510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191184

B Applicant

SSI Diagnostica A/S

C Proprietary and Established Names

ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test
S. pneumoniae and *L. pneumophila* Urinary Antigen Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MJH	Class II	21 CFR 866.3300 - Haemophilus Spp. Serological Reagents	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for the detection *S. pneumoniae* and *L. pneumophila* antigens in human urine and *S. pneumoniae* and *S. pneumoniae* antigens in human CSF.

B Measurand:

S. pneumoniae and *L. pneumophila* antigens or whole organism

C Type of Test:

Qualitative lateral flow assay

III Intended Use/Indications for Use:

A Intended Use(s):

The ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test is an in vitro, rapid, lateral flow test, also known as a lateral flow immunochromatographic assay, intended for the qualitative detection of Streptococcus pneumoniae and Legionella pneumophila antigens in urine specimens from patients with symptoms of pneumonia. The assay is intended to aid in diagnosis of *S. pneumoniae* and *L. pneumophila* serogroup 1 infections. The assay is further intended to aid in the diagnosis of *S. pneumoniae* infections by detection of *S. pneumoniae* antigen in cerebrospinal fluid (CSF). Results from the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test should be interpreted in conjunction with the patient's clinical evaluation and other diagnostic methods.

B Indication(s) for Use:

Same as Intended Use(s)

C Special Conditions for Use Statement(s):

Rx Only

D Special Instrument Requirements:

None

IV Device/System Characteristics:

A Device Description:

The ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test is a lateral flow test for the qualitative detection of *S. pneumoniae* in human urine and CSF samples and *L. pneumophila* (primarily serogroup 1) antigens in human urine samples. The test is an aid in diagnosis of pneumococcal pneumonia caused by *S. pneumoniae* or *Legionella* pneumonia (Legionnaires' disease) , in conjunction with culture and other clinical findings.

B Principle of Operation:

The assay is performed by adding three (3) large free-falling drops (120 µL) of patient urine or CSF are diluted with two (2) large free-falling drops (90 µ L) of buffer reagent in a tube. The test strips are introduced into each tube containing either patient samples or controls. After fifteen (15) minutes of sample incubation on the absorbing pad, the test is removed, read and the visual results interpreted. Colored beads bind to the captured antigens, causing the development of red and blue lines respectively. When there are no bacterial antigens present, there are no red/blue

lines in the test area. As the sample migrates through the membrane a purple/gray line develops in the control (C) area, which consists of goat anti-rabbit antibodies. This built-in procedural control provides evidence that the test was performed properly, and the sample and reagents have migrated through the device strip. If the control line does not appear or if any of the lines are not fully developed the test is invalid.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Binax NOW Legionella Urinary Antigen Test

B Predicate 510(k) Number(s):

K070522

C Comparison with Predicate(s):

Device & Predicate Device(s):	K191184	K070522
Device Trade Name	ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test	Binax NOW Legionella Urinary Antigen Test
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test is an in vitro lateral flow test, also known as a lateral flow immunochromatographic assay, intended for the qualitative detection of *Streptococcus pneumoniae* and *Legionella pneumophila* antigen in urine specimens from patients with symptoms of pneumonia. The test is intended to aid in diagnosis of either *S. pneumoniae* or *L. pneumophila* serogroup 1. The assay is further intended to aid in the diagnosis of *S. pneumoniae* infections by detection of *S. pneumoniae* antigen in cerebrospinal fluid (CSF). Results from the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen should be interperted in conjunction with the	The BinaxNOW Legionella Urinary Antigen Test is an *in vitro* rapid immuno-chromatographic assay for the qualitative detection of Legionella pneumophila serogroup 1 antigen in urine specimens from patients with symptoms of pneumonia. It is intended to aid in the presumptive diagnosis of Legionella infection (Legionnaires Disease) caused by *L. pneumophila* serogroup 1 in conjunction with culture and other methods.

	patient's clinical evaluation and other diagnostic methods.	
Measurement Principle	Rapid Lateral flow test	same
Read Method	Visual	same
Capture antibody	Rabbit polyclonal	same
Assay interpretation	Qualitative	same
Read time	15 min	same
General Device Characteristic Differences		
Sample type	Urine and CSF	Urine
Measured analyte	*S. pneumoniae and* *L. pneumophila*	*L. pneumophila*
Sample type	Urine, Urine preserved and CSF	Urine

VI Standards/Guidance Documents Referenced:

CLSI EP07-A2 Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition, November 2005

CLSI EP12-A2 User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline— Second Edition

CLSI EP17-A2 Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline, September 2009

FDA Guidance Document- Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics

Guidance for Industry and Food and Drug Administration Staff. Document issued on September 25, 2018.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Reproducibility of the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test was determined using a 12-member masked specimen panel, consisting of six urine

specimens, three CSF specimens, and three controls. Of the six urine specimens, two were negative specimens, two were *L. pneumophila* moderate positive specimens, (3 - 4x higher than the C_{95}), one was a *S. pneumoniae* low positive specimen, (1 - 2 x LoD), and one was a *S. pneumoniae* moderate positive specimen (3 - 4x higher than the C_{95}). Of the three CSF specimens tested, one was a true negative specimen, one was a *S. pneumoniae* low positive specimen, (1 - 2 x LoD), and one was a *S. pneumoniae* moderate positive specimen (3 - 4x higher than the $C_{95)}$. ,Urine and CSF samples were spiked using a known concentration of *S. pneumoniae* or *L. pneumophila* purified antigen to achieve the desired concentration. Testing was performed at two independent laboratories and on-site at SSI. Samples were tested twice a day in triplicate over a five-day period by multiple technicians at each site using multiple kit lots, with a positive control included with each individual test and a negative control tested with each sample panel of masked specimens. Concordance with the expected result for all true negative samples was 99.7% (354/355). For urine, concordance for *L. pneumophila* panel members was 99.4% (356/358) and for *S. pneumoniae* panel members 100% (180/180). For *S. pneumoniae* CSF panel members, concordance was 99.4% (178/179). The test had an invalid rate of 0.74% (1072/1080). The results for reproducibility testing were acceptable.

2. Linearity:
   Not Applicable.

3. Analytical Specificity/Interference:
   Cross Reactivity: Urine
   The ImmuView *S. pneumoniae* and *L. pneumophila* Urine Antigen Test was evaluated for cross-reactivity with the organisms listed in Table 1 below. *S. pneumoniae* and *L. pneumophila* purified antigen was spiked into clinically negative urine at 2-3 x LoD. The organisms listed below were spiked at concentration of $>10^8$ CFU/mL and viruses at a range from $10^{3.3}$ to $10^{8.25}$ $TCID_{50}$ units per 0.2 mL.

   Table 1. Organisms tested for cross-reactivity

Acinetobacter spp.(4)	*Lactobacillus rhamnosus*
Bacillus subtilis	*Lactobacillus sp.*
Bordetella pertussis	*Listeria monocytogenes*
Moraxella catarrhalis	*Morganella morganii*
Candida albicans (4)	*Moraxella osloensis*
Citrobacter freundii	*Mycoplasma genitalium*
Cornyebacterium sp.	*Neisseria gonorrhoeae (3)*
Cornyebacterium urealyticum	*Neisseria lactamica*
Enterobacter cloacae (3)	*Neisseria meningitidis*
Escherichia coli (10)	*Proteus mirabilis (2)*
Enterococcus faecalis (7)	*Proteus vulgaris*
Enterococcus faecium	*Pseudomonas aeruginosa (4)*
Enterococcus durans	*Pseudomonas stutzeri*
Gardnerella vaginalis	*Pseudomonas spp. (2)*
Hemophilus influenzae type a-f and non caps (11)	*Salmonella bredeney*
Haemophilus parainfluenzae	*Salmonella Thompson*
Adenovirus 2,	*Salmonella typhimurium*

Chlamydophila pneumoniae (2)	*Serratia marcescens*
Chlamydia trachomatis	*Staphylococcus epidermidis*
Cytomegalovirus	*Salmonella glostrup*
Enterovirus D68	*Streptococcus mutans (2)*
Herpes Simplex 1,2	*Streptococcus parasanguis*
Influenza A (H1N1 and H3N2) virus	*Streptococcus sanguinis*
Influenza B Virus	*Streptococcus aureus (6)*
Parainfluenza virus 1,2,3 (3)	*Streptococcus epidermidis (5)*
Respiratory Syncytial Virus A	*Streptococcus saprophyticus (3)*
Klebsiella oxytoca (2)	*Stenotrophomonas maltophilia*
Klebsiella pneumoniae (3)	*Streptococcus gr. A, B, C, F, L and G (16)*
Legionella pneumophila sg3	*Streptococcus mitis*
Lactobacillus catenaforme	

Cross Reactivity: CSF
ImmuView *S. pneumoniae* and *L. pneumophila* Urine Antigen Test was evaluated for cross-reactivity with the organisms listed in Table 2 below. The organisms were tested with and without *S. pneumoniae* purified antigen spiked into clinically negative CSF at 2-3 x LoD. The organisms listed below were spiked at concentration of $>10^8$ CFU/mL.

Table 2. Organisms used for Cross-reactivity testing in CSF.

E. coli (5)	*Staphylococcus aureus*
Hemophilus influenza type a-f and non caps (7)	*Streptococcus* Gr A
Listeria monocytogenes	*Streptococcus agalactiae* (GBS) serogroup g Ia, Ib, II, III (4)
Measles	*Streptococcus mitis*
Neisseria meningitidis Gr. B, D and W135 (3)	

No significant cross reactivity was observed during the study.

Interfering substances: Urine:
ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test was evaluated for interfering substances with the substances and concentrations listed in Table 3. Testing was conducted using negative urine and negative urine spiked with both *S. pneumoniae* and *L. pneumophila* antigen at 2-3x LoD. None of the substances were observed to interfere with the performance of the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen test.

Table 3 Interfering substances evaluated in urine

Agent	Concen.	Agent	Concen.
Acetaminophen	0.1mg/mL	Leucocytes	>250 cells/mL
Acetylsalicyclic acid	0.1mg/mL	Miconazole	5%
Amantadine	0.03mg/mL	Mix (pH, whole blood, protein and glucose) (H)	
Amoxicillin	0.075mg/mL	Mix (pH, whole blood, protein and glucose) (M)	
Amphotericin B	0.22mg/mL	Mix (pH, whole blood, protein and glucose) (L)	
Antihistamine	0.22mg/mL	Mucin	0.086mg/mL
Ascorbic acid (C-Vitamin)	1mg/mL	Oseltamivir (Tamiflu)	0.03mg/mL
Augmentin (Amoxicillin-Clavulanate)	0.22mg/mL	Oxalic acid	0.01%
Azithromycin	0.012mg/mL	pH (acidic)	4
Beet root	20%	pH (neutral)	7
Beet root	1.17%	pH (basic)	9
Beet root	0.01%	Plasma	90%
Bilirubin	0.2mg/mL	Plasma	50%
Bromhexin/cough drops/couch syrup	0.22mg/mL	Plasma	10%
Caffeine	15mg/mL	Prednisone	0.22mg/mL
Chlorophyll	0.11mg/mL	Protein (albumin) (H)	10mg/mL
Chlorophyll	0.04mg/mL	Protein (albumin) (M)	5mg/mL
Chlorophyll	0.01mg/mL	Protein (albumin) (L)	0.6mg/mL
Ciprofloxacin	0.22mg/mL	Pyridium	1mg/mL
Decongestant	0.22mg/mL	Rifampicin	0.09mg/mL
Corticosterone (Corticosteroids)	0.015mg/mL	Spinach	1%
Erythromycin	0.067mg/mL	Tobacco purified	0.4mg/mL
Glucose (H)	20mg/mL	Triglycerides	4mg/mL
Glucose (M)	10mg/mL	Urea	20mg/mL
Glucose (L)	3mg/mL	Vaginal contraceptive gel	5%
Hemoglobin	5mg/mL	Vancomycin	0.1mg/mL
Human albumin	35mg/mL	Water-based personal lubricant	5%
Human red blood cells 10% Washed pooled cells	10%	White blood cells	10%
Ibuprofen	0.1mg/mL	Whole blood	10%
Itraconazole	0.22mg/mL	Whole blood	15%

No interference was observed during the study.

Interfering substances: CSF

ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test was tested with interfering agents at different concentrations. Substances were tested with artificial CSF and artificial CSF spiked with *S. pneumoniae* antigen at 2-3x LoD. Table 4 list the interfering substances tested.

Table 4. Interfering substances evaluated in CSF

Agent	Concentration	Agent	Concentration
Glucose (H)	1mg/mL	Glucose (H)	1mg/mL
Glucose (M)	0.5mg/mL	Glucose (M)	0.5mg/mL
Glucose (L)	0.1mg/mL	Glucose (L)	0.1mg/mL
Red blood cells (H)	15%	Red blood cells (H)	15%
Red blood cells(M)	10%	Red blood cells(M)	10%
Red blood cells (L)	5%	Red blood cells (L)	5%
Protein (H)	60mg/mL	Protein (H)	60mg/mL
Protein (M)	30mg/mL	Protein (M)	30mg/mL
Protein (L)	10mg/mL	Protein (L)	10mg/mL
White blood cells	$10.6x10^6$/mL	White blood cells	$10.6x10^6$/mL
White blood cells	$5.3x10^6$/mL	White blood cells	$5.3x10^6$/mL
White blood cells	$2.7x10^6$/mL	White blood cells	$2.7x10^6$/mL
White blood cells	$1.8x10^6$/mL	White blood cells	$1.8x10^6$/mL
White blood cells	$0.9x10^6$/mL	White blood cells	$0.9x10^6$/mL
Bilirubin	15%	Bilirubin	15%
Bilirubin	10%	Bilirubin	10%
Bilirubin	5%	Bilirubin	5%
Plasma	15%	Plasma	15%
Plasma	10%	Plasma	10%
Plasma	5%	Plasma	5%

No interference was observed during the study.

4. Assay Reportable Range:
   Not Applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   Sample Stability study
   Specimen stability was evaluated for both fresh and preserved samples. Samples were preserved in either Boric acid or piperazine-N,N'-bis(2-ethanesulfonic acid) (PIPES). For the analysis, a panel with a total of 105 samples were prepared as listed in Table 5 below. Low positive samples represented 1 - 2x LoD and Moderate positives represented 4x LoD.

Table 5. Panel used for Sample Stability Testing

Panel	Test times	Condition
Neg urine (N=5)	T0, 1, 2 and 7 days	2-8 ºC and ~30 ºC
Neg urine with Boric acid (N=5)		
Neg urine with PIPES (N=5)		
S. pneumoniae low pos urine (N=10)		
S. pneumoniae low pos urine with Boric acid (N=10)		
S. pneumoniae low pos urine with PIPES (N=10)		
S. pneumoniae Mod pos urine (N=5)		
S. pneumoniae Mod pos urine with Boric acid (N=5)		
S. pneumoniae Mod pos urine with PIPES (N=5)		
L. pneumophila low pos urine (N=10)		
L. pneumophila low pos urine with Boric acid (N=10)		
L. pneumophila low pos urine with PIPES (N=10)		
L. pneumophila Mod pos urine (N=5)		
L. pneumophila Mod pos urine with Boric acid(N=5)		
L. pneumophila Mod pos urine with PIPES (N=5)		

Fresh samples were tested at time 0 then stored at refrigeration (2ºC - 8ºC) and room temperatures (~30ºC). Subsequent testing was performed at 1, 2 and 7 days. Testing was conducted following the instructions in the proposed package insert. The results for antigen stability indicated that use of preservative supports stable test performance over the course of 7 days for either refrigeration or room temperature storage. Fresh urine samples remained positive only 83% of the time when tested at 48 hours. Urine samples without preservative must be tested within 24 hours of collection.

Frozen sample stability

Stability of frozen urine samples compared to fresh samples was established using panels prepared with *S. pneumoniae/L. pneumophila* antigen at Low (1-2x LoD) and moderate (3-4x LoD) antigen concentrations, *S. pneumoniae/L. pneumophila* whole organism at low (1-2x LoD) concentration. and true negative samples. Urine specimens were prepared with and without preserved. Samples were stored at -20ºC for 7 days and were tested at 0, 1, 2, and 7 days. The results showed that all positive samples remained positive and negative samples remained negative throughout the study.

Freeze/Thaw study

A study was conducted to determine stability after 5 freeze/thaw cycles using a 110 urine specimen panel described in Table 6. below. Samples were not tested using a preservative. The results showed that up to 5 freeze/thaw cycles did not significantly impact the performance of the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test. The package insert will indicate that if samples are not tested fresh, frozen urine samples may be tested after no more than 5 freeze/thaw cycles.

Table 6. Freeze/Thaw Panel

Panel	Replicates
S. pneumoniae Strong pos (5x LoD)	10
L. pneumophila Strong pos (5x LoD)	10
S. pneumoniae Weak pos (1-2 x LoD)	30
L. pneumophila. Weak pos (1-2 x LoD)	30
S. pneumoniae High neg (<1 x LoD)	10
L. pneumophila High neg (<1 x LoD)	10
True Negative	10

6. Detection Limit:

The limit of detection (LoD) for the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test was determined by spiking purified antigen or whole organisms into unpreserved urine and preserved urine (boric acid or PIPES). The concentration of purified antigen was reported in pg/mL for *S. pneumoniae* and µg/mL for *L. pneumophila,* and for whole organisms as CFU/mL. LoD was defined as the concertation the yields at least a positive result in 95% of performed tests. Table 7 lists the LoD values for antigen and whole organism in urine for *S. pneumoniae* and *L. pneumophila*. The use of preservatives (boric acid or PIPES) did not significantly impact the LoD.

Table 7. LoD for *S. pneumoniae* and *L. pneumophila*

Test material	**LoD**
S. pneumoniae antigen	62.5 pg/mL
L. pneumophila SG 1 (Philadelphia) antigen	0.025 µg/mL
L. pneumophila SG 1 (Bellingham) antigen	0.5 µg/mL
S. pneumoniae (serotype 1)	10^5 CFU/mL
L. pneumophila SG1 (Philadelphia)	10^4 CFU/mL
L. pneumophila SG 1 (Bellingham)	10^5 CFU/mL

The LoD in CSF for the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test was determined by spiking whole organisms into clinically negative human CSF. The concentration of *S. pneumoniae* using whole organisms is reported in CFU/mL. LoD was defined as the concertation the yields at least a positive result in 95% of performed tests in CSF. The study data show that the LoD for *S. pneumoniae* in CSF is 10^3 CFU/mL. The LoD for *L. pneumophila* was not evaluated.

Inclusivity

The reactivity of three additional *S. pneumoniae* serotypes, 3, 5 and 37, was evaluated. The samples were prepared by spiking clinically negative urine with antigen or whole organism. Testing was conducted around the previously established LoD in replicates of 6 to determine the lowest concentration that provided a positive result 100% of the time.

The reactivity of four Pontiac and three non-Pontiac strains of *L. pneumophila* was evaluated. Samples were prepared by spiking clinically negative urine with antigen or whole organism. Testing was conducted around the previously established the LoD in replicates of 20 or 6 to determine the lowest concentration that provided a positive result 100% of the time. The reactivity of three additional *L. pneumophila* subgroups 3, 6,8,10 and 12, was evaluated. The

samples were prepared by spiking clinically negative urine with antigen or whole organism. Testing was conducted well above the established LoD in replicates of 6 to determine the lowest concentration that provided a positive result 100% of the time. Table 8 below summarizes the Inclusivity results for *S. pneumoniae* and *L. pneumophila*

Table 8. Summary of Inclusivity Testing

Streptococcus pneumoniae in urine		
Subgroup	Antigen Concentration (µg/mL)	Whole Organism Concentration (CFU/mL)
type 1	ND*	10^4
type 3	0.001	10^4
type 5	0.010	10^5
type 37	0.0001	ND*

Legionella pneumophila in urine				
Subgroup	Pontiac/Non-Pontiac	Species	Concentration (µg/mL)	Concentration (CFU/mL)
SG1	Pontiac	Knoxville	0.100	10^5
SG1	Pontiac	Allentown/France	0.005	ND*
SG1	Pontiac	Benidorm	ND*	10^4
SG1	Pontiac	Philadelphia	0.010	10^4
SG1	Non-Pontiac	OLDA/Oxford	0.001	ND*
SG1	Non-Pontiac	Camperdown	0.315	ND*
SG1	Non-Pontiac	Heysham	1.250	ND*
SG3			250	ND*
SG6			250	ND*
SG8			250	ND*
SG10			250	ND*
SG12			7.8	ND*

*ND = Not tested

7. Assay Cut-Off:

   Not Applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   See Clinical Studies section below.

2. Matrix Comparison:

   Not Applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Clinical Agreement for Prospective Urine Samples

Prospectively collected patient urine samples (n = 306) from two different sites (Spain and Denmark) were tested with both the ImmuView *S. pneumoniae* and *L. pneumophila* Urinary Antigen Test and two FDA cleared lateral flow urine antigen tests (one per antigen) as comparator assays. Fresh urine samples were from patients at risk of having community acquired pneumonia. The results from each site were pooled and analyzed by analyte. Of the 306 patients, 179 were from Spain and 127 from Denmark. The patient population consisted of 141 females and 165 males, ranging in age from 18-95 years old. The results of this prospective method comparison test for *S. pneumoniae* antigen found in urine are noted in Table 9. Boiling of samples for discrepant resolution did not change any of the results or performance. Table 10 notes the results of this prospective method comparison test for *L. pneumophila* antigen found in urine.

Table 9. *S. pneumoniae* Prospective Study

ImmuView	Comparator Positive	Comparator Negative	Total
Positive	72	6	78
Negative	3	225	228
Positive percent agreement	96.0% (72/75)	95% CI (88.9%-98.6%)	
Negative percent agreement	97.4% (225/231)	95% CI (94.5-98.8%)	

Table 10. *L. pneumophila* Serogroup 1 Prospective Study

ImmuView	Comparator Positive	Comparator Negative	Total
Positive	3	0	3
Negative	0	303	303
Positive percent agreement	100.0% (3/3)	95% CI (43.9%-92.9%)	
Negative percent agreement	100.0% (303/303)	95% CI (98.8%-100%)	

Clinical Sensitivity/Specificity for Retrospective Urine Samples

To further characterize test performance, 100 frozen urine samples from patients previously determined to be *S. pneumoniae* blood culture positive were tested. In total there were 48 samples from Sweden and 52 samples from Denmark. These results are described in Table 11. Discrepant results were boiled, and the results are footnoted below.

Table 11. *S. pneumoniae* Retrospective Sample Testing (urine)

ImmuView	Blood Culture Positive	Blood Culture Negative	Total
Positive	78[a]	4	82
Negative	22	217[b]	239
Sensitivity	78.0% (78/100)	95% CI (68.9%-85%)	
Specificity	98.1% (217/221)	95% CI (95.4%-99.3%)	

[a] After boiling three samples turned positive (81/100)
[b] After boiling one false positive turned negative (218/221)

To further characterize test performance, 98 stored frozen urine samples from patients previously determined to be *Legionella* respiratory culture positive. A total of 55 urine samples were from Europe and 43 urine samples were from patients within the United States. These results are described in Table 12.

Table 12. *L. pneumophila* Serogroup 1 Retrospective Sample Testing (urine)

ImmuView	Sputum Culture Positive	Sputum Culture Negative	Total
Positive	86[c]	1	87
Negative	12	239[d]	251
sensitivity	87.8% (86/98)	95% CI (79.8%-92.9%)	
specificity	99.6% (239/240)	95% CI (97.7%-99.9%)	

[c] After boiling two samples turned negative (84/98)
[d] After boiling one sample tuned negative (240/240)

The clinical specificity of the test was established by testing known negative (culture confirmed negative) urine samples collected from 3 sites, one in the U.S. and two in Europe.

Clinical sensitivity and specificity - CSF

The sensitivity of the *S. pneumoniae* test line was obtained by testing leftover (retrospective) CSF specimens from US and European patients suspected of meningitis. Testing was conducted for contrived specimens were of human CSF spiked with antigen and negative CSF.

Retrospective specimens.

Nine CSF specimens known positive for *S. pneumoniae* were tested at two U.S. labs with 113 samples previously determined to be negative. Samples were blinded and the testing was performed by three operators on different days. Five CSF specimens known positive for *S. pneumoniae* were tested at one European laboratory with 56 samples previously determined to be negative. Samples were blinded and tested by one operator on multiple days. Results are in table 13 below.

Table 13. Retrospective CSF test results

ImmuView	*S. pneumoniae* Culture positive (CSF)	*S. pneumoniae* Culture negative (CSF)	Total
S. pneumoniae Positive	13	7	20
S. pneumoniae Negative	1	162	163
Sensitivity	92.9% (13/14)	95% CI (68.5%-98.7%)	
Specificity	95.9% (162/169)	95% CI (91.7%-98.0%)	

The sensitivity of device *L. pneumophila* test line was not evaluated in this study as *Legionella* is an exceptionally rare etiology for meningitis, and CSF is not included as a matrix for meningitis testing in the device Intended Use.

Contrived CSF testing

Additional human CSF testing was conducted using whole organisms spiked into human CSF. Testing was conducted with the ImmuView test and the comparator for the following contrived samples: 25 samples with *S. pneumoniae* whole organism near the LoD, 25 samples with *S. pneumoniae* whole organism across a clinically relevent range, and 10 negative CSF samples. The positive percent agreement and negatuive percent agreemnt for the both the ImmuView test and the comparator test was 100%, 50/50 for PPA and 10/10 for NPA. Table 14 summarizes these results.

Table 14 Contrived CSF results (*S. pneumoniae* whole organism spiked into human CSF)

ImmuView	*S. pneumoniae* Contrived Positive	*S. pneumoniae* Contrived Negative	Total
ImmuView *S. pneumoniae* Positive	50	0	50
ImmuView *S. pneumoniae* Negative	0	10	10
Positive percent agreement	100%	95% CI (92.9%-100%)	
Negative percent agreement	100%	95% CI (72.2%-100%)	

2. Clinical Specificity:

   See section C.1. above.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   See section C.1. above.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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