510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
K173376

B. Purpose for Submission:
The purpose of this submission is to show that the ASI RPR Test for syphilis run on the ASI Evolution instrument is substantially equivalent to the ASI RPR Test for syphilis run on the ASiManager-AT and to obtain clearance for the ASI Evolution.

C. Measurand:
Antibodies to plasma reagin (cardiolipin and lecithin).

D. Type of Test:
The ASI Automated RPR Test for syphilis run on the ASI Evolution instrument is a macroscopic non-treponemal flocculation test that is performed in a 48-well microtiter plate and interpreted by an instrument algorithm analyzing a high resolution digital image of each well.

E. Applicant:
Arlington Scientific, Inc.

F. Proprietary and Established Names:
ASI Automated RPR Test for syphilis
ASI Evolution

G. Regulatory Information:

1. Regulation section:
   21 CFR §866.3820 – *Treponema pallidum* nontreponemal test reagents

2. Classification:
   Class II

3. Product code:
   GMQ, Antigens, Nontreponemal, All
   JQT, Densitometer/scanner (integrating, reflectance, tlc, radiochromat.) clinical

4. Panel:
   Microbiology (83)

H. Intended Use:

1. Intended use(s):
   The ASI Automated RPR (rapid plasma reagin) Test for Syphilis, for use on the ASI Evolution Automated Syphilis Analyzer, is a qualitative nontreponemal flocculation test for the detection of reagin antibodies in human serum and plasma as a screening test for serological evidence of syphilis. All reactive RPR test samples should be further tested with a treponemal test. The ASI Automated RPR Test for Syphilis for use on the ASI Evolution produces only a reactive or non-reactive result and does not report RPR titers for reactive samples.
   The ASI Automated RPR Test for Syphilis is for professional use only. The test is intended to be used for *in vitro* diagnostic testing.

   The ASI Evolution is intended to be used as a fully automated analyzer to objectively interpret the results of the ASI automated RPR test for syphilis. The ASI Evolution is designed to provide standardized test interpretation and to provide for storage, retrieval, and transmittal of the test results. It is intended to be acquired, possessed and used only by health care professionals. The ASI Evolution analyzer, in conjunction with the ASI Automated RPR Test is intended to be used for in vitro diagnostic testing. The ASI Automated RPR Test for Syphilis for use on the ASI Evolution produces only a reactive or non-reactive result and does not report RPR titers for reactive samples.

2. Indication(s) for use:
   Same as Intended Use

3. Special conditions for use statement(s):
   For Prescription Use Only

4. Special instrument requirements:
   ASI Evolution

I. Device Description:

The ASI Evolution is an instrument that automates the dispensing of serum or plasma samples and the dispensing of carbon antigen reagent. The instrument also automates the RPR agglutination measurement and image processing algorithm using an internal CCD camera.

ASI Automated RPR Test for Syphilis includes the following reagents:

- Carbon Antigen - 0.003% cardiolipin, 0.020–0.022% lecithin, 0.09% cholesterol, charcoal (activated) as visual enhancer, phosphate buffer, 0.1% sodium azide as preservative and stabilizers.
- Controls (Reactive, Weak Reactive, Nonreactive) - Human serum or defibrinated plasma (liquid), with 0.1% sodium azide as preservative.

Additional materials required but not supplied include clean de-ionized H_20.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ASI RPR Card Test for Syphilis on the ASiManager- AT

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

   K851504

3. Comparison with predicate:

Table 1: Device Similarities

Item	**ASI Evolution**	**ASiManager-AT**
Reagent Technology	Flocculation Test	Same
Antigen	Cardioliping, lecithin, cholesterol	Same
Reported Results	Reactive, Nonreactive, Titer	Same
Results Interpretation	Automated	Same
Sample Type	Serum or Plasma	Same
Controls	Reactive, Weak Reactive, Nonreactive	Same

Table 2: Device Differences

Item	**ASI Evolution**	**ASiManager-AT**
Intended Use	The ASI Automated RPR (rapid plasma reagin) Test for Syphilis, for use on the ASI Evolution Automated Syphilis Analyzer, is a qualitative nontreponemal flocculation test for the detection of reagin antibodies in human serum and plasma as a screening test for serological evidence of syphilis. All reactive RPR test samples should be further tested with a treponemal test. The ASI Automated RPR Test for Syphilis for use on the ASI Evolution produces only a reactive or non-reactive result and does not report RPR titers for reactive samples. The ASI Automated RPR Test for Syphilis is for professional use only. The test is intended to be used for *in*	The ASI RPR (rapid plasma reagin) Card Test for Syphilis is a qualitative and semiquantitative nontreponemal flocculation test for the detection of reagin antibodies in human serum and plasma as a screening test for serological evidence of syphilis. This test is also intended for use in screening blood donors and cadaveric (non-heart beating) donor specimens for tissue donation when the test is read and interpreted with the ASiManager-AT. The ASI RPR Card Test for Syphilis is for professional use only. The ASiManager-AT is intended to be used as an integrated digital particle analyzer to objectively interpret the results of the ASI RPR Card Test for

	vitro diagnostic testing. The ASI Evolution is intended to be used as a fully automated analyzer to objectively interpret the results of the ASI automated RPR test for syphilis. The ASI Evolution is designed to provide standardized test interpretation and to provide for storage, retrieval, and transmittal of the test results. It is intended to be acquired, possessed and used only by health care professionals. The ASI Evolution analyzer, in conjunction with the ASI Automated RPR Test is intended to be used for *in vitro* diagnostic testing. The ASI Automated RPR Test for Syphilis for use on the ASI Evolution produces only a reactive or non-reactive result and does not report RPR titers for reactive samples.	Syphilis. The ASiManager-AT is designed to provide standardized test interpretation and to provide for storage, retrieval, and transmittal of the test results. It is intended to be acquired, possessed and used only by health care professionals. The ASiManager-AT is intended to be used for *in vitro* diagnostics, blood donor and cadaveric (non-heart beating) donor screening.
Technology Instruments	The ASI Evolution is an integrated digital particle analyzer designed to objectively interpret certain agglutination tests manufactured by Arlington Scientific, Inc. (ASI). The ASI Evolution fully automates the sample and reagent handling steps of the test procedure. Laboratory professionals use the ASI Evolution to provide standardized test interpretation using criteria that define reactive and nonreactive agglutination reactions. The same proprietary interpretive algorithm used in the predicate device (ASiManager-AT) is used in the ASI Evolution. The ASI Evolution employs a camera to create a highly sensitive and high-resolution image of the agglutination immunoassay. This image is then analyzed by the proprietary software algorithm to interpret the agglutination pattern.	The ASiManager-AT is an integrated digital particle analyzer designed to objectively interpret certain slide agglutination tests manufactured by Arlington Scientific, Inc. (ASI). Qualitative and semiquantitative tests are performed by laboratory professionals who use the ASiManager-AT to provide standardized test interpretation using criteria that define reactive and nonreactive agglutination reactions. The ASiManager-AT employs a camera to create a highly sensitive and high-resolution image of the agglutination immunoassay. This image is then analyzed by the proprietary software algorithm to interpret the agglutination pattern. The ASiManager-AT further provides tools that enable the creation, storage, retrieval and transmittal of the test

	The ASI Evolution further provides tools that enable the creation, storage, retrieval and transmittal of the test results.	results.
Sample Processing	Automated	Manual
Test Container/Surface	48 well plastic microtiter plate	30, 15, or 10 well plastic coated test card
RPR Carbon Antigen Reagent Volume	110 µl	105 µl

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

EP05-A3, Evaluation of Precision of Quantitative Measurement Methods; Approved Guideline, Third Edition
EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition
EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline, Third Edition (For Matrix Comparison only)
EP12-A2 – User Protocol for Evaluation of Qualitative Test Performance – Second Edition
EP15-A3, User Verification of Precision and Estimate of Bias, Approved Guideline, Third Edition
EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline

L. Test Principle:

The ASI Evolution system automates sample processing and measurement of RPR agglutination tests for syphilis. The instrument automatically dispenses serum or plasma samples and ASI Evolution carbon antigen reagent into micro-well plates. Reactions occur in plastic 48-well plates.

The Analyzer automates the following stages of the RPR test:

- Fluid Handling: aspirating and dispensing fluid volumes between 2µL and 500µL
- Mixing: the plate carriers mix in a circular motion at two speeds (~400 rpm and ~100 rpm)
- Timing: the instrument will process the tests in a prescribed time allotment, with each step timed appropriately
- Image Capture: the instrument's camera will record images of each completed test
- Image processing: the software processes and stores data of the test result image

- Reporting: the software reports and records the numerical and qualitative results of each test

The user must perform the following tasks:

- Loading sample tubes into the sample rack
- Loading the sample rack into the unit
- Refilling the prime bottle with D.I. Water
- Placing the reagent and diluent in their respective positions in the permanent rack
- Loading and unloading 48-well plates

The result is analyzed through an image processing algorithm from images taken with an internal CCD camera. The camera first takes high quality images of each well in the microplates using light reflectance. The image is then analyzed by software that has been developed with an optical recognition feature that identifies each well boundary and ensures it is in the correct position, then followed by a software algorithm that interprets the agglutination pattern to determine the sample result. All images are stored on the hard drive and results are labeled reactive or non-reactive.

Barcode labeled patient samples can be imported with the use of a hand-held barcode scanner. The Analyzer is designed to process up to 192 samples (4 plates). A printout or file export is provided after the results are determined. The reactive samples can be batched for determination of titers using another protocol contained in the instrument software.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   All analytical study data was captured as either reactive or non-reactive results. No RPR titers were performed during the studies. Any data that is listed as expected result, for titered samples, refers to simply a reactive result, not a titer.

   a. Precision/Reproducibility:

   Precision
   Precision testing of the ASI RPR Test for syphilis run on the ASI Evolution instrument was performed. A human serum panel consisting of 10 frozen samples spanning the measuring range of the test was assayed on one reagent lot. One hundred ninety-two aliquots of each same sample were placed in each well of four (4) 48-well plates (total of 40 plates). The four plates for each sample were run on the instrument at the same time. The analyte titers of the samples used are described in table 3 below.

Table 3: Precision Study Serum Panel

Sample ID	RPR Titer (previously determined)
R7C21R	1:8
N7D04	Not Reactive
11114B	1:1
11114C	1:1
11114F	1:1
02287	Not Reactive
08296	1:256
11114D	1:1
W7E26R	1:2
N7H03	Not Reactive

The data from ASI Automated RPR Test for syphilis run on the ASI Evolution instrument was analyzed for total precision. The % expected result and the 95% Confidence Interval are summarized below:

Table 4: Precision Study Results with the ASI Automated RPR Test for syphilis on the ASI Evolution

Sample Titer	N	Total Precision	
		% Expected Result	95% Confidence Interval
1:8	192	100%	98.04% - 100%
Not Reactive	192	100%	98.04% - 100%
1:1	192	100%	98.04% - 100%
1:1	192	100%	98.04% - 100%
1:1	192	100%	98.04% - 100%
Not Reactive	192	100%	98.04% - 100%
1:256	192	100%	98.04% - 100%
1:1	192	100%	98.04% - 100%
1:2	192	100%	98.04% - 100%
Not Reactive	192	100%	98.04% - 100%

Reproducibility

Reproducibility testing was performed at each of three (3) US testing facilities using 3 lots of the ASI RPR Test for syphilis run on the ASI Evolution instrument. All 3 lots were run at each site by each operator. A serum panel consisting of 7 samples spanning the measuring range were assayed in 2 replicates per run, 6 runs per day over 5 days (2 reps x 6 runs x 5 days x 3 sites = 180 total data points per sample).

Table 5: Reproducibility Sample Panel

Sample	RPR Titer (previously determined)
02287	Non-Reactive
N6K14	Non-Reactive
05225B	1:2
07035	1:4
05225A	1:8
R7C21R	1:8
07117	1:16

The data was analyzed for % agreement with expected result at each site and the 95% Confidence Interval. Because agreement with expected results was 100% there was no observed variation by user, day, site, or lot. The results are summarized below in table 6:

Table 6: Reproducibility Study data for the ASI RPR Test for syphilis run on the ASI Evolution

RPR			Site 1		Site 2		Site 3		Total	
Sample	Sample #	N	Expected Result	95% Confidence Interval	% Expected Result	95% Confidence Interval	% Expected Result	95% Confidence Interval	% Expected Result	95% Confidence Interval
RPR nonreactive	02287	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR nonreactive	N6K14	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR reactive 1:2	05225B	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR reactive 1:4	07035	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR reactive 1:8	05225A	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR reactive 1:8	R7C21R	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100
RPR reactive 1:16	07117	180	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (60/60)	93.98 - 100	100% (180/180)	97.91 - 100

b. Linearity/assay reportable range:

N/A

Not applicable; this is a qualitative assay

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

Traceability:

Because there are no calibrators for the reagents no traceability study was needed.

Calibrator

The assay is calibrated only for the settings of the camera. To do this a black calibrator plate is placed into the instrument and a calibration program is run to adjust the camera

settings according to an algorithm in the software. The user has no control over the calibration process. The user determines only when to initiate the process. Calibration is recommended every 3 months.

Controls

The controls for this assay are external and include one negative control, one weak reactive control and one reactive control. All controls are made of human serum or plasma and preserved with 0.01% sodium azide. Reactive and weak reactive controls are made from the human serum or plasma of syphilis infected individuals containing reagin antibodies. The control set is tested for hepatitis B antigen, HIV-1, HIV-2, and hepatitis C virus to ensure absence of these infectious agents. The controls should be run according to local, state and/or federal regulations or accreditation requirements and the laboratory's standard Quality Control Procedures.

Stability:

Stability studies have been performed to support the following claims:

Sample Stability:

Sample stability was performed in the original submission for the reagents (K851504). The serum and EDTA plasma storage conditions are listed below.

- Serum samples should be tested within five (5) days of collection. Samples should be stored at 2-8° C.
- Serum samples that require longer than five (5) days storage must be removed from the red cells and stored at -20° C or below until testing.
- Plasma samples should be tested withing five (5) days of collection. Samples should be stored at 2-8°C.
- Plasma samples stored longer than five (5) days at 2-8° C should not be used in the assay because of the potential for false reactive results.

Kit Stability:

The following are the stability claims for the ASI Automated RPR Test for Syphilis:

- Kit Stability was previously determined in the original submission for the reagents (K851504)
- Additionaly studies demonstrated stability of the reagents on board the ASI Evolution instrument for 8 hours.

Testing was conducted using four different samples:

- RPR nonreactive sample
- RPR reactive 1:2 tittered sample (low reactive)
- RPR reactive 1:16 tittered sample (moderate reactive)
- RPR reactive 1:64 tittered sample (high reactive)

Each sample was aliquoted to allow for two operators to run each sample in triplicate at each time point.

For this study, reagent was placed on the instrument at the beginning of the day, from storage at 2-8°C, and the sample panel was tested. The reagents were then left on the instrument for 8 hours and the sample panel was then tested using the reagents stored on the instrument. This process was repeated over 5 days, using the same reagent bottles. At the end of each day the reagents were placed at 2-8°C. The testing results are presented in table 8 below.

Table 8: On-board Stability Testing Data

Sample	Expected Results	Results					% Agreement
		ASI Evolution					
Morning		Day 1	Day 2	Day 3	Day 4	Day 5	
Non-Reactive	NR	3/3	3/3	3/3	3/3	3/3	100%
1:2	R	3/3	3/3	3/3	3/3	3/3	100%
1:16	R	3/3	3/3	3/3	3/3	3/3	100%
1:64	R	3/3	3/3	3/3	3/3	3/3	100%
After 8 hours on-board instrument							
Non-Reactive	NR	3/3	3/3	3/3	3/3	3/3	100%
1:2	R	3/3	3/3	3/3	3/3	3/3	100%
1:16	R	3/3	3/3	3/3	3/3	3/3	100%
1:64	R	3/3	3/3	3/3	3/3	3/3	100%

Fresh vs. Frozen Study:

Testing was performed to evaluate the performance of frozen samples, compared to fresh sample. Twenty non reactive samples and 40 reactive samples were chosen and each sample was split into two aliquots. One aliquot was stored at 2-8°C and the other was frozen for 1 month. Fresh samples were tested within 5 days of storage and frozen samples were tested after one month. All samples were allowed to reach room temperature before testing. Results of the testing of fresh and frozen samples are shown below.

Table 9: Frozen vs. Refrigerated Testing Results

Sample Titer	N	Fresh Samples	Frozen Samples
		% Expected Result (# expected result/N)	% Expected Result (# expected result/N)
Not Reactive	20	100% (20/20)	100% (20/20)
1:1	20	100% (20/20)	100% (20/20)
1:2	5	100% (5/5)	100% (5/5)
1:4	5	100% (5/5)	100% (5/5)
1:8	3	100% (3/3)	100% (3/3)
1:16	2	100% (2/2)	100% (2/2)
1:32	2	100% (2/2)	100% (2/2)
1:64	2	100% (2/2)	100% (2/2)

1:128	1	100% (1/1)	100% (1/1)
All Reactive Samples	40	100% (40/40)	100% (40/40)

Carryover:
This study was designed to test for potential carryover of sample when using the ASI Evolution. Two samples were used, a highly reactive RPR (1:64) sample and nonreactive sample. Twenty four (24) aliquots of each sample were prepared, with enough volume to be tested 5 times. Testing was performed in one plate, alternating 24 aliquots of the highly reactive sample with 24 aliquots of the nonreactive sample. One plate was run each day for five days, using one lot of reagents. No carryover was observed during testing. Test results are shown below.

Table 10: Carryover Study Data

Sample Titer	N	Day 1	Day 2	Day 3	Day 4	Day 5
		% Expected Result (# expected result/N)	% Expected Result (# expected result/N)	% Expected Result (# expected result/N)	% Expected Result (# expected result/N)	% Expected Result (# expected result/N)
Not Reactive	24	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)
1:64	24	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)	100% (24/24)

d. Detection limit:

Not applicable

e. Analytical specificity:

Interfering Substances and Cross Reactivity
An interfering substances and cross reactivity study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the ASI Evolution and the ASI Automated RPR Test for Syphilis. Known clinical serum or EDTA plasma samples were purchased representing the specimen categories listed below. These samples were then tested on the ASI Evolution instrument to evaluate their cross-reactivity with the RPR reagent.

Table 11: Cross-Reactivity/Interfering Stubstances Study Data

Specimen Category	Number of Samples Tested	Expected Result	# of samples with expected result/ # of samples tests
Anti-Nuclear Antibodies (+) Syphilis (-)	3	Non-reactive	3/3
Anti-Streptolysin O (+) Syphilis (-)	2	Non-reactive	2/2
C-Reactive Protein (+) Syphilis (-)	2	Non-reactive	2/2
Infectious Mono (+) Syphilis (-)	3	Non-reactive	3/3
Rheumatoid Factor (+) Syphilis (-)	12	Non-reactive	12/12
Rubella (+) Syphilis (-)	12	Non-reactive	12/12
Lyme antibody (+) Syphilis (-)	12	Non-reactive	12/12
HIV (+) Syphilis (-)	50	Non-reactive	50/50
Bilirubin 20 mg/dl	2	Non-reactive	2/2
Hemoglobin 10 mg/ml	2	Non-reactive	2/2
Triglycerides 1000mg/dl	2	Non-reactive	2/2
HIV (+) Syphilis (+)	24	Reactive	24/24

No interference was observed with any of the substances tested.

2. Comparison studies:

   a. Method comparison with predicate device:

   The results of the ASI Automated RPR Test for Syphilis on the ASI Evolution were compared to test results using the ASI RPR Test on the ASiManager-AT. For additional details on the study see the "Clinical Studies" section below.

3. Clinical studies:

   a. Clinical Sensitivity and Specificity:

   Clincical performance was evaluated at three sites from June 2017 to September 2017 using a total of 1078 prospective and retrospective serum samples and 1003 retrospective plasma samples. Samples were obtained from referenece laboratories and commercial suppliers who collected samples in the US. No invalid results or instrument errors were observed during the clinical study.

   The samples tested included 1068 prospective serum samples, 10 retrospective serum samples, 1003 retrospective plasma samples, 143 clinically diagnosed syphilis patients, and 250 pregnant women. Of the total number of 2474 samples tested in the entire clinical study there were no invalid results. The calculated rate of invalid results in this study was 0.0%.

   Performance with Prospectively Collected Specimens

   Prospective specimens were collected and tested at two different Public Health

Laboratories. Serum samples were collected, de-identified and run on both the ASI Evolution and ASiManager-AT following the appropriate package insert instructions. Positive and negative controls were run on each day of testing.

One thousand sixty eight (1068) serum samples were randomly selected from prospective specimens that were collected at the public health laboratories. Patients were infants (<1 year) to 100 years with 324 females (30.3%), 739 males (69.2%) and 5 patients with unreported sex (0.5%).

The positive percent agreement (PPA) and the negative percent agreement (NPA) of the ASI Evolution using the ASI Automated RPR Test for Syphilis, in prospectively collected samples, when compared to the previously FDA cleared RPR assay, ASiManager-AT ASI RPR Test for Syphilis, along with the 95% confidence interval are shown in table 12.

Table 12: Prospective Serum Sample Results for ASI Automated RPR Test for Syphilis on the ASI Evolution vs. FDA cleared comparator

Prospective Samples		ASI RPR Card Test for Syphilis on the ASiManager-AT Result		
		Reactive	Non-Reactive	Total
ASI Automated RPR Test for Syphilis on the ASI Evolution Result	Reactive	114	1	115
	Non-Reactive	1	952	953
	Total	115	953	1068

PPA: 99.13% (95% CI: 95.24%-99.85%)
NPA: 99.90% (95%CI: 99.41%-99.98%)

Performance with Retrospective/Pre-Selected Samples

Retrospective samples were purchased by Bio-Rad from multiple vendors. Testing was conducted in-house. Serum and sodium citrate plasma samples were frozen and de-identified.

A total of 10 retrospective serum samples and 1003 retrospective sodium citrate plasma samples were tested. The positive percent agreement (PPA) and the negative percent agreement (NPA) of the ASI Evolution using the ASI Automated RPR Test for Syphilis, in retrospective serum and plasma samples, when compared to the previously FDA cleared RPR assay, ASiManager-AT using the ASI RPR Test for Syphilis, along with the 95% confidence interval are shown in tables 13 and 14 below.

Table 13: Retrospective Serum Sample Results for ASI Automated RPR Test for Syphilis on the ASI Evolution vs. FDA cleared comparator

Retrospective Serum Samples		ASI RPR Card Test for Syphilis on the ASiManager-AT Result		
		Reactive	Non-Reactive	Total
ASI Automated RPR Test for Syphilis on the ASI Evolution Result	Reactive	7	0	7
	Non-Reactive	0	3	3
	Total	7	3	10

PPA: 100% (95% CI: 59.04% - 100%)
NPA: 100% (95% CI: 29.24% - 100%)

Table 14: Retrospective Plasma Sample Results for ASI Automated RPR Test for Syphilis on the ASI Evolution vs. FDA cleared comparator

Retrospective Sodium Citrate Plasma Samples		ASI RPR Card Test for Syphilis on the ASiManager-AT Result		
		Positive	Negative	Total
ASI Automated RPR Test for Syphilis on the ASI Evolution Result	Reactive	10	0	10
	Non-Reactive	0	993	993
	Total	10	993	1003

PPA: 100% (95% CI: 69.15% - 100%)
NPA: 100% (95% CI: 99.63% - 100%)

Performance in Samples from Pregnant Women

A total of 280 pregnant women were tested in this study. The women were 15 – 41 years old and covered all three trimesters of pregnancy. Two hundred fifty samples were prospectively collected, 30 samples were preselected pregnant women positive for syphilis. The positive percent agreement (PPA) and the negative percent agreement (NPA) of the ASI Evolution using the ASI Automated RPR Test for Syphilis, when compared to the previously FDA approved RPR assay, ASiManager-AT using the ASI RPR Test for Syphilis, along with the 95% confidence interval are shown in the table below.

Table 15: Pregnant Women Sample Results for ASI Automated RPR Test for Syphilis on the ASI Evolution vs. FDA cleared comparator

Pregnant Women		ASI RPR Card Test for Syphilis on the ASiManager-AT Result		
		Positive	Negative	Total
ASI Automated RPR Test for Syphilis on the ASI Evolution Result	Reactive	30	0	30
	Non-Reactive	0	250	250
	Total	30	250	280

PPA: 100% (95% CI:88.65% - 100%)
NPA: 100% (95% CI: 98.49% - 100%)

Performance in Medically Diagnosed Individuals

The performance of the ASI Evolution was evaluated with samples from subject who were medically diagnosed with primary, secondary, or latent syphilis. The diagnosis of syphilis and the stage of the disease were made by a licensed physican based on the patient's clinical sypmptoms, medical history, and laboratory test results at the time of diagnosis. Samples were collected from 143 individuals diagnosed with primary, secondary, or latent syphilis with treatment status. All samples gave valid results. The positive percent agreement (PPA) and the negative percent agreement (NPA) of the ASI Evolution using the ASI Automated RPR Test for Syphilis, when compared to the previously FDA approved RPR assay, ASiManager-AT using the ASI RPR Test for Syphilis, along with the 95% confidence interval are shown in the table below.

Table 16: Medically Diagnosed Individuals, Treated and Untreated, Results for ASI Automated RPR Test for Syphilis on the ASI Evolution vs. clinical status

Syphilis Phase	Treatment Status	N	Reactivity in Medically Diagnosed Syphilis Patients	
			ASI Evolution vs. ASiManager	95% Confidence Interval
Primary	Untreated	25	100% (25/25)	86.28% - 100%
	Treated	18	100% (18/18)	81.47% - 100%
Secondary	Untreated	25	100% (25/25)	86.28% - 100%
	Treated	25	100% (25/25)	86.28% - 100%
Latent	Untreated	25	100% (25/25)	86.28% - 100%
	Treated	25	100% (25/25)	86.28% - 100%
All Phases	Untreated	75	100% (75/75)	95.13% - 100%
	Treated	68	100% (68/68)	94.65% - 100%
Total		**143**	**100% (143/143)**	**97.38% - 100%**

4. Clinical cut-off**:**
   Not Applicable.

5. Expected values/Reference range:
   A total of 1068 specimens were collected prospectively from the intended use population and tested with the ASI Evolution. The syphilis prevalence, stratified by gender and age group, is presented below.

Table 17: Prevalence of Syphilis Among Subjects Sent for Syphilis Testing

Age (years)	Gender	N	ASI Automated RPR Test for Syphilis on the ASI Evolution Results			
			Reactive (N)	% Reactive	Non-Reactive (N)	% Non-Reactive
<21	Female	45	0	0%	45	100%
	Male	55	4	7%	51	93%
21-30	Female	140	12	9%	128	91%
	Male	283	43	15%	240	85%
31-40	Female	85	2	2%	83	98%
	Male	231	30	13%	201	87%
41-50	Female	29	2	7%	27	93%
	Male	90	12	13%	78	87%
51-60	Female	17	2	12%	15	88%
	Male	64	7	11%	57	89%
>61	Female	4	0	0%	4	100%
	Male	16	0	0%	16	100%
Unknown Age	Female	4	0	0%	4	100%
	Male	0	0	N/A	0	N/A
Various Ages*	Unknown Sex	5	0	0%	5	100%
Overall 0 - 100	Female	324	18	6%	306	94%
	Male	739	96	13%	643	87%
Total		**1068**	**114**	**11%**	**954**	**89%**

*20, 28, 29, 30, 46

The syphilis prevalence in this clinical study was 11%.

N. Instrument Name:

ASI Evolution, software version 1.0

O. System Descriptions:

1. Device Description
   The ASI Evolution is an integrated digital particle analyzer designed to objectively interpret certain slide agglutination tests manufactured by Arlington Scientific, Inc. (ASI). The ASI Evolution fully automates the sample and reagent handling steps of the test procedure. Qualitative and semi-quantitative tests are performed by laboratory professionals who use the ASI Evolution to provide standardized test interpretation using criteria that define reactive and nonreactive agglutination reactions.

   The ASI Evolution employs a camera to create a highly sensitive and high-resolution

image of the agglutination immunoassay. This image is then analyzed by the proprietary software algorithm to interpret the agglutination pattern.

2. Principle of Operation
   The ASI RPR Test is a macroscopic nontreponemal flocculation test to be used for the detection of reagin. The microparticulate carbon RPR antigen enhances the visual discrimination between reactive and nonreactive results. The reagin-type antibody binds with the antigen that is composed of a complex of cardiolipin, lecithin and cholesterol particles with activated charcoal. The result of this antigen-antibody reaction is macroscopic flocculation. This test kit is intended to be used in conjunction with the ASI Evolution Automated Syphilis Analyzer.

3. Modes of Operation
   The assay is fully automated.

4. Calibration
   The firm included in their latest software build the ability to calibrate exposures per well using a grey intensity target (on empty wells). Users can verify that the grey intensity (shade) stays within the allowed range when the picture is taken.

5. Software
   a. FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types: **YES_X_** or **NO__**

   b. Level of Concern: Moderate

   c. Device Hazard Analysis
      The firm provided a Failure Mode and Effects Criticality Analysis (FMECA) to examine the likelihood of each failure mode's occurrence during operation of the device, and their effect on patient results.

   d. Software Description
      The software for the ASI Evolution analyzes agglutination tests, which are interpreted through image processing algorithms from images taken with a CCD camera. The image results are passed to an integrated PC and software to provide an easy to use application for reviewing and distributing results.

      The ASI Evolution software algorithm determines a 'Reactive' or 'Nonreactive' result based on the following criteria—
      - If the numerical number is less than or equal to 50 the result is 'Nonreactive'.
      - If the numerical number is greater than or equal to 51, the test is 'Reactive'.

   e. Software Requirements Specifications
      The firm's SRS documents describes functional features of the software. It

highlights what functions should be implemented in the ASI Evolution software. The firm indicated that the software will run on a windows based computer, and will have sufficient processing power to complete all necessary, user required operation. The firm stated that future versions of their software may be updated to run with newer operating systems.

f. EMC Testing and Standards
The firm provided test report showing compliance to IEC 61010-1 for general safety requirements of electrical equipment. The firm also provided the test report showing compliance to IEC 61010-2-101 for safety requirements for IVD medical, electrical equipment.

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

Not Applicable

Q. Proposed Labeling:

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

R. Conclusion:

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