510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K201438

B Applicant

Arlington Scientific, Inc. (ASI)

C Proprietary and Established Names

ASI Evolution
ASI Automated RPR Test for Syphilis

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GMQ	Class II	21 CFR 866.3820 - Treponema Pallidum Nontreponemal Test Reagents	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

The purpose of the submission was to provide data in support of modifications made to the result interpretation algorithm. The changes were necessary due to an identified bug in the software which, on a rare occasion, could allow for a false negative result. All other functionality of the algorithm is unchanged.

B Measurand:

Nontreponemal antibodies (plasma reagin).

C Type of Test:

Qualitative and Semi-quantitative flocculation test

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

The ASI Automated RPR (rapid plasma reagin) Test for Syphilis, for use on the ASI Evolution Automated Analyzer, is a qualitative and semi-quantitative flocculation test for the detection of nontreponemal antibodies in human serum and plasma to aid in the diagnosis of syphilis. All reactive RPR test samples should be further tested with a treponemal test to determine serological evidence of syphilis infection. The test is intended to be used for *in vitro* diagnostic testing.

The ASI Automated RPR Test for Syphilis is for professional use only.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
ASI Evolution Automated Analyzer

IV Device/System Characteristics:

A 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, including fluid handling, mixing, timing, image capture, image processing and result reporting.

The RPR (rapid plasma reagin) Test for Syphilis is sold in two kit sizes, 480 tests and 4800 tests. Each reagent kit contains RPR Carbon Antigen, three Controls (Reactive, Weak Reactive and Nonreactive) and 48-well Microwell Plates.

The test uses serum or plasma samples which are loaded directly onto the analyzer along with microwell plates in the designated area. The instrument automatically dispenses the specified sample volume and the reagents into the microwells where the reaction occurs. The instrument can accommodate up to 4 microwell plates and process up to 192 samples, including controls.

The ASI Evolution further provides tools that enable the creation, storage, retrieval and transmittal of the test results.

B Principle of Operation:

The ASI Evolution employs a camera to create a high-resolution image of an agglutination immunoassay. The software has been developed with an optical recognition feature capable of recognizing each well boundary to ensure accurate positioning prior to image capture. The image is then analyzed by the proprietary software algorithm that interprets the agglutination pattern based on the number and size of the carbon particles in the image. This count is then compared to preset parameters to determine the test result. If the value is below the parameter, it is interpreted as Nonreactive, and if the value is above the parameter, it is interpreted as Reactive. All images are stored on the hard drive and results are labeled reactive or non-reactive. This interpretation is then displayed on the User Interface.

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

C Instrument Description Information:

1. Instrument Name:

   ASI Evolution Automated Analyzer

2. Specimen Identification:

   Barcode or manual.

3. Specimen Sampling and Handling:

   Direct from the sample collection tube.

4. Calibration:

   Not required.

5. Quality Control:

   Three Controls are included in the reagent kit: Reactive, Weak Reactive and Nonreactive.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ASI Automated RPR Test for Syphilis on the ASI Evolution

B Predicate 510(k) Number(s):

K182391

C Comparison with Predicate(s):

Device & Predicate Device(s):	K201438	K182391
Device Trade Name	ASI Automated RPR Test for Syphilis using ASI Evolution (Modified)	ASI Automated RPR Test for Syphilis on the ASI Evolution (Original)
General Device Characteristic Similarities		
Intended Use/Indications for Use	The ASI Automated RPR (rapid plasma reagin) Test for Syphilis, for use on the ASI Evolution Automated Analyzer, is a qualitative and semiquantitative flocculation test for the detection of nontreponemal antibodies in human serum and plasma to aid in the diagnosis of syphilis. All reactive RPR test samples should be further tested with a treponemal test to determine serological evidence of syphilis infection. The test is intended to be used for in vitro diagnostic testing. The ASI Automated RPR Test for Syphilis is for professional use only.	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 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.

Technology	Macroscopic flocculation with a digital particle Reader based on reflectance technology and image capture using CCD camera.	Same
Sample Processing	Fully automated	Same
Analyte	Nontreponemal antibody to *T. pallidum* (rapid plasma reagin)	Same
Sample Type	Serum and Plasma	Same
Quality Controls	Reactive, Weak Reactive, Nonreactive Controls are provided with the reagent kit.	Same
Result Interpretation	Automated	Same
Throughput	192 Samples (including Controls)	Same
General Device Characteristic Differences		
Software	The "clump finder" algorithm was modified to keep large aggregates intact.	Designed to divide large aggregates, when encountered, into smaller aggregates.
	Corrected a bug in the weighting function that assigns a numerical value to an aggregate by size.	A weighting function assigns a numerical value to an aggregate by size and the algorithm bins clusters, where each bin has an assigned weighted value, according to size.
Catalog Number for Commercial Distribution	Two separate catalog numbers created for commercial distribution: (a) for sale to diagnostic laboratories, and (b) for sale to blood donor screening laboratories.	One catalog number for diagnostic use and for blood screening.

VI Standards/Guidance Documents Referenced:

161010-1	International Electrotechnical Commission (IEC)	Standard for Safety Electrical Equipment for Measurement, Control, and Laboratory use; Part 1: General Requirements	Issued: 2010-06 Ed: 3	2010/06/01
CAN CSA C22.2 61010-1	Canadian Standards Association (CSA)	Standard for Safety of Electrical Equipment for Measurement, Control and Laboratory Use; Part 1: General Requirement	Ed: 2	Issued 2004/07/01

IEC 61010-2-101	International Electrotechnical Commission (IEC)	Safety Requirements for Electrical Equipment for Measurement, Control and Laboratory Use – Part 2-101: Particular Requirements for in vitro diagnostic (IVD) Medical Equipment	Ed:1.0	2002/01/01
IEC 61326-1	International Electrotechnical Commission (IEC)	Electrical Equipment for Measurement, Control and Laboratory Use EMC Requirements Part 1: General Requirements	Ed: 1.0	2005/12/01
IEC 61326-2-6	International Electrotechnical Commission (IEC)	Electrical Equipment for Measurement, Control and Laboratory Use EMC Requirements Part 2-6: Requirements for - in vitro diagnostic (IVD) medical equipment	Ed: 1.0	Issued 2005/12/01
13485:2003 with 14971:2007 Risk Management Guidance	International Organization for Standardization	Medical devices – Quality management systems – Requirements for regulatory purposes Medical devices – Application of risk management to medical devices	2003 2007	2003/2007
21 CFR 820	U.S. Food and Drug Administration (FDA)	Quality System Regulation 21 CFR Part 820 Medical Devices, Current Good Manufacturing Practices (CGMP)	Final Rule	1996/10/07

VII Performance Characteristics:

A Analytical Performance:

1. Precision/Reproducibility:

   Precision and reproducibility of the ASI Automated RPR Test for Syphilis performed on the ASI Evolution was initially demonstrated and reviewed under K173376.

To demonstrate the reproducibility of the system after the interpretation algorithm was modified, a study was conducted testing seven serum samples with a range of RPR titers. The testing was performed over five testing days using three lots of Carbon Antigen each day. Each sample was tested in duplicate, in two runs per day for a total of 60 measurements per sample (5 days x 2 runs/day x 2 replicates x 3 lots of Carbon Antigen). The sample panel consisted of two nonreactive samples, two samples with a titer of 1:2, one sample with a titer of 1:4, one sample with a titer of 1:8 and one sample with a titer of 1:16. All tests gave expected results. A summary of the reproducibility data is shown below.

Summary of Reproducibility Results

	Sample RPR Status (Manual)	Sample ID	N	% Agreement with Expected Result	95% Confidence Interval
1	RPR nonreactive	10159A	60	100% (60/60)	94.0 - 100
2	RPR nonreactive	06127	60	100% (60/60)	94.0 - 100
3	RPR reactive 1:2	10159D	60	100% (60/60)	94.0 - 100
4	RPR reactive 1:2	W9P19R	60	100% (60/60)	94.0 - 100
5	RPR reactive 1:4	10159C	60	100% (60/60)	94.0 - 100
6	RPR reactive 1:8	10159E	60	100% (60/60)	94.0 - 100
7	RPR reactive 1:16	R0B03R	60	100% (60/60)	94.0 - 100

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   See K173376.

4. Assay Reportable Range:

   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   See K173376.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

8. Accuracy (Instrument):

   Not applicable.

9. Carry-Over:

   See K173376.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A comparison of the digital interpretation of results from the ASI Evolution using the original interpretation algorithm to the interpretation made by the ASI Evolution using the new interpretation algorithm was conducted by testing 1,762 retrospective samples (872 serum and 890 plasma). All samples were deidentified and the testing was performed over multiple days by multiple operators, using one lot of Carbon Antigen. Reactive, Weak Reactive and Nonreactive controls were run on each day of testing. The results are presented below, by matrix.

RPR Results with the Modified vs. Original Interpretation Algorithm in Plasma

		ASI Evolution (Original)		
ASI Evolution (Modified)		**Reactive**	**Nonreactive**	**Total**
	Reactive	119	1	120
	Nonreactive	5	765	770
	Total	124	766	890
	PPA=96.0% (119/124); 95% CI: 90.9%-98.3%			
	NPA=99.9% (765/766); 95% CI:99.3%-100%			

RPR Results with the Modified vs. Original Interpretation Algorithm in Serum

		ASI Evolution (Original)		
ASI Evolution (Modified)		**Reactive**	**Nonreactive**	**Total**
	Reactive	91	6	97
	Nonreactive	0	775	775
	Total	91	781	872
	PPA=100% (91/91); 95% CI: 96.0%-100%			
	NPA=99.2% (765/768); 95% CI:98.3%-99.7%			

RPR Results with the Modified vs. Original Interpretation Algorithm, Combined

		ASI Evolution (Original)		
ASI Evolution (Modified)		**Reactive**	**Nonreactive**	**Total**
	Reactive	210	7	217
	Nonreactive	5	1540	1545
	Total	215	1547	1762
	PPA=97.7% (210/215); 95% CI: 94.7%-99.0%			
	NPA=99.6% (1540/1547); 95% CI:99.1%-99.8%			

There were 12 samples that gave discordant results (6 serum and 6 plasma) between the two versions of the interpretation algorithm. These samples were tested with the TPPA assay (treponemal test) as well as with the manual RPR. The results of both treponemal testing and manual RPR testing were consistent with the results obtained using the modified algorithm, as shown below.

Supplemental Testing of Discordant Samples

Sample ID (coded)	Original Algorithm	New Algorithm	Treponemal Testing	Manual RPR Testing
GL0475634	Reactive	Nonreactive	Nonreactive	Nonreactive
JK0521018	Reactive	Nonreactive	Nonreactive	Nonreactive
LB0302794	Reactive	Nonreactive	Nonreactive	Nonreactive
GA1468206	Nonreactive	Reactive	Reactive	Reactive (1:8)
GL0475247	Reactive	Nonreactive	Nonreactive	Nonreactive
FD0974464	Nonreactive	Reactive	Reactive	Reactive (1:8)
AB1320706	Nonreactive	Reactive	Reactive	Reactive (1:4)
FD0965477	Nonreactive	Reactive	Reactive	Reactive (1:128)
GL0587386	Nonreactive	Reactive	Reactive	Reactive (1:8)
LC0812942	Nonreactive	Reactive	Reactive	Reactive (1:2)
AU483009	Nonreactive	Reactive	Reactive	Reactive (1:4)
FD09300106	Reactive	Nonreactive	Nonreactive	Nonreactive

Additional investigation of the images from the 12 discordant samples revealed the following:

1. The seven samples that were Reactive by the modified algorithm and Nonreactive by the original algorithm, were found to be misidentified by the original algorithm due to the identified “bug” in the software.
2. The five samples that were Reactive by the original algorithm and Nonreactive by the modified algorithm, were all found to have a bubble or an artifact in the test well, which was mis-identified by the original algorithm as a “clump.” The image analysis of the modified interpretation algorithm is able to account for these in the aggregation totals.

2. Interpretation of Images by the Software

The modified algorithm was evaluated using a bank of well images that have been collected from multiple ASI Evolution analyzers. The images were passed through the algorithm and the interpretation result was given as Nonreactive or Reactive. A total of 18,017 images were passed through the algorithm. These included 8,631 reactive images and 9,386 nonreactive images. The results were compared to those obtained when tested on the ASI Evolution using

the original unmodified software. The results from this study along with positive and negative percent agreements (PPA and NPA, respectively), are shown below.

Image Interpretation of Banked Well Images (Multiple Analyzers)
Modified Algorithm vs. Original Algorithm

		ASI Evolution (Original)		
ASI Evolution (Modified)		**Reactive**	**Nonreactive**	**Total**
	Reactive	8,618	7	8,625
	Nonreactive	13	9,379	9,392
	Total	8,631	9,386	18,017
	PPA=99.9% (8,618/8,631); 95% CI: 99.7%-99.9%			
	NPA=99.9% (9,379/9,386); 95% CI:99.9%-100%			

3. Challenge Panel
   The interpretation algorithm was further evaluated with 30 clinical samples representing "challenge" samples. These samples tested Nonreactive with the original algorithm but were Reactive with a manual RPR test. The archived images of these samples were reassessed with the new interpretation algorithm and all samples were interpreted as Reactive.

4. Testing of Pregnant Women
   Serum samples from pregnant women were tested on the ASI evolution using the modified interpretation algorithm. The results were compared to the results obtained with the ASI RPR Card test on the ASiManager-AT. There were 250 specimens with Nonreactive results and 30 specimens with Reactive results. There was 100% agreement between the results obtained with both test systems.

5. Matrix Comparison:

   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   See K173376.

2. Clinical Specificity:

   See K173376.

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

   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable

F Other Supportive Instrument Performance Characteristics Data:

Automated End-point Titration

In order to evaluate the titer functionality of the ASI Automated RPR on the ASI Evolution and to assess the accuracy of the semiquantitative test procedure, nine samples with known RPR reactivity were first evaluated by manual RPR titer method and then run in the TITER mode on the ASI Evolution using the modified software. The test panel consisted of the following samples:

End-point Test Panel

Sample	Sample ID	Sample Type	Manual RPR Results with Titer
1	06127	Normal Human Serum	Nonreactive (NR)
2	10159A	Nonreactive Control	Nonreactive (NR)
3	10159E	Human Serum	Reactive (1:8)
4	10159D	Human Serum	Reactive (1:2)
5	W9P19R	Weak Reactive Control	Reactive (1:2)
6	R0B03R	Reactive Control	Reactive (1:8)
7	01140	Human Serum	Reactive (1:64)
8	10159	Human Serum	Reactive (1:128)
9	10189C	Human Serum	Reactive (1:256

Each sample was tested in eight replicates on 10 different days, for a total of 80 data points for each sample. Acceptance criteria were: (a) all Nonreactive samples must be Nonreactive on the ASI Evolution, and (b) all Reactive samples must generate a titer result that is within one titer of the manual RPR titer result. All samples generated expected results, as shown in the table below.

RPR End-point Titer (Modified Algorithm)

Sample	RPR End-point (Manual)	Nonreactive	1:1 (Neat)	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512
1	Nonreactive	80										
2	Nonreactive	80										
3	1:2			43	37							
4	1.2			58	22							
5	1:8					65	15					
6	1:8				20	55	5					
7	1:64							17	46	17		
8	1:128								26	53	1	
9	1:256									35	40	5

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.