**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION MEMORANDUM**

**A. 510(k) Number:**

K181288

**B. Purpose for Submission:**

Clearance of a new device

**C. Measurand:**

White blood cell count (WBC) and percent neutrophil count (NEUT%)

**D. Type of Test:**

Enumeration of WBCs and NEUT%

**E. Applicant:**

Athelas Inc.

**F. Proprietary and Established Names:**

Athelas One

**G. Regulatory Information:**

1. Regulation section:

   21 CFR 864.5220, Automated differential cell counter

2. Classification:

   Class II

3. Product code:

   GKZ, Counter, differential cell

4. Panel:

   Hematology (81)

## H. Intended Use:

1. Intended use(s):

   Athelas One is indicated for use for quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary or $K_2$EDTA venous whole blood. The Athelas One system is for In Vitro Diagnostic use only. The Athelas One is only to be used with Athelas One Test Strips. The Athelas One is indicated for use in clinical laboratories and for point of care settings. The Athelas One is only indicated for use in adult populations (aged 21 and older).

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Athelas One analyzer

## I. Device Description:

The Athelas One is an automated cell counter system which consists of: the Athelas One analyzer and the Athelas One Test Strips. The Athelas One system is intended to analyze capillary whole blood and anticoagulated venous whole blood collected in $K_2$EDTA collection tubes.

The Athelas One Tests Strips collects a blood sample (capillary or collected in $K_2$EDTA anticoagulant) to generate a layer of cells for counting and image analysis. The Athelas One Test Strips are comprised of an upper optical panel, lower optical panel and a stain coated region containing methylene blue and cresyl violet stains. The test strip channel is optically clear for the camera module to take pictures of the cells in the blood sample.

A smartphone/tablet with the Athelas controlling mobile application is required to initiate a test with the Athelas One System. The smartphone/tablet models compatible to initiate testing are those devices supporting iOS 9, 10, and 11, or Android 7, 8, and 9. In addition, the smartphone/tablet with the Athelas controlling mobile application is required to view test results.

## J. Substantial Equivalence Information:

1. Predicate device name(s):

   Sysmex XE-5000 Automated Hematology Analzyer

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

   K071967

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| Item | Candidate<br>Athelas One<br>K181288 | Predicate<br>Sysmex XE-5000<br>K071967 |
| Intended Use | Athelas One is indicated for use for quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary or $K_2$EDTA venous whole blood. The Athelas One system is for In Vitro Diagnostic use only. The Athelas One is only to be used with Athelas One Test Strips. The Athelas One is indicated for use in clinical laboratories and for point of care settings. The Athelas One is only indicated for use in adult populations (aged 21 and older). | The Sysmex XE-5000 is an automated hematology analyzer for in-vitro diagnostic use in screening patient populations found in clinical laboratories. The XE-5000 classifies and enumerates the same parameters as the XE-2100 using whole blood as described below, cord blood for HPC and has a body fluid mode for body fluids. The Body Fluid mode analyzes WBC-BF, RBC-BF, MN%/#, PMN%/# and TC-BF in body fluids (cerebrospinal fluids (CSF), serous fluids, and synovial fluids with EDTA as needed). WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMP %/#, MONO %/#, EO%/#, BASO %/#, NRBC, RDW-SD, RDW-CV, MPV, RET %/#, IRF, IG%/#, HPC#, RET-He, IPF, WBC-BF, RBC-BF, MN%/#, PMN%/#, TC-BF#. |
| Intended Use Settings | Point of care, clinical laboratory | Clinical laboratory |
| Specimen Type | Capillary whole blood and $K_2$EDTA venous whole blood | Same in addition to body fluids (CSF, serous fluids, and synovial fluids) |
| Parameters | WBC, NEUT% | WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMP %/#, MONO %/#, EO%/#, BASO %/#, NRBC, RDW-SD, RDW-CV, MPV, |

| Similarities | | |
|---|---|---|
| Item | Candidate<br>Athelas One<br>K181288 | Predicate<br>Sysmex XE-5000<br>K071967 |
| | | RET %/#, IRF, IG%/#, HPC#, RET-He, IPF, WBC-BF, RBC-BF, MN%/#, PMN%/#, TC-BF#. |

| Differences | | |
|---|---|---|
| Item | Candidate<br>Athelas One<br>K181288 | Predicate<br>Systex XE-5000<br>K071967 |
| Test Principle | A microfluidic test strip channel creates a stained monolayer of WBCs. Multiple images are taken of the monolayer and the cells are counted and classified by computer vision based image analysis. | Performs analyses using the following methods: RF/DC detection method, Sheath Flow DC dectection method, and flow cytometry methods using a semiconductor laser. |
| Controls/Calibrators | ATH-CHECK (Three level control)<br>Factory Calibrated | e-Check (XE) (Three level control)<br>XE Calibrator (X Cal) |
| Sample Processing | Internet connected device for processing results on Cloud server | Processing of results occurs locally in device |
| Sample Volume | 3.5 µL | 130–200 µL depending on operation mode |
| Measurement Range | WBC: 1.0–20 $x10^3$/µL | WBC: 0.0–440 $x10^3$/µL |
| Calibration | Factory calibrated, no further calibration | Automtic and manual calibration using e-Check (XE) control material |

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

CLSI H26-A2: Validation, Verification and Quality Assurance of Automated Hematology Analyzers; Approved Guideline – Second Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline – First Edition

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measreument Procedures – Approved Guideline – Second Edition

CLSI EP14-A2: Evluation of Matrix Effects; Approved Guideline – Second Edition

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline – First Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in Clinical Laboratory; Approved Guideline – Third Edition

## L. Test Principle:

The Athelas One system consists of the Athelas One analyzer and Athelas One test strips. The Athelas One test strips serve as both a sample container and a reaction chamber. A capillary whole blood sample or whole blood specimen anticoagulated in $K_2$EDTA of 3.5 µL is pipetted or directly transferred via fingerstick to the Athelas One test strip which automatically spreads the sample into a monolayer. The pre-coated stain within the strip chamber interacts with the monolayer of blood and stains the WBCs. The Athelas One test strip is inserted into the Athelas One analyzer which utilizes a proximity sensor to lock in place. A servo stabilizes and auto-focuses the blood sample, and then a stage actuator scans the strip across various fields while the optical module takes multiple images of the cells across the monolayer. The images of the blood sample are transmitted to the server where they are analyzed using a locked down image processing algorithm. The algorithm recognizes the nucleation and WBCs to generate a WBC count and NEUT% result based on the concentrations and types of cells present. The WBC count and NEUT% is then returned to the user via the controlling mobile application on an authorized lab or hospital device.

## M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   *a. Precision/Reproducibility:*

   <u>Repeatability</u>: The repeatability study was conducted in accordance with CLSI EP05-A3 and CLSI H26-A2 at one internal site.The study was conducted with nine whole blood samples collected in $K_2$EDTA. The samples spanned the reportable range of the Athelas One analyzer including clinically important ranges and were tested using three lots of test strips, three operators and five analyzers. Ten replicates were measured for each sample per lot per operator for a total of 90 measurements per sample. Results were analyzed for both WBC count and NEUT% for the following variances using a mixed ANOVA model. All results met the pre-defined acceptance criteria. Table 1 presents results for WBC count and Table 2 presents results for NEUT%.

**Table 1. Precision (Repeatability) for WBC Count**

| Sample | Mean Value ($x10^3/\mu L$) | N | Repeatability | | Between-Lot | | Between-Instrument | | Between-Operator | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) |
| 1 | 2.20 | 90 | 0.12 | 5.62 | 0.00 | 0.00 | 0.00 | 0.00 | 0.04 | 1.70 | 0.13 | 5.87 |
| 2 | 3.75 | 90 | 0.20 | 5.42 | 0.00 | 0.00 | 0.01 | 0.36 | 0.02 | 0.60 | 0.20 | 5.46 |
| 3 | 4.12 | 90 | 0.20 | 4.78 | 0.00 | 0.00 | 0.06 | 1.43 | 0.04 | 1.02 | 0.21 | 5.09 |
| 4 | 5.11 | 90 | 0.25 | 4.96 | 0.00 | 0.00 | 0.14 | 2.73 | 0.10 | 1.87 | 0.30 | 5.96 |
| 5 | 7.89 | 90 | 0.33 | 4.18 | 0.06 | 0.78 | 0.09 | 1.14 | 0.15 | 1.94 | 0.38 | 4.82 |
| 6 | 10.01 | 90 | 0.50 | 5.01 | 0.00 | 0.00 | 0.10 | 0.98 | 0.19 | 1.91 | 0.55 | 5.45 |
| 7 | 14.64 | 90 | 0.66 | 4.51 | 0.19 | 1.27 | 0.00 | 0.00 | 0.00 | 0.00 | 0.69 | 4.69 |
| 8 | 17.52 | 90 | 0.70 | 3.97 | 0.00 | 0.00 | 0.17 | 0.95 | 0.26 | 1.49 | 0.76 | 4.34 |
| 9 | 23.33 | 90 | 1.01 | 4.33 | 0.77 | 3.31 | 0.20 | 0.87 | 0.43 | 1.82 | 1.36 | 5.81 |

**Table 2. Precision (Repeatability) for NEUT%**

| Sample | Mean Value ($x10^3/\mu L$) | N | Repeatability | | Between-Lot | | Between-Instrument | | Between-Operator | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD $x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) |
| 1 | 50.78 | 90 | 3.36 | 6.62 | 0.33 | 0.64 | 0.43 | 0.84 | 0.82 | 1.61 | 3.50 | 6.90 |
| 2 | 60.98 | 90 | 3.61 | 5.92 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 3.61 | 5.92 |
| 3 | 69.52 | 90 | 3.14 | 4.52 | 0.29 | 0.42 | 0.17 | 0.24 | 0.70 | 1.01 | 3.24 | 4.66 |
| 4 | 55.25 | 90 | 3.11 | 5.64 | 0.00 | 0.00 | 1.09 | 1.97 | 3.01 | 5.44 | 4.46 | 8.08 |
| 5 | 71.57 | 90 | 2.54 | 3.55 | 0.00 | 0.00 | 1.14 | 1.60 | 1.79 | 2.49 | 3.31 | 4.62 |
| 6 | 68.57 | 90 | 2.58 | 3.76 | 0.00 | 0.00 | 0.92 | 1.34 | 1.51 | 2.21 | 3.13 | 4.56 |
| 7 | 50.27 | 90 | 2.96 | 5.89 | 1.17 | 2.33 | 0.81 | 1.61 | 0.73 | 1.45 | 3.37 | 6.69 |
| 8 | 34.60 | 90 | 3.49 | 10.09 | 0.30 | 0.87 | 0.00 | 0.00 | 3.08 | 8.90 | 4.66 | 13.48 |
| 9 | 72.11 | 90 | 2.24 | 3.11 | 1.46 | 2.02 | 0.41 | 0.57 | 0.00 | 0.00 | 2.70 | 3.75 |

Reproducibility: The reproducibility study was conducted in accordance to CLSI EP05-A3 over 20 days across three sites (two external, one interal), with three analyzers (one per site), three lots of test strips, two operators per site and one lot of quality control (QC) materials (ATH-CHECK quality control material) consisting of three levels (low, medium, high). Each testing site performed two runs per day and two replicates per run. A total of 80 readings were generated at each site for each level of QC (2 runs x 20 days x 2 replicates = 80 readings). All results met pre-defined acceptance criteria. Tables 1–3 summarizes the reproducibility results for the ATH-CHECK QC material (low, medium and high) at all study sites combined.

**Table 1. Precision (Reproducibility) for ATH-CHECK – Low**

| Parameter | Mean Value ($10^3/\mu L$) | N | Within-Run | | Between-Run | | Between-Day | | Between-Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) |
| WBC | 2.746 | 240 | 0.140 | 5.097 | 0.000 | 0.000 | 0.060 | 2.175 | 0.018 | 0.673 | 0.153 | 5.583 |
| NEUT% | 50.781 | 240 | 2.680 | 5.278 | 1.239 | 2.440 | 1.305 | 2.570 | 1.197 | 2.356 | 3.443 | 6.780 |

**Table 2. Precision (Reproducibility) for ATH-CHECK – Medium**

| Parameter | Mean Value (K/µL) | N | Within-Run | | Between-Run | | Between-Day | | Between-Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) | SD ($x10^3/\mu L$) | CV (%) |
| WBC | 7.546 | 240 | 0.339 | 4.492 | 0.112 | 1.479 | 0.080 | 1.062 | 0.230 | 3.049 | 0.432 | 5.726 |
| NEUT% | 29.990 | 240 | 3.015 | 6.030 | 0.932 | 1.865 | 0.833 | 1.666 | 0.728 | 1.457 | 3.344 | 6.689 |

**Table 3. Precision (Reproducibility) for ATH-CHECK – High**

| Parameter | Mean Value (K/µL) | N | Within-Run | | Between-Run | | Between-Day | | Between-Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | SD ($x10^3$/µL) | CV (%) | SD ($x10^3$/µL) | CV (%) | SD $x10^3$/µL) | CV (%) | SD ($x10^3$/µL) | CV (%) | SD ($x10^3$/µL) | CV (%) |
| WBC | 15.246 | 240 | 0.656 | 4.300 | 0.000 | 0.000 | 0.460 | 3.014 | 0.532 | 3.491 | 0.961 | 6.305 |
| NEUT% | 50.832 | 240 | 2.967 | 5.838 | 0.000 | 0.000 | 0.947 | 1.864 | 1.139 | 2.241 | 3.316 | 6.525 |

*b. Linearity/assay reportable range:*

Assay reportable range: WBC: 1.0–25.0 $x10^3$/µL

Linearity: The objective of the linearity study was to assess the linear correlation of the Athlelas One WBC concentration across the reportable range (stated above). Ten samples were analyzed in four replicates across the reportable range and tested on four analyzers with one test strip lot. The samples were obtained by pooling together one low WBC concentration $K_2$EDTA whole blood sample (0.8 $x10^3$/µL) and one high WBC concentration $K_2$EDTA whole blood sample (38.6 $x10^3$/µL) in specific proportions. The best fitting regressional model was a first order model and linearity was demonstrated for the range presented below:

| Parameter | Linear Range |
|---|---|
| WBC ($x10^3$/µL) | 0.08–38.6 |

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

Controls: Control materials to be used with the Athelas One System are the ATH-CHECK Quality Control Materials, which are comprised of three levels (low, medium, high).

Whole blood stability: Whole blood stability was evaluated on the Athelas One device by conducting a 48-hour stability study on nine different $K_2$EDTA venous blood samples with low (0.53 $x10^3$/µL), normal (4.0–10.0 $x10^3$/µL) , and high (>10 $x10^3$/µL) WBC levels with one test strip lot and four Athelas one analyzers. The study was designed in accordance with recommendations from CLSI EP25-A. After baseline WBC and NEUT% was established by running samples in triplicate at time 0 (T0), each sample was divided into two identical aliquots. Aliquot 1 was stored at refrigerated temperature (2–8ºC) and aliquot 2 was stored at room temperature (20–25ºC). Triplicate measurements were run subsequently at each time point for both refrigerated and room temperature samples. The results were analyzed for measurand with pre-defined maximum allowable drift criteria. Based on the outcome of the whole blood stability study, the whole blood sample stability for both WBC and NEUT% parameters are 24 hours at refrigerated temperature (2–8ºC) and 24 hours at room temperature (20–25ºC).

Test Strip Stability: A 16-week test strip stability study was conducted to assess the shelf-life stability of the Athelas test strips. The strips were tested weekly over 16 weeks to substantiate a 14-week stability claim. The study was designed in accordance with recommendations from CLSI EP25-A. In particular, the study was

conducted over 16 weeks, across two test strip lots, four analyzers, two replicates, and one lot of quality control materials. Each week, two replicates per two lots of strips across 3 levels of control fluid were performed. Statistically significant degradation/drift over the 105 day study ($p > 0.05$) as recommended by the CLSI EP25-A regression slope analysis was not observed. The stability duration for all samples can be set to 98 days with no observed degradation at 105 days, the last time point of the study.

*d. Detection limit:*

Limit of Blank (LoB): This study was conducted in accordance with CLSI EP17-A2 using five blank samples containing diluent. The LoB was assessed with two strip lots, two instruments, over three days and two replicates per sample (for each strip lot, day and instrument combinations) and 60 total blank replicates per lot (across all blank samples, days and instruments). Each day, two replicates of each sample were measured per strip lot and instrument combinations.

Limit of Detection (LoD): This study was conducted in accordance with CLSI EP17-A2. The LoB was established by evaluating five diluted fresh whole blood samples to create low WBC count samples (0.3–0.5 $x10^3/\mu L$). The samples were assessed with two strip lots, two instruments for over three days. Two replicates per sample (for each strip lot, day and instrument combinations) and 60 total replicates per reagent lot (across all samples, days and instruments) were obtained. On each day, two replicates of each sample were measured per strip lot and instrument combination.

Limit of Quantification (LoQ): The study was conducted in accordance with CLSI EP17-A2. The LoQ was established with four diluted $K_2$EDTA whole blood samples to reach an approximate WBC concentration of 0.45 $x10^3/\mu L$ with two strip lots, one instrument, for over three days with three replicates per sample.

| Parameter | LoB | LoD | LoQ |
|---|---|---|---|
| WBC ($10^3/\mu L$) | 0.000 | 0.079 | 0.440 |

*e. Analytical specificity:*

A study was conducted to determine the interference level of the following interferents with the hematology results of the Athelas One System. Fresh whole blood samples collected in $K_2$EDTA were contrived with the interferents listed below where 16 measurements were obtained per interferent. The interference study results demonstrated that the following interferents do not interfere with test results up to the following concentrations:

| Interferents | Concentration |
|---|---|
| Triglyceride Rich Lipoproteins | 500 mg/dL |
| Hemolysate | 500 mg/dL |
| Protein | 8 g/dL |
| Levodopa | 20 mg/L |
| Methyldopa | 71 µmol/L |
| Metronidazole | 701 µmol/L |
| Acetylsalicyclic Acid | 3.62 mmol/L |
| Phenylbutazone | 400 mg/L |
| Rifampicin | 78.1 µmol/L |
| Cyclosporine | 5 mg/L |
| Acetaminophen | 1324 µmol/L |
| Heparin | 3000 U/L |
| Ibuprofen | 2425 µmol/L |
| Bilirubin C | 5 mg/dL |
| Bilirubin F | 15 mg/dL |

*f. Assay cut-off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

The method comparison study was conducted at three U.S. point of care clinical sites to assess the performance of the Athelas One versus the Sysmex XE-5000. Each site had a minimum of three operators, three lots of test strips, and three Athelas One analyzers. In total, 312 unique patient samples were analyzed on the Athelas One system, where 113 samples were analyzed with capillary whole blood (direct from fingerstick) and 195 samples were analyzed with $K_2$EDTA venous whole blood. The method comparison study included both normal and abnormal patient samples at each site. Passing-Bablok regression analysis was conducted for each individual site as well as all sites combined. All results were within the pre-defined acceptance criteria. Tables 1 and 2 presented below demonstrate the correlation and estimated bias of the Athelas One and System XE-5000 for each site and all sites combined:

**Table 1. Method Comparison – Individual Site Results**

| Site | Parameter | Result Range | N | (r) | Slope (95% CI) | Intercept (95% CI) | Mean Bias | Mean % Bias |
|---|---|---|---|---|---|---|---|---|
| 1 | WBC (x$10^3$/µL) | 1.1–23.0 | 107 | 0.99 | 0.985 (0.945, 1.024) | -0.097 (-0.285, 0.133) | -0.163 | -2.86% |
| 1 | NEUT% | 15.0–87.31 | 107 | 0.97 | 0.940 (0.911, 0.981) | 2.646 (-0.222, 4.714) | 0.226 | 0.93% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2 | WBC (x$10^3$/µL) | 2.0–18.94 | 104 | 0.98 | 0.983 (0.918, 1.048) | -0.041 (-0.394, 0.384) | -0.080 | -1.50% |
| 2 | NEUT% | 9.0–88.43 | 104 | 0.95 | 0.981 (0.919, 1.042) | 2.647 (-1.437, 6.255) | 0.988 | 1.50% |
| 3 | WBC (x$10^3$/µL) | 1.4–22.0 | 101 | 0.99 | 0.977 (0.950, 1.012) | -0.055 (-0.276, 0.116) | -0.211 | -2.57% |
| 3 | NEUT% | 8.0–92.89 | 101 | 0.96 | 0.998 (0.955, 1.043) | 0.641 (-2.765, 4.065) | 0.708 | 1.11% |

**Table 2. Method Comparison – Combined Site Results**

| Parameter | Result Range | N | (r) | Slope (95% CI) | Intercept (95% CI) | Mean Bias | Mean % Bias |
|---|---|---|---|---|---|---|---|
| WBC (x$10^3$/µL) | 1.1–23.0 | 312 | 0.99 | 0.978 (0.958, 1.000) | -0.042 (-0.159, 0.086) | -0.151 | -2.31 |
| NEUT% | 8.0–92.89 | 312 | 0.96 | 0.980 (0.953, 1.003) | 1.855 (0.530, 3.677) | 0.636 | 1.18 |

Bias at medical decision levels for WBC and NEUT% parameters at each site and all sites combined were assessed and all samples met the pre-defined acceptance criteria.

*b. Matrix comparison:*

The matrix comparison study was conducted to assess the comparison of capillary whole blood and venous whole blood collected in $K_2$EDTA anticoagulant on the Athelas One. A total of 59 patients were included in the study where each patient provided a capillary whole blood sample and venous whole blood sample collected in $K_2$EDTA anticoagulant. Patient samples included both normal and abnormal samples covering medical decision points of WBCs. Passing-Bablok regression analysis was performed and results demonstrated to be within the pre-defined acceptance criteria.

3. Clinical studies:

*a. Clinical Sensitivity:*

Not applicable

*b. Clinical specificity:*

Not applicable

*c. Other clinical supportive data (when a. and b. are not applicable):*

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

   Adult reference intervals for the WBC and NEUT% parameters on the Athelas One were verified using 120 healthy donors (N=60 males, N=60 females) utilizing $K_2$EDTA whole blood samples. Confidence intervals for the reference limits were calculated using a 90% probability.

| Parameter | Male (N = 60) | | Female (N = 60) | |
|---|---|---|---|---|
| | Lower Limit | Upper Limit | Lower Limit | Upper Limit |
| WBC ($x10^3/\mu L$) | 3.91 | 10.90 | 4.49 | 12.68 |
| NEUT% | 41.0 | 70.7 | 42.9 | 74.3 |

**N. Instrument Name:**

Athelas One

**O. System Descriptions:**

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X_____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes ___X_____ or No _____

2. Software:

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

   Yes ___X_____ or No _____

3. Specimen Identification:

   Before a test can be performed, the Athelas One prompts the end user to input a patient identifier, which is manual entry. This prompt is a mandatory function.

4. Specimen Sampling and Handling:

   Capillary whole blood or venous whole blood collected in $K_2$EDTA anticoagulant may be used. A drop of blood is collected via fingerstick using a lancet, and held against a Athelas One Test Strip. If pre-collected, $K_2$EDTA samples are used, mix all specimen

tubes thoroughly on a mechanical mixer for at least two minutes or invert the tube 10–20 times by hand. The specimen can be stored at room temperature for 2 hours or in a refrigerator for 24 hours. If the specimen has been refrigerated, it should be warmed to room temperature prior to mixing.

5. Calibration:

   The Athelas One is factory calibrated and is fully functional upon unpackaging.

6. Quality Control:

   ATH-CHECK QC material is provided at three levels (low, normal and high) which includes preserved human leukocytes (neutrophils, lymphocytes, basophils, eosinophils, monocytes) along with the other components of whole blood (RBCs, platelets) in proportions expected in human whole blood.

   Value Assignment: Value assignment for the ATH-CHECK QC materials was based on data collected across three Athelas One analyzers conducted at three separate sites, with six operators. Each site ran two runs per day and two replicates per run. Standard deviation from the study was used to determine the range of each parameter of ATH-CHECK QC material through the formula value range = mean ± 3.0*SD.

   Open-Vial Stability: The open-vial stability study was conducted with two ATH-CHECK QC lots, three QC levels per lot (low, medium, high), two vials per lot and three instruments. Five time points (days 0, 2, 4, 7 and 8) were included in the study and three replicates per measurement point were obtained. Results demonstrated an open-vial stability of 7 days.

   Closed-Vial Stability: The closed-vial stability study was conducted with two ATH-CHECK QC lots, three QC levels per lot (low, medium, high), two vials per lot and three instruments. Nine time points (days 0, 2, 4, 7, 8, 10, 12, 15, 16) across the closed-vial testing period of 16 days and three replicates per measurement point were obtained. Results demonstrated a closed-vial stability of 15 days.

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

Flagging Comparison Study: This study was conducted to assess the flagging capabilities (distributional and morphological) of the Athelas One compared to the Sysmex XE-5000 utilizing patient samples covering a range of abnormal conditions. This study was performed with 312 patient samples from either capillary whole blood or venous whole blood collected in $K_2$EDTA anticoagulant. Results met the pre-defined acceptance crtieria. Summarized data is presented below for both distributional flags as well as morphological flags.

*Distributional Flags*

The results of the Athelas One WBC distributional flagging (leukocytosis, leukocytopenia)

compared to the Sysmex XE-5000 were divided into two categories: 1) No flags, negative judgement and 2) patients with positive distributional abnormalities with flags present, positive judgement.

| | | Sysmex XE-5000 | | |
|---|---|---|---|---|
| | | **Positive (Abnormal)** | **Negative (Normal)** | **Total** |
| **Athelas One** | **Positive (Abnormal)** | 34 | 4 | 38 |
| | **Negative (Normal)** | 5 | 269 | 274 |
| | **Total** | 39 | 273 | 312 |

%Positive Agreement (Sensitivity) = 87.2%; 95% CI: 72.57, 95.70
%Negative Agreement (Specificity) = 98.5%; 95% CI: 96.29, 99.60
%Overall Agreement = 97.12%; 95% CI: 94.59, 98.67

*Morphological Flags*

The results of the Athelas One WBC morphological flagging (nucleated RBCs, platelet clumps, etc.) compared to the Sysmex XE-5000 were divided into two categories: 1) No flags, negative judgement and 2) patients with positive distributional abnormalities with flags present, positive judgement.

| | | Sysmex XE-5000 | | |
|---|---|---|---|---|
| | | **Positive (Abnormal)** | **Negative (Normal)** | **Total** |
| **Athelas One** | **Positive (Abnornal)** | 90 | 7 | 97 |
| | **Negative (Normal)** | 9 | 206 | 215 |
| | **Total** | 99 | 213 | 312 |

%Positive Agreement (Sensitivity) = 90.91%; 95% CI: 83.44, 95.76
%Negative Agreement (Specificity) = 96.71%; 95% CI: 93.35, 98.67
%Overall Agreement = 94.87%; 95% CI: 91.81, 97.04

**Q. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

**R. Conclusion:**

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