510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K182391

B. Purpose for Submission:

To expand the intended use of the ASI Automated RPR (rapid plasma reagin) Test for Syphilis performed on the ASI Evolution instrument, previously 510(k)-cleared under K173376, to include a semi-quantitative claim for the determination of reagin antibody endpoint titers in human serum and plasma samples.

C. Measurand:

Antibodies to plasma reagin (cellular lipids and lecithin).

D. Type of Test:

The ASI Automated RPR Test for Syphilis run on the ASI Evolution instrument is a nontreponemal flocculation test that is performed in a 48-well microtiter plate and interpreted by the ASI Evolution instrument using a high-resolution camera and embedded pattern recognition software algorithm that analyzes the algglutination pattern of each microtiter well.

E. Applicant:

Arlington Scientific, Inc.

F. Proprietary and Established Names:

ASI Automated RPR Test for Syphilis
ASI Evolution Automated Syphilis Analyzer
ASI Evolution

G. Regulatory Information:

1. Regulation Section:

   21 CFR §866.3820 – *Treponema pallidum* nontreponemal test reagents

2. Classification:

   Class II

3. Product Code(s):

   GMQ – Antigens, nontreponemal, all
   JQT – Densitometer/scanner (integrating, reflectance, TLC, or radiochromatogram) for clinical use

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 and semi-quantitative 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 is for professional use only. The test is intended to be used for *in vitro* diagnostic testing and blood donor screening.

   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 for Syphilis is intended to be used for *in vitro* diagnostic testing and blood donor screening.

2. Indication(s) for Use:

   Same as intended use

5. Special Conditions for Use Statement(s):

   For prescription use only

6. Special Instrument Requirements:

   ASI Evolution

I. Device Description:

1. Overview:

The ASI Automated RPR Test for Syphilis performed on the ASI Evolution is an automated nontreponemal flocculation test for the detection of reagin antibodies in human serum and plasma. Reagin antibodies, if present in human serum or plasma, bind to the carbon RPR test antigen which is composed of complexed cardiolipin, lecithin, and cholesterol particles in the presence of activated charcoal. Flocculation of the antibody-antigen complex and coagglutination with charcoal particles allows visualization of an agglutionation pattern that is distinguishable from non-reactive test samples.

The ASI Evolution instrument provides full automation of the sample and reagent handling steps of the test procuedure, and objective interpretation of test results via a high-resolution internal CCD camera and an embedded agglutination pattern recognition software. The ASI Evolution reports a qualitative test result (reactive or non-reactive) for each microtiter well and semi-quantitative endpoint titers of serially diluted samples.

Performance data supporting the qualitative claim for the ASI Automated RPR Test for Syphilis run on the ASI Evolution was previously submitted and reviewed by FDA under K173376. Detailed descriptions of the analytical and clinical study designs and test results which were conducted to support the qualitative claim are available in the K173376 decision summary document. Data presented in the sections below are limited to the studies that were required to demonstrate that the ASI Auotmated RPR Test for Syphilis run on the ASI Evolution can accurately determine semi-quantiative reagin antibody endpoint titers.

2. Materials Provided:

The 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, Non-reactive) - Human serum or defibrinated plasma (liquid), with 0.1% sodium azide as preservative.

3. Materials Required but Not Provided:

Additional materials required for the ASI Auotmated RPR Test for Syphilis but not provided include:

- Deionized water
- ASI Evolution instrument system

J. Substantial Equivalence Information:

1. Predicate Device Name(s):

   Gold Standard Diagnostics AIX1000 Rapid Plasma Reagin (RPR) Automated Test System

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

   K150358

3. Comparison with Predicate:

Table 1: Device Similarities

	Similarities	
	Device	**Predicate**
Item	**ASI Automated RPR Test for Syphilis on the ASI Evolution K182391**	**Gold Standard Diagnostics AIX1000 RPR Automated Test System K150358**
Regulation	866.3820	Same
Product Code	GMQ	Same
Device Class	II	Same
Technology	Nontreponemal macroscopic flocculation test	Same
Antigen	cardiolipin, lecithin, and cholesterol with activated carbon	Same
Intended Use	The ASI Automated RPR (rapid plasma reagin) Test for Syphilis, for use on the ASI Evolution Automated Syphilis Analyzer, is a qualitative and semi-quantitative 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 is for professional use only. The test is intended to be used for *in vitro* diagnostic testing and blood donor screening. The ASI Evolution is intended to be used as a fully automated analyzer to	The Gold Standard Diagnostics AIX1000 Rapid Plasma Reagin (RPR) Automated Test System is a non-treponemal flocculation test that can qualitatively determine the presence of reagin antibodies in human serum. It may be used to aid in the diagnosis of syphilis when used in conjunction with supplemental treponemal laboratory tests and other clinical information. This test may also be used to detect non-treponemal antibodies in samples serially diluted to estabilish titer information. This test is not intended for screening blood or tissue donors.

	Similarities	
	Device	**Predicate**
	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 for Syphilis is intended to be used for *in vitro* diagnostic testing and blood donor screening.	
Sample Processing	Automated	Same
Result Interpretation	Automated	Same
Test Format	48-well microtiter plate	Same
Test Capacity	192 samples	Same
Result Reporting	Qualitative, semi-quantiative titers	Same

Table 2: Device Differences

	Differences	
	Device	**Predicate**
Item	**ASI Automated RPR Test for Syphilis on the ASI Evolution K182391**	**Gold Standard Diagnostics AIX1000 RPR Automated Test System 510(k)# K150358**
Sample Type	Serum or plasma	Serum only
Indications for use	Used for *in vitro* diagnostic testing and blood donor testing	Used for *in vitro* diagnostic testing only
Controls	Reactive, weak reactive, non-reactive	Reactive and non-reactive
Instrumentation and Software	ASI Evolution equipped with a CCD camera and proprietary pattern recognition algorithm	AIX1000 equipped with an HD camera and proprietary pattern recognition algorithm

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

- EP012-A2. User Protocol for Evaluation of Qualitative Test Performance: Approved Guideline-Second Edition.
- EP05-A3. Evaluation of Precision of Quantitative Measurement Methods: Approved Guideline-Third Edition.

L. Test Principle:

The ASI Automated RPR Test for Syphilis is a fully automated, high-throughput

macroscopic nontreponemal flocculation test that detects reagin antibodies in human serum or plasma samples. The test kit is intended to be used with the ASI Evolution system.

The ASI Evolution is an integrated digital particle analyzer designed to automate the sample and reagent handling steps of the test procedure and objectively interpret the test results of the ASI Automated RPR Test for Syphilis. 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 microtiter plates using light reflectance. The image is then analyzed by software developed with an optical recognition feature that identifies each well boundary to ensure it is in the correct position, and interprets the agglutination pattern to determine the sample result.

To complete the ASI Automated RPR Test for Syphilis the user must perform the following tasks:

- Load sample tubes into the sample rack
- Load the sample rack into the unit
- Refill the prime bottle with deionized water
- Place the reagent and diluent in their respective positions in the permanent rack
- Load and unload 48-well microtiter plates.

To complete the ASI Autotmated RPR Test for Syphilis the analyzer automates the following steps:

- Aspirate and dispense sample fluid and carbon RPR antigen
- Perform mixing of the reaction
- Time each procedural step appropriately
- Capture and record images of each completed test
- Process and store data of the test result image
- Report and record the qualitative and numerical results of each test.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   Analytical studies supporting the qualitative detection of reagin antibodies in human plasma and serum by the ASI Automated RPR Test for Syphilis performed on the ASI Evolution were previously submitted and reviewed under K173376. Details pertaining to the study protocols and resulting data are available in the K173376 decision summary document. In addition to the previously conducted studies, validation testing to support the semi-quantitative claim for the determination of reagin antibody endpoint titers in human serum and plasma was performed. A description of the study protocol and a summary of the test results are provided below.

   Endpoint Titer Validation

   A randomized and blinded panel of 10 human serum samples with known reagin antibody endpoint titers, as determined by the ASI RPR Card Test for Syphilis on the ASiManager-AT, was tested with the ASI Automated RPR Test for Syphilis on the ASI Evolution using

the semi-quantitative test procedure. The reactive samples had titers ranging from 1:1 to 1:256. Each sample panel member was tested a minimum of 80 times, in-house, on at least five different days by one operator using a single ASI Evolution instrument. To meet the acceptance criteria, all non-reactive samples were required to yield non-reactive test results, while all reactive samples were required to yield test results within one dilution above or below the known titer. The results of the semi-quantitative analysis are shown below.

Table 3: Results from Endpoint Titer Validation Study

Endpoint Titer Results												
Sample Reactivity	Non-reactive	Neat (1:1)	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	% Agreement within +/- 1 titer (95% C.I.)
06127 (Non-reactive)	80	0	0	0	0	0	0	0	0	0	0	100% (95.49% - 100%)
N8E23 (Non-reactive)	80	0	0	0	0	0	0	0	0	0	0	100% (95.49% - 100%)
W6A16R (1:2)	0	7	69	4	0	0	0	0	0	0	0	100% (95.49% - 100%)
W8B01R (1:2)	0	0	75	5	0	0	0	0	0	0	0	100% (95.49% - 100%)
R7F01R (1:8)	0	0	0	0	76	4	0	0	0	0	0	100% (95.49% - 100%)
R8B01R (1:8)	0	0	0	32	48	0	0	0	0	0	0	100% (95.49% - 100%)
07117 (1:16)	0	0	0	0	5	75	0	0	0	0	0	100% (95.49% - 100%)
08188 (1:64)	0	0	0	0	0	0	0	87	1	0	0	100% (95.89% - 100%)
07098 (1:128)	0	0	0	0	0	0	0	5	82	1	0	100% (95.89% - 100%)
08296 (1:256)	0	0	0	0	0	0	0	0	21	65	4	100% (95.98% - 100%)

Non-reactive test results were observed for all 160 non-reactive samples. In addition, all reactive samples produced test results that were within one dilution of the known reagin antibody titer for an overall percent agreement of 100%.

2. Comparison studies:

Method comparison with predicate device

Clinical performance of the ASI Automated RPR Test for Syphilis on the ASI Evolution for the qualitative claim was evaluated under K173376. The study cohort consisted of 1068 prospective serum samples, 10 retrospective serum samples, 1003 retrospective plasma samples, 143 clinically diagnosed syphilis patients, and 250 pregnant women. For additional details and study results, please refer to the K173376 decision summary document.

N. Instrumentation/System Description

1. Instrument Name

ASI Evolution

2. System Description

The ASI Evolution instrument system is an integrated digital particle analyzer designed to objectively interpret certain slide agglutination tests manufactured by Arlington Scientific, Inc. (ASI). The system is capable of fully automating the sample and reagent handling steps of test procedures as well as digital acquisition and interpretation of agglutination patterns. This system design removes assay subjectivity, reduces errors, enables the review of past data, and speeds up the overall test procedure.

3. Software

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

a. Level of Concern

Moderate

b. Software Description

The software for the ASI Evolution instrument 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 "Non-reactive" result based on the following criteria:

- If the numerical number is less than or equal to 50 the result is "Non-reactive."
- If the numerical number is greater than or equal to 51, the test is "Reactive."

The "Reactive" or "Non-reactive" outputs of the software determine the qualitative assay result. When running the semi-quantitative titer protocol, the software uses the same cutoffs described above to distinguish between a "Reactive" and "Non-reactive" sample well. The endpoint titer value is equivalent to the highest dilution at which the serially diluted sample produces a "Reactive" test result.

c. Specimen Identification

Barcode labeled patient samples can be imported with the use of a hand-held barcode scanner.

d. Specimen Sampling and Handling

e. 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.

f. Quality Control

Quality control is conducted using external reactive, weak-reactive and non-reactive controls that are provided with the ASI Automated RPR Test for Syphilis.

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