83 (Microbiology)

H. Intended Use:

1. Intended use(s):

The Clearview Advanced™ Strep A test is a rapid chromatographic immunoassay for the qualitative detection of Strep A antigen from throat swab specimens as an aid in the diagnosis of Group A Streptococcal infection.

2. Indication(s) for use:

The Clearview Advanced™ Strep A test is a rapid chromatographic immunoassay for the qualitative detection of Strep A antigen from throat swab specimens as an aid in the diagnosis of Group A Streptococcal infection.

3. Special conditions for use statement:

For prescription use only.

4. Special instrument requirements:

None

I. Device Description:

The Clearview Advanced™ Strep A test is a qualitative, lateral flow immunoassay for the detection of Streptococcus A (Strep A) carbohydrate antigen directly from a throat swab sample. The contents of the test kit are as follows:

- 30 Test Packs: Each pack includes 1 Test Strip, 1 coated Extraction Tube, and 1 Workstation
- 30 Sterile Swabs
- 31 Reagent 1 (R1) Vials
- 1 Positive Control (Nonviable Group A Streptococci; 0.09% NaN₃)
- 1 Negative Control (Nonviable Group C Streptococci; 0.09% NaN₃)
- 1 Package Insert

J. Substantial Equivalence Information:

1. Predicate device name(s):

Genzyme OSOM Ultra Strep A Test

2. Predicate K number(s):

K992658

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the qualitative detection of Strep A antigen from throat swab specimens	Same
Specimen	Throat swab	Same
Assay technique	Chromatographic immunoassay	Same

Differences		
Item	Device	Predicate
Labeled antibody location	Extraction tube coated with conjugate antibodies	Dual label technology-antibodies coated at 2 separate locations on the device
Results read	3 mins	5 mins

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

N/A

L. Test Principle:

To perform the test, Reagent 1 (R1) is added to the extraction tube, which is coated with a mixture of conjugate antibodies and a lytic enzyme extraction reagent. The lytic enzyme is mixed with colloidal gold conjugated to rabbit anti-Strep A and a second colloidal gold control conjugate antibody. The reagents are dried onto the bottom of an extraction tube forming a red spot. The extraction/conjugate pellet is resuspended with R1 and the throat swab is added to the extraction tube. The Strep A antigen is extracted from the sample and the swab is removed. The test strip is immediately placed in the extracted sample. If Group A Streptococcus is present in the sample, it will react with the anti-Strep A antibody conjugated to the gold particle. The complex will then be bound by the anti-Strep A capture antibody and a visible red test line will appear, indicating a positive result. To serve as an on-board procedural control, the blue line observed at the control site prior to running the assay will turn red, indicating that the test has been performed properly. If Strep A antigen is not present or present at very low levels, only a red control line will appear. If the red control line does not appear, or remains blue, the test result is invalid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Binax, Inc. conducted a masked reproducibility study of the Clearview Advanced™ Strep A test at three separate sites to demonstrate inter-site and intra-site reproducibility of test results obtained by six trained lab technicians. Each technician was provided with masked coded panels and tested six replicates of true negative samples (diluent only), moderate positive samples (positive 100% of the time), Limit of Detection (LoD) samples (C_{95} concentration, positive 95% of the time); and samples near the cut-off (C_{50} concentration, positive 50% of the time) per day on 5 different days. Each operator performed positive and negative control testing each day that sample panels were tested. The results of the reproducibility study were as follows:

Overall Percent Detection by Site for All Sample Types

Sample	Site 1 Detection	Site 2 Detection	Site 3 Detection	Overall Detection
Diluent (True Negative)	0% (0/60)	0% (0/60)	0% (0/59)*	0% (0/179)
1×10^5 (Moderate Positive)	100% (60/60)	98% (59/60)	100% (60/60)	99% (179/180)
1×10^4 (LOD/ C_{95} Concentration)	100% (60/60)	100% (60/60)	83% (50/60)	94% (170/180)
3.2×10^3 (Near the cut-off/ C_{50} Concentration)	80% (48/60)	58% (34/59)*	10% (6/60)	49% (88/179)

*2 invalid results excluded from the data analysis

Samples around the cut-off produce positive results sometimes and negative results sometimes. This variability is not necessarily due to site or operator disparities.

The specimens (samples) used to study variability consisted of a dilution series prepared from a 1×10^9 organisms/mL stock of *Streptococcus pyogenes*. 10µl of solution at various concentrations were inoculated onto sterile foam tipped swabs and dried for > 3 hours in a humidity-controlled environment. Each swab was individually pouched and assembled into blind panels. LoD studies were used to derive the sample concentrations tested.

b. *Linearity/assay reportable range:*

N/A

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

Sample storage and transport media (Amies and Stuart media) studies were conducted to support the storage conditions (time and temperature) of swabs prior to testing, and to support use of swabs stored in various types of transport media for testing in the Clearview Advanced Strep A assay. Swabs were inoculated at three concentrations of bacterial load, 5×10^8 , 1×10^5 and 1×10^4 organisms/test. Five swabs for each concentration per time point and temperature were evaluated in the assay with and without transport media. For blank swabs (no bacterial inoculation), two replicates were evaluated. All results were interpreted by 2 operators.

The swabs were stored at either 4°C or 30°C and tested at 4 hours, 24 hours, and 48 hours. Additionally, all swabs were tested immediately (within 15 minutes) of returning the swab to media or sheath. Positive and negative controls were run on each day of testing and yielded expected results. Results showed that all swabs not inoculated (no bacteria) tested negative in the Clearview Advanced™ Strep A test while all positive swabs generated a positive result. Thus tested media does not appear to interfere with the Clearview Advanced™ Strep A test performance and is appropriate for transport and storage of throat swab specimens intended for use with the Clearview Advanced™ Strep A test. Expected results were obtained at all temperatures and time points tested. The results indicate that Clearview Advanced™ Strep A Test performance is not impacted by the storage conditions tested in this study and recommended in the “Specimen Collection and Handling” section of the package insert.

d. *Detection limit:*

A concentrated stock (1×10^9 organisms/mL) of inactivated *Streptococcus pyogenes* (ATCC #19615) was spiked onto sterile foam swabs. Following coating, the swabs were dried in humidity controlled conditions and then run in the assay. Ten operators each interpreted two devices per dilution for 20 interpretations per dilution. The LoD of the Clearview Advanced Strep A test was determined to be 1×10^4 organisms per test.

Clearview Advanced™ LOD Study Results

Level (Organisms/Test)	Number Detected	% Detection
1×10^5	20/20	100
1×10^4 (LOD, C ₉₅)	18/20	90
7.5×10^3	15/20	75
3.2×10^3 (Cut-Off, C ₅₀)	10/20	50
1×10^3 (High Negative, C ₅)	1/20	5
Strep C (True Negative)	0/20	0
Diluent	0/20	0

e. Analytical specificity:

Cross-Reactivity

Potentially cross reacting organisms, obtained from The American Type Culture Collection (ATCC), were grown in culture and diluted to a final concentration of 1×10^7 - 1×10^8 organisms. Subsequently, all dilutions were tested in duplicate, using the Clearview Advanced™ test.

Cross-Reactivity Results

Organism (ATCC #)	Concentration (organisms/test)	
	1×10^8	1×10^7
<i>Streptococcus</i> Group B (31475)	-	-
<i>Streptococcus</i> Group C (12388)	-	-
<i>Streptococcus</i> Group F (12392)	-	-
<i>Streptococcus</i> Group G (12394)	-	-
<i>Streptococcus aeruginosus</i> (700231)	-	-
<i>Streptococcus mitis</i> (49456)	-	-
<i>Streptococcus mutans</i> (25175)	-	-
<i>Streptococcus oralis</i> (35037)	-	-
<i>Streptococcus pneumoniae</i> (49136)	-	-
<i>Streptococcus sanguis</i> (10556)	-	-

<i>Streptococcus salivarius</i> (13419)	-	-
<i>Arcanobacterium haemolyticum</i> (9345)	-	-
<i>Bordetella pertussis</i> (9797)	-	-
<i>Candida albicans</i> (10231)	-	-
<i>Corynebacterium diphtheriae</i> (12812)	-	-
<i>Enterococcus faecalis</i> (49474)	-	-
<i>Enterococcus faecium</i> (12952)	-	-
<i>Escherichia coli</i> (25922)	-	-
<i>Fusobacterium necrophorum</i> (25286)	-	-
<i>Haemophilus parahaemolyticus</i> (10014)	-	-
<i>Haemophilus parainfluenzae</i> (33392)	-	-
<i>Haemophilus influenzae</i> (49144)	-	-
<i>Klebsiella pneumoniae</i> (33495)	-	-
<i>Moraxella catarrhalis</i> (25238)	-	-
	Concentration (organisms/test)	
Organism (ATCC #)	1 x 10⁸	1 x 10⁷
<i>Moraxella lacunata</i> (11748)	-	-
<i>Neisseria gonorrhoeae</i> (49226)	-	-
<i>Neisseria lactamica</i> (23970)	-	-
<i>Neisseria meningitidis</i> (13077)	-	-
<i>Neisseria mucosa</i> (92981)	-	-
<i>Neisseria sicca</i> (9913)	-	-
<i>Neisseria subflava</i> (19243)	-	-
<i>Proteus vulgaris</i> (33420)	-	-
<i>Pseudomonas aeruginosa</i> (15442)	-	-
<i>Serratia marcescens</i> (13880)	-	-
<i>Staphylococcus aureus</i> (12600)	-	-
<i>Staphylococcus epidermidis</i> (14990)	-	-

<i>Staphylococcus haemolyticus</i> (29970)	-	-
<i>Yersinia enterocolitica</i> (9610)	-	-

None of the bacteria, viruses, or yeast tested cross reacted in the Clearview Advanced™ Strep A test at concentrations ranging from 10^7 to 10^8 organisms/test.

Interfering Substances

In this study, the sponsor measured and diluted each potentially interfering substance and split into aliquots. One aliquot was spiked with *S. pyogenes* to a final concentration of 2.5×10^4 organisms/test. The second aliquot contained no bacteria. Sterile foam swabs were dipped into each aliquot and allowed to absorb the liquid for up to 5 minutes prior to evaluation in the Clearview Advanced™ Strep A test. All aliquots were run in triplicate in the Clearview Advanced™ Strep A test. If interference was observed, testing was repeated at a reduced concentration to determine the highest concentration at which there was no interference. Positive and negative controls were run each day of testing and yielded the expected results. The results were as follows:

Interfering Substances Study Results

Substance	Testing Concentration	<i>S. pyogenes</i> (2.5×10^4)	OTC / Diluent Only
OTC Mouthwashes			
Listerine Antiseptic	20%	+	-
Listerine Cool Mint	20%	+	-
Crest Pro-Health Clean Night Mint	20%	+	-
OTC Lozenges			
Sucrets Complete (Cool Citrus)	10%	+	-
Halls Cherry Mentholypus	10%	+	-
Halls Plus Mentholypus	10%	+	-
Cepacol Cherry Sore Throat	10%	+	-
OTC Throat Sprays			
Cepacol Dual Relief	20%	+	-
Chloraseptic Max	20%	+	-
OTC Cough Syrups			
Tylenol Cough and Sore Throat	10%	+	-
Tussin (Guaifenesin Syrup) Rite	0.1%	+	-

Robitussin (Guaifenesin Syrup)	1%	+	-
Robitussin Nighttime Cough,	10%	+	-
Children's Dimetapp Cough Plus	10%	+	-
Children's Dimetapp DM Elixir	10%	+	-
ACTIVE INGREDIENTS			
Acetaminophen (Tylenol)	10mg/mL	+	-
Brompheniramine Maleate	5mg/mL	+	-
Chlorpheniramine Maleate	5mg/mL	+	-
Dextromethorphan HBr	5mg/mL	+	-
Diphenhydramine HCl	5mg/mL	+	-
Doxylamine Succinate	1mg/mL	+	-
Guaifenesin (Guaicol glyceryl	20mg/mL	+	-
Ibuprofen (Advil)	10mg/mL	+	-
Phenylephrine HCl	5mg/mL	+	-

None of the products tested produced false positive or false negative test results in the Clearview Advanced™ Strep A test at the concentrations listed.

f. Assay cut-off:

The assay cut off is 1×10^4 organisms per test

2. Comparison studies:

a. Method comparison with predicate device:

N/A

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical Sensitivity:

In the clinical study, the sponsor evaluated 297 throat swab specimens using the Clearview Advanced™ Strep A. One test result was deemed invalid, thus Clearview Advanced Strep A test performance was compared to culture on 296 of these samples.

Performance of the Clearview Advanced™ Strep A test vs. Culture is presented by patient age, below.

Clearview Advanced Strep A Test Performance v. Culture by Subject Age

	SENSITIVITY			SPECIFICITY	
Age	% Sens	95%CI		% Spec	95%CI
≤17 Yrs	92.0% (104/113)	85.6- 95.8%		94.6% (157/166)	90.0- 97.1%
≥18 Yrs	75.0% (3/4)	30.1- 95.5%		100% (13/13)	77.2-100%
Overall	91.5% (107/117)	85.0- 95.3%		95.0% (170/179)	90.7- 97.3%

Results showed that ninety-four percent (94%) of the throat swab specimens tested were collected from pediatric subjects (≤ 17 years old) while 6% were collected from adults (≥ 18 years old). There were no statistical differences in Clearview Advanced™ Strep A test performance between adult and pediatric subjects.

The overall Clinical Sensitivity and Specificity of the device are as follows:

Clinical Sensitivity and Specificity

		Culture		
		Positive	Negative	Total
Clearview Advanced Strep A Test	Positive	107	9	116
	Negative	10	170	180
	Total	117	179	296

Sensitivity: 91.5% (85.0% to 95.3%)*

Specificity: 95.0% (90.7% to 97.3%)*

* denotes 95% Confidence Interval

b. Clinical specificity:

See Clinical Performance Studies, section 3(a) for clinical sensitivity and specificity.

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:

The sponsor states that approximately 15% of pharyngitis in children ages 3 months to 5 years is caused by Group A beta-hemolytic Streptococcus. In school-aged children and adults, the incidence of Strep throat infection is about 40%. This disease usually occurs in the winter and early spring in temperate climates. Sponsor indicated that the expected range was established in the literature, and provided copies of supporting references.

N. Proposed Labeling:

The labeling is sufficient and it 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.