## 5.0 510(k) Summary

## 5.1 Preparation Date: 12/21/2017

**Submitted By**

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**5.2 Trade Name –** ASI RPR TEST FOR SYPHILIS FOR USE ON THE ASI EVOLUTION

**Regulation section:** (21 CFR 866.3820) *Treponema pallidum* test reagents

**Classification: Class II**

**Product Code: GMQ**

**Panel: Microbiology**

**5.3 Predicate Device(s) –** Gold Standard Diagnostics AIX1000 (K150358) and ASiManager-AT (K111356)

**5.4 SUMMARY AND EXPLANATION:** *Treponema pallidum*, the etiological agent of syphilis, induces the production of at least two types of antibodies in human infection: anti-treponemal antibodies that can be detected by FTA-ABS antigen, and anti-nontreponemal antibodies (reagin) that can be detected by RPR antigen.

**PRINCIPLE OF THE PROCEDURE:** 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.

**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 semiquantitative 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 that uses light reflectance 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 ASI Evolution further provides tools that enable the creation, storage, retrieval and transmittal of the test results.

**Intended Use –** The **ASI Automated RPR** (rapid plasma reagin) **Test** for syphilis 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 for use on the ASI Evolution analyzer. The ASI RPR Test for Syphilis is for professional use only. The test is intended for use in screening blood donors.

**5.5 Summary of Comparison Data –** A comparison of the digital interpretation of the results of testing samples with the ASI RPR Test for Syphilis using the **ASI Evolution** and the ASiManager-AT by trained laboratory professionals was conducted to show substantial equivalence.

The following data are the results from three testing sites:

**Combined (serum and plasma) Prospective Sample Testing - 1000 Samples**

| | | **ASI Evolution** | |
|---|---|---|---|
| | | Reactive | Nonreactive |
| ASiManager-AT Results | Reactive | 12 | 4* |
| | Nonreactive | 0 | 984 |

* Note - All 16 reactive prospective samples had confirmatory testing done using the Trinity Biotech CAPTIA Syphilis (T. Pallidum)-G test. Four of the reactive samples did not confirm. These samples were the same four samples that the ASI Evolution reported as nonreactive. The same 4 samples were also nonreactive with BD Macro-Vue RPR Card nontreponemal test. The ASiManager-AT results were incorrect.

**Combined (serum and plasma) Retrospective Sample Testing – 1,861 Samples**

Known Infected

| | | ASI Evolution | | |
|---|---|---|---|---|
| | | Reactive | Nonreactive | Total |
| ASiManager-AT Results | Reactive | 817 | 0 | 817 |
| | Nonreactive | 0 | 0 | 0 |
| | Total | 817 | 0 | 817 |

Known Uninfected

| | | ASI Evolution | | |
|---|---|---|---|---|
| | | Reactive | Nonreactive | Total |
| ASiManager-AT Results | Reactive | 0 | 0 | 0 |
| | Nonreactive | 0 | 1,044 | 1,044 |
| | Total | 0 | 1,044 | 1,044 |

Table 1

| Site | Prospective random samples | | Retrospective samples[3] | | | | A panel of known reactivity[3] | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | | | Plasma | | Serum | | Serum | | |
| | Plasma[1] | Serum[2] | Known infected | Known Uninfected | Known infected | Known Uninfected | Known infected | Known Uninfected | |
| A | 500 | 0 | 0 | 0 | 0 | 0 | 400 | 48 | 948 |
| B | 100 | 400 | 0 | 0 | 0 | 0 | 400 | 48 | 948 |
| C | 0 | 0 | 410 | 993 | 7 | 3 | 400 | 48 | 1,861 |
| Total | 600 | 400 | 410 | 993 | 7 | 3 | **1,200** | **144** | **3,757** |

1 – There were3 concordant reactive results.

2 – There were 9 concordant reactive results and 4 discordant results (ASI Evolution nonreactive and ASiManager-AT reactive).

3 – All tests gave the expected results.

# ASI Evolution Performance Characteristics

## Positive Agreement

Using the data from the composite performance results above, the positive agreement of the **ASI Evolution** can be calculated using the following formula:

**Positive Agreement = TR/(TR+FN)**

where

**TR** = the number of samples that test reactive by both the ASI Evolution and ASiManager-AT.

**FN** = the number of samples that test nonreactive by the ASI Evolution and reactive by the ASiManager-AT.

Using this formula the overall positive agreement is calculated as:

829/(833 + 0) = 99.52
95% CI: (98.76%, 99.87%)

Serum positive agreement is calculated as:

PPA = 416/420 = 99.05%
95% CI: (97.58%, 99.74%)

EDTA (203) and Sodium Citrate (210) plasma positive agreement is calculated as:

413/(413 + 0) = 100%
95% CI: (99.11%, 100%)

## Negative Agreement

Using the data from the composite performance results above the negative agreement of the **ASI Evolution** can be calculated using the following formula:

**Negative Agreement = TN/(TN+FR)**

where

**TN** = the number of samples that test nonreactive by both the ASI Evolution and ASiManager-AT.

**FR** = the number of samples that test reactive by the ASI Evolution and nonreactive by the ASiManager-AT.

Using this formula the overall negative agreement is calculated as:

2028/(2028 + 0) = 100%
95% CI: (99.82%, 100%)

Serum negative agreement is calculated as:

438/(438 + 0) = 100%
95% CI: (99.16%, 100%)

All plasma samples combined (EDTA and citrate) negative percentage agreement:

1590/1590 = 100%
95% CI: (99.77%, 100%)

Conclusion:

The performance of the ASI Evolution is substantially agreement to the performance of the ASiManager-AT.

## Sensitivity

Using the data from the performance results of the retrospective samples supplied by ASI of known infected status above, the sensitivity of the **ASI Evolution** in a blood bank setting can be calculated using the following formula:

**Sensitivity = TR/(TR+FN)**

where

**TR** = True Reactive, the number of samples that test reactive which actually are reactive.

**FN** = False Nonreactive, the number of samples that test nonreactive which actually are reactive.

Each laboratory was supplied with a panel of 400 known reactive samples. Each panel was made up of the same samples but different aliquots. Each sample was from a different and unique patient or donor. The samples were numbered R1-R400 and contained 0.5 ml each. These samples were purchased from blood banks and commercial vendors. The samples were tested by the respective facility that the sample was purchased from or vendor using RPR testing to determine the exact status of the sample. The samples were tested by ASI using the ASI RPR Test for Syphilis and the ASiManager-AT to verify the reactivity before being sent to the participating laboratory. Only the testing done at ASI will be used to calculate the sensitivity so that the same samples tested at the other sites that were duplicate samples are not used to make the determination. The other 17 reactive retrospective samples tested at ASI will also be used. These samples were purchased from blood banks and commercial vendors. The samples were tested by the respective facility that the sample was purchased from or vendor using RPR testing to determine the exact status of the sample. The samples were tested by ASI using the ASI RPR Test for Syphilis and the ASiManager-AT to verify the reactivity before being sent to the participating laboratory. Additional 400 known reactive plasma samples were tested (200 EDTA and 200 citrated plasma samples). From Table 1, 410 plasma samples and 407 serum samples with known reactive status were tested with ASI Evolution.

Using the formula from above, the sensitivity is calculated as:

ASI Evolution results:
Serum = 407/407 = 100%; 95% CI: (99.10%, 100%)
Plasma = 410/410 = 100%; 95% CI: (99.10%, 100%)

## Specificity

Using the data from the prospective samples, the specificity of the **ASI Evolution** can be calculated using the following formula:

**Specificity = TN/(TN+FR)**

where

**TN** = True Nonreactive, the number of samples that test nonreactive which actually are nonreactive.

**FR** = False Reactive, the number of samples that test reactive which actually are nonreactive.

Specificity was calculated from the prospective studies excluding confirmed reactive samples. From Table 1, 597 = 600-3 plasma samples and 391 = 400-9 serum samples were used to calculate specificity with ASI Evolution.

Using the formula from above, the specificity is calculated as:

ASI Evolution results:

Serum = 391/391 = 100%; 95% CI: (99.06%, 100%)
Plasma = 597/597 = 100%; 95% CI: (99.38%, 100%)

## Repeatability

Repeatability is defined as the variation in measurements taken by a single instrument on the same item and under the same conditions.

The interpretation of 14 samples using the ASI RPR Test for Syphilis and the **ASI Evolution** were evaluated for reactivity. The testing requirements were as follows:

1. All qualitative testing was conducted according to the proper procedure.
2. Each qualitative sample was tested 192 times.

A total of 10 samples were evaluated to determine repeatability of reactivity. Of the 10 samples, 7 were reactive and 3 were nonreactive. The reactive samples had titers of 1:1 (4 samples), 1:2 (1 sample), 1:8 (1 sample) and 1:256 (1 sample). Each of the 10 samples was repeated 192 times to evaluate the reactivity using the **ASI Evolution**. An aliquot of the same sample was dispensed into 192 tubes. All 192 tubes were placed

into the ASI Evolution and the run was performed. In this manner all 192 wells were tested with the same sample to show well to well and plate to plate repeatability. Refer to Table 18-14.

Table 18-14

| Sample | | | Result | | % Agreement |
|---|---|---|---|---|---|
| | Sample ID | Titer | | | |
| 1 | R7C21R | 1:8 | R | 192/192 | 100% |
| 2 | N7D04 | NR | NR | 192/192 | 100% |
| 3 | 11114B | 1:1 | R | 192/192 | 100% |
| 4 | 11114C | 1:1 | R | 192/192 | 100% |
| 5 | 11114F | 1:1 | R | 192/192 | 100% |
| 6 | 02287 | NR | NR | 192/192 | 100% |
| 7 | 08296 | 1:256 | R | 192/192 | 100% |
| 8 | 11114D | 1:1 | R | 192/192 | 100% |
| 9 | W7E26R | 1:2 | R | 192/192 | 100% |
| 10 | N7H03 | NR | NR | 192/192 | 100% |

The data above show that the **ASI Evolution** gives an objective and standardized interpretation of the test results with a high degree of repeatability.

Repeatability testing was conducted at each test site. The testing consisted of:

- Testing seven (7) samples, 2 - RPR nonreactive sample, a RPR reactive 1:2 titered sample, a RPR reactive 1:4 titered sample, a RPR reactive 1:8 titered sample, and a RPR reactive 1:16 titered sample.
- Each sample was run in duplicate within the panel.
- Each sample was tested each day for five non-consecutive days by an operator with experience in performing the ASI RPR Test for Syphilis and operating the ASI Evolution.
- Each sample was tested a second time on each of the days referenced above separated by approximately 2 hours.
- Testing at each site was performed on the same ASI Evolution.

The results of the testing are contained in Table 18-15:

Table 18-15 Site 1 – San Diego Blood Bank

| Sample | Expected | Results | | | | | % Agreement Positive |
|---|---|---|---|---|---|---|---|
| | | ASiManager-AT #1 | | | | | |
| | Date | 07/27/2017 | 07/29/2017 | 07/31/2017 | 08/02/2017 | 08/04/2017 | |
| 1 – (07035) | R | R | R | R | R | R | 100% |
| 2 – (05225A) | R | R | R | R | R | R | 100% |
| 3 – (05225B) | R | R | R | R | R | R | 100% |
| 4 – (07117) | R | R | R | R | R | R | 100% |
| 5 – (02287) | NR | NR | NR | NR | NR | NR | 100% |
| 6 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 7 – (R7C21R) | R | R | R | R | R | R | 100% |
| 8 – (05225B) | R | R | R | R | R | R | 100% |
| 9 – (02287) | NR | NR | NR | NR | NR | NR | 100% |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10 – (07117) | R | R | R | R | R | R | 100% |
| 11 – (07035) | R | R | R | R | R | R | 100% |
| 12 – (R7C21R) | R | R | R | R | R | R | 100% |
| 13 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 14 – (05225A) | R | R | R | R | R | R | 100% |

Table 18-16 Site 2 – Interstate Blood Bank

| Sample | Expected | Results | | | | | % Agreement Positive |
|---|---|---|---|---|---|---|---|
| | | ASiManager-AT #1 | | | | | |
| | Date | 08/31/2017 | 09/02/2017 | 09/04/2017 | 09/06/2017 | 09/08/2017 | |
| 1 – (07035) | R | R | R | R | R | R | 100% |
| 2 – (05225A) | R | R | R | R | R | R | 100% |
| 3 – (05225B) | R | R | R | R | R | R | 100% |
| 4 – (07117) | R | R | R | R | R | R | 100% |
| 5 – (02287) | NR | NR | NR | NR | NR | NR | 100% |
| 6 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 7 – (R7C21R) | R | R | R | R | R | R | 100% |
| 8 – (05225B) | R | R | R | R | R | R | 100% |
| 9 – (02287) | NR | NR | NR | NR | NR | NR | 100% |
| 10 – (07117) | R | R | R | R | R | R | 100% |
| 11 – (07035) | R | R | R | R | R | R | 100% |
| 12 – (R7C21R) | R | R | R | R | R | R | 100% |
| 13 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 14 – (05225A) | R | R | R | R | R | R | 100% |

Table 18-17 Site 3 – Arlington Scientific, Inc.

| Sample | Expected | Results | | | | | % Agreement Positive |
|---|---|---|---|---|---|---|---|
| | | ASiManager-AT #1 | | | | | |
| | Date | 07/12/2017 | 07/14/2017 | 07/17/2017 | 08/19/2017 | 08/21/2017 | |
| 1 – (07035) | R | R | R | R | R | R | 100% |
| 2 – (05225A) | R | R | R | R | R | R | 100% |
| 3 – (05225B) | R | R | R | R | R | R | 100% |
| 4 – (07117) | R | R | R | R | R | R | 100% |
| 5 – (02287) | NR | NR | NR | NR | NR | NR | 100% |
| 6 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 7 – (R7C21R) | R | R | R | R | R | R | 100% |
| 8 – (05225B) | R | R | R | R | R | R | 100% |
| 9 – (02287) | NR | NR | NR | NR | NR | NR | 100% |
| 10 – (07117) | R | R | R | R | R | R | 100% |
| 11 – (07035) | R | R | R | R | R | R | 100% |
| 12 – (R7C21R) | R | R | R | R | R | R | 100% |
| 13 – (N6K14) | NR | NR | NR | NR | NR | NR | 100% |
| 14 – (05225A) | R | R | R | R | R | R | 100% |

**The data shows a very high degree of repeatability.**

## Reproducibility

Reproducibility is defined as the variation in measurements taken by multiple instruments on the same item and under the same conditions.

The interpretation of 10 samples using the ASI RPR Test for Syphilis and the **ASI Evolution** were evaluated for reactivity. The testing requirements were as follows:

1. Each sample was tested 192 times.
2. The same samples and reagents were used on all three instruments

A total of 10 samples were evaluated to determine reproducibility of reactivity between the three instruments. Of the 10 samples, 7 were reactive and 3 were nonreactive. The reactive samples had titers of 1:1 (4 samples), 1:2 (1 sample), 1:8 (1 sample) and 1:256 (1 sample). Each of the 10 samples was repeated 192 times to evaluate the reactivity using the **ASI Evolution**. An aliquot of the same sample was dispensed into 192 tubes. All 192 tubes were placed into the ASI Evolution and the run was performed. In this manner all 192 wells were tested with the same sample to show well to well and plate to plate repeatability. Refer to Table 18-14. The data are shown in Table 18-18.

Table 18-18

| | Sample | Expected | Results | | | | | | % Agreement |
|---|---|---|---|---|---|---|---|---|---|
| | Sample ID | Titer | Evolution 1 | | Evolution 2 | | Evolution 3 | | |
| 1 | R7C21R | 1:8 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 2 | N7D04 | NR | NR | 192/192 | NR | 192/192 | NR | 192/192 | 100% |
| 3 | 11114B | 1:1 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 4 | 11114C | 1:1 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 5 | 11114F | 1:1 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 6 | 02287 | NR | NR | 192/192 | NR | 192/192 | NR | 192/192 | 100% |
| 7 | 08296 | 1:256 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 8 | 11114D | 1:1 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 9 | W7E26R | 1:2 | R | 192/192 | R | 192/192 | R | 192/192 | 100% |
| 10 | N7H03 | NR | NR | 192/192 | NR | 192/192 | NR | 192/192 | 100% |

The data above show that the **ASI Evolution** gives an objective and standardized interpretation of the test results with a high degree of reproducibility. **The ASI Evolution has a high degree of reproducibility.**

## Cross Reactivity/Interfering Substances

A study was conducted to evaluate potential interference or cross reactivity from different disease conditions. Results are listed below:

| Specimen Category | Number of Samples | Expected Result | Result |
|---|---|---|---|
| ANA (+) Syphilis (-) | 3 | NR | NR |
| ASO (+) Syphilis (-) | 2 | NR | NR |
| CRP (+) Syphilis (-) | 2 | NR | NR |
| Infectious Mono (+) Syphilis (-) | 3 | NR | NR |
| RF (+) Syphilis (-) | 12 | NR | NR |
| Rubella (+) Syphilis (-) | 12 | NR | NR |
| Lyme's (+) Syphilis (-) | 12 | NR | NR |
| HIV (+) Syphilis (-) | 50 | NR | NR |
| HIV (+) Syphilis (+) | 24 | R | R |
| Pregnancy (+) Syphilis (-) | 250 | NR | NR |
| Pregnancy (+) Syphilis (+) | 30 | R | R |

| | | | |
|---|---|---|---|
| Bilirubin 20 mg/dl | 2 | NR | NR |
| Hemoglobin 10 mg/ml | 2 | NR | NR |
| Triglycerides 1000mg/dl | 2 | NR | NR |

The positive infectious mono samples were heterophil positive. EBV testing was not conducted.

The study showed no interference.

## Carry-Over

A study was conducted to evaluate if contamination of a nonreactive sample due to carry-over from an adjacent reactive sample can occur.

- Testing was conducted at:
  - Arlington Scientific, Inc.
- Testing was conducted using two different samples:
  - RPR reactive 1:64 tittered sample (high reactive) – 06237
  - RPR nonreactive sample – Lot 06127
- The same samples were used for all testing.
- The same lot of carbon antigen was used – Lot CA7D24R
- Each test run was completed each day for five days by an operator with experience in performing the ASI RPR Card Test for Syphilis and operating the ASI Evolution.
- The test consisted of alternating 24 aliquots of the samples listed above in the sample rack and completing a run of 48 tests. Testing was performed on the same ASI Evolution.

The results of the testing are contained in tables below:

Table 1

| Sample | Well Number | Expected | Results | | | | |
|---|---|---|---|---|---|---|---|
| | | | ASiManager-AT #1 | | | | |
| | | Date | 08/11/17 | 08/14/17 | 08/15/17 | 08/16/17 | 08/17/17 |
| 06237 | P1:A1 | R | R | R | R | R | R |
| 06127 | P1:A2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:A3 | R | R | R | R | R | R |
| 06127 | P1:A4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:A5 | R | R | R | R | R | R |
| 06127 | P1:A6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:A7 | R | R | R | R | R | R |
| 06127 | P1:A8 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:B1 | R | R | R | R | R | R |
| 06127 | P1:B2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:B3 | R | R | R | R | R | R |
| 06127 | P1:B4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:B5 | R | R | R | R | R | R |
| 06127 | P1:B6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:B7 | R | R | R | R | R | R |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 06127 | P1:B8 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:C1 | R | R | R | R | R | R |
| 06127 | P1:C2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:C3 | R | R | R | R | R | R |
| 06127 | P1:C4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:C5 | R | R | R | R | R | R |
| 06127 | P1:C6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:C7 | R | R | R | R | R | R |
| 06127 | P1:C8 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:D1 | R | R | R | R | R | R |
| 06127 | P1:D2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:D3 | R | R | R | R | R | R |
| 06127 | P1:D4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:D5 | R | R | R | R | R | R |
| 06127 | P1:D6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:D7 | R | R | R | R | R | R |
| 06127 | P1:D8 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:E1 | R | R | R | R | R | R |
| 06127 | P1:E2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:E3 | R | R | R | R | R | R |
| 06127 | P1:E4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:E5 | R | R | R | R | R | R |
| 06127 | P1:E6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:E7 | R | R | R | R | R | R |
| 06127 | P1:E8 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:F1 | R | R | R | R | R | R |
| 06127 | P1:F2 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:F3 | R | R | R | R | R | R |
| 06127 | P1:F4 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:F5 | R | R | R | R | R | R |
| 06127 | P1:F6 | NR | NR | NR | NR | NR | NR |
| 06237 | P1:F7 | R | R | R | R | R | R |
| 06127 | P1:F8 | NR | NR | NR | NR | NR | NR |

Using this data the following evaluations can be made:

1. All testing results were as expected.

There was no contamination or carry-over.