March 22, 2022

Athelas Inc.
Tanay Tandon
Chief Executive Officer
67 East Evelyn Avenue
Mountain View, California 94041

Re: K200828
Trade/Device Name: Athelas Home
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated Differential Cell Counter
Regulatory Class: Class II
Product Code: GKZ
Dated: November 25, 2021
Received: November 29, 2021

Dear Tanay Tandon:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Min Wu, Ph.D.
Chief
Hematology Branch
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K200828

Device Name

Athelas Home

Indications for Use *(Describe)*

The Athelas Home is indicated for the quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary whole blood. The Athelas Home system is for In Vitro Diagnostic use and for prescription use only. The Athelas Home is only to be used with Athelas Home Test Strips. The Athelas Home is indicated for use by patients and caregivers within home settings with results viewable by health care professionals. The Athelas Home is intended for patients at risk of neutropenia. For patients with psychiatric conditions, clinical judgement should be exercised when deciding the end-user, based on the instructions for use (IFU) of Athelas Home, the treating physician should determine which patients are competent to perform the test by themselves. The Athelas Home is indicated for adult populations only (aged 21 and older).

Results obtained with the Athelas Home should not be the sole basis for patient diagnosis, treatment or management of leukopenia and neutropenia. All results should be evaluated by a healthcare provider.

The Athelas Home is intended to be used by a single person and should not be shared.

Prescription Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5 - 510(k) Summary

Date Prepared:
Jan 17th, 2021

Submitter:
Tanay Tandon (Athelas)
Company: Athelas Inc.
Address: 160 S Whisman Ave. Mountain View, CA 94041
Email Address: tanay@athelas.com

Proprietary Trade name:
Athelas Home

Common name:
Automated differential cell counter.

Classification name:
Automated differential cell counter (21 CFR 864.5220, Product Code GKZ)

Indicated use:
The Athelas Home is indicated for the quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary whole blood. The Athelas Home system is for In Vitro Diagnostic use and for prescription use only. The Athelas Home is only to be used with Athelas Home Test Strips. The Athelas Home is indicated for use by patients and caregivers within home settings with results viewable by health care professionals. The Athelas Home is intended for patients at risk of neutropenia. For patients with psychiatric conditions, clinical judgement should be exercised when deciding the end-user, based on the instructions for use (IFU) of Athelas Home, the treating physician should determine which patients are competent to perform the test by themselves. The Athelas Home is indicated for adult populations only (aged 21 and older).

Results obtained with the Athelas Home should not be the sole basis for patient diagnosis, treatment or management of leukopenia and neutropenia. All results should be evaluated by a healthcare provider.

The Athelas Home is intended to be used by a single person and should not be shared.

Prescription Use Only.

Substantial Equivalence:

Predicate: Athelas One, Automated Haematology Analyzer (K181288)

Comparison with predicate:

Similarities		
Item	Device: Athelas Home	Predicate: Athelas One
Intended Use	The Athelas Home is indicated for the quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary whole blood. The Athelas Home system is for In Vitro Diagnostic use and for prescription use only. The Athelas Home is only to be used with Athelas Home Test Strips. The Athelas Home is indicated for use by patients and caregivers within home settings with results viewable by health care professionals. The Athelas Home is intended for patients at risk of neutropenia. For patients with psychiatric conditions, clinical judgement should be exercised when deciding the end-user, based on the instructions for use (IFU) of Athelas Home, the treating physician should determine which patients are competent to perform the test by themselves. The Athelas Home is indicated for adult populations only (aged 21 and older). Results obtained with the Athelas Home should not be the sole basis for patient diagnosis, treatment or management of leukopenia and neutropenia. All results should be evaluated by a healthcare provider. The Athelas Home is intended to be used by a single person and should not be shared. Prescription Use Only.	Athelas One is indicated for use for quantitative determination of white blood cells (**WBC**) and Neutrophil percentages (**NEUT%**) in capillary or K2EDTA 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).
Specimen Type	Capillary Whole Blood	Capillary and Venous Whole Blood
Modes of Operation	Single mode of operation for capillary samples	Single mode of operation for both venous and capillary samples
Software/Hardware	Internet connected device for processing results on cloud server.	Internet connected device for processing results on cloud server.
Sample Volume	3.5 µL	3.5 µL

Measurement Range	WBC: 1 - 25K/µL	WBC: 1 - 25K/µL
Calibration	Factory calibrated and automatic calibration at the beginning of each test. No manual calibration by the end user.	Factory calibrated and automatic calibration at the beginning of each test. No manual calibration by the end user.
Test Principle	A microfluidic test strip channel creates a stained monolayer of white blood cells. Multiple images are taken of the monolayer and the cells are counted and classified by computer vision based image analysis.	A microfluidic test strip channel creates a stained monolayer of white blood cells. Multiple images are taken of the monolayer and the cells are counted and classified by computer vision based image analysis.
Parameters	WBC, NEUT%	WBC, NEUT%
Target Population	Only Adult (all those 21 and older).	Only Adult (all those 21 and older).
Reagents	Cresyl Violet, Methylene Blue Stain (pre-loaded/coated dry and contained in test strip)	Cresyl Violet, Methylene Blue Stain (pre-loaded/coated dry and contained in test strip)
Controls/ Calibrators	Auto-Check 3-Level Gridded Strip OR ATH-CHECK (3 level control)	ATH-CHECK (3 level control)

Differences		
Item Name	Device: Athelas Home	Predicate: Athelas One
Intended use sites	Home, Point of Care, Clinical Laboratory	Point of Care, Clinical Laboratory
Result Viewing	Results are remotely and securely transmitted to the prescribing physician or healthcare provider.	Results are shown on the mobile/tablet application used for system operation.
Remote Lockout Capability	Yes	No

Description of Device:

The Athelas Home is identical to the Athelas One K181288 in its technology, all software, the analytes measured, all components, and usage process. The Athelas Home has additional software and quality control safeguards to enable at-home usage of the device. Additionally, results generated from the Athelas Home are not shown to end-patients, rather are transmitted via the software directly to their healthcare provider. The Athelas Home also has Remote Lockout capabilities, such that a healthcare provider or manufacturer can remotely lock-out a device for safety in usage.

Athelas Home is indicated for the quantitative determination of white blood cells (WBC) and Neutrophil percentages (NEUT%) in capillary whole blood. The Athelas Home system is for In Vitro Diagnostic use and for prescription use only. The Athelas Home is only to be used with

Athelas Home Test Strips. The Athelas Home is indicated for use by patients and clinicians within home and point-of-care settings, with results viewable by health care professionals only. The Athelas Home is indicated for operation by adult populations only (aged 21 and older).

The Athelas Home is not indicated to completely replace a patient's monitoring regimen on reference lab systems. Prescribers should continue monitoring patients using traditional lab-based means as deemed necessary and possible.

The Athelas Home is not indicated to return results directly to patients. The Athelas Home directly transfers results to a health-care professional for interpretation and analysis.
The Athelas Home is not indicated to directly diagnose or assist in disease management. Rather, the Athelas Home should be used to quantify WBC and Neut% only, with all decision making owned by the physician as per standard of care.

The Athelas Home uses image processing and microfluidics in order to measure WBC and NEUT% values from whole blood in point-of-care and home settings. For further technological details refer to Athelas One K181288 application.

The precision/bias goals of the device are provided below:

Target Evaluation Criteria:

WBC Precision: 7.5% CV above 2K/μL WBC. 0.25 K/μL SD below 2K/μL WBC.
WBC Bias/Error: ±7.5% error above 2K/μL WBC. ±0.25 K/μL error below 2K/μL WBC.

Neutrophil % Precision: 5% SD OR 15% CV
Neutrophil % Bias: ±10% bias or ±5% Neut% total error (whichever larger).

These targets were chosen based on CLSI clinical precision/bias recommendations for WBC and Neut%. Constant value targets were set to account for asymptotically increasing percent imprecision towards lower concentrations as per the poisson distribution.

Description of Intended Setting:

The Athelas Home is indicated to be used within a patient's home in a stationary and dry location. The Athelas Home labeling (Proposed Labeling Section 13) highlights the specific conditions (temperature, humidity) for storage and operation, which are identical to the FDA-cleared Athelas One (K181288).

Summary of Technological Characteristics Compared to Predicate Devices:

The Athelas Home is identical to the Athelas One in its technology, all software, the analytes measured, all components, and usage process. The Athelas Home has additional software and quality control safeguards to enable at-home usage of the device. Additionally, results generated

from the Athelas Home are not shown to end-patients, rather are transmitted via the software directly to their healthcare provider. The Athelas Home also has Remote Lockout capabilities, such that a healthcare provider or manufacturer can remotely lock-out a device for safety in usage.

Testing: Bench, Clinical testing, At-Home testing, and Flex Testing were conducted to showcase substantial equivalence between the Athelas Home and predicate device.

As per Agency guidance in presubmission (Q190305), studies from the Athelas One were used to support the Athelas Home because the devices are identical.

Bench

Within-run Precision/Reproducibility

From K181288 Athelas One

Within-run Precision Repeatability

Precision studies were performed using K2EDTA whole blood samples around medical decision levels and the upper and lower limit of the analytical measuring range. The study was conducted with nine whole blood samples, three different operators and three different test strip lots. Care was taken to include both normal and abnormal samples.

Three operators and three test strip lots were used in conjunction. Per operator, per lot, ten replicates of each sample were tested and the results were recorded. 90 tests were run per sample, with 810 tests run in total. The mean, standard deviation (SD), and coefficient of variation (CV) were calculated for each sample. All results met the predefined specifications (CV%) for precision (targets shown on below table as well).

WBC Summarized

Sample	Mean Value (K/µL)	N	Repeatability		Between-Lot		Between-Instrument		Between-Operator		Total		Target Evaluation		
			SD (K/µL)	CV (%)	SD (K/µL)	CV (%)	SD (K/µL)	CV (%)	SD (K/µL)	CV (%)	SD (K/µL)	CV (%)	Target Metric	Experiment Value	Target Value
1	2.20	90	0.12	5.62	0.00	0.00	0.00	0.00	0.04	1.70	0.13	5.87	CV	5.87%	7.50%
2	3.75	90	0.20	5.42	0.00	0.00	0.01	0.36	0.02	0.60	0.20	5.46	CV	5.46%	7.50%
3	4.12	90	0.20	4.78	0.00	0.00	0.06	1.43	0.04	1.02	0.21	5.09	CV	5.09%	7.50%
4	5.11	90	0.25	4.96	0.00	0.00	0.14	2.73	0.10	1.87	0.30	5.96	CV	5.96%	7.50%
5	7.89	90	0.33	4.18	0.06	0.78	0.09	1.14	0.15	1.94	0.38	4.82	CV	4.82%	7.50%
6	10.01	90	0.50	5.01	0.00	0.00	0.10	0.98	0.19	1.91	0.55	5.45	CV	5.45%	7.50%
7	14.64	90	0.66	4.51	0.19	1.27	0.00	0.00	0.00	0.00	0.69	4.69	CV	4.69%	7.50%
8	17.52	90	0.70	3.97	0.00	0.00	0.17	0.95	0.26	1.49	0.76	4.34	CV	4.34%	7.50%
9	23.33	90	1.01	4.33	0.77	3.31	0.20	0.87	0.43	1.82	1.36	5.81	CV	5.81%	7.50%

Precision Reproducibility (between run)

Precision/Reproducibility studies were performed on the Athelas One Whole Blood Manual Mode using three levels of ATH-check quality control material (Low, Normal and High). The 20-day study used three sites, with three analyzers (one instrument per site), three lots of test strips, and one lot of quality control materials (all levels). We performed two runs per day and two replicates per run with two operators per site. A total of 80 readings were generated at each site for each level of control (2 runs x 20 days x 2 replicates = 80 readings). As per Agency recommendation results were analyzed using ANOVA analysis and taking into account the nested design of the study.

Low

Low

Overall Summary Table

Measurand	Mean Value	N	Within-Run		Between-Run		Between-Day		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%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

Medium

Medium

Overall Summary Table

Measurand	Mean Value	N	Within-Run		Between-Run		Between-Day		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%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 %	49.990	240	3.015	6.030	0.932	1.865	0.833	1.666	0.728	1.457	3.344	6.689

High

High

Overall Summary Table

Measurand	Mean Value	N	Within-Run		Between-Run		Between-Day		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%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 %	50.823	240	2.967	5.838	0.000	0.000	0.947	1.864	1.139	2.241	3.316	6.525

A site by site analysis was also conducted as per Agency recommendation, also falling within evaluation criteria. Overall reproducibility levels were found to meet the acceptance criteria of 7.5% CV for WBC and 5% SD or 15% CV for Neutrophils across all three levels and all sites.

At-Home Precision Study

An additional precision repeatability (within-run) study was conducted to showcase the precision performance of the Athelas Home specifically by at-home users. The study design recommended by the Agency was for samples to be collected in duplicate by home users in home environments and analyzed for CV% to confirm that evaluation criteria for precision were still met.

Patients were instructed to conduct two tests on the Athelas Home following the labeling process. Patients were instructed to collect both samples within 5 minutes of each other following the Athelas Home labeling, filling two unique test strips. This was known as the **in-home whole blood self-test group.**

A separate group of patients were provided with Athelas Home Quality Control material and asked to use the dropper on the Quality Control Material vial to conduct 3 replicates for the

assigned sample to the given patient. This was known as the **in-home quality control material self-testing group.**

The evaluation criteria is shown below:

WBC Targets (Evaluation Criteria)

Range (WBC)	Target	Statistic
0 - 2K	0.25 K/µL	Standard Deviation
2K +	7.5%	CV %

CV% was calculated for the two groups (patient blood samples, and quality control material) combined as well as independently in order to evaluate against the Evaluation Criteria. Per-recommendation of CLSI EP05-A3, the primary analyte (WBC) was used for precision evaluation.

The results indicate that the At-Home Precision Repeatability studies met their pre-set evaluation criteria for WBC CV% and NEUT% precision (7.5% CV for WBC and 5% SD for NEUT% or 15% CV for NEUT%).

Patient In-home Whole Blood Studies Self-Test

The in-home whole blood study consisted of 24 patients, and 2 replicates per sample.

Patient Run Number	Replicate 1 WBC	Replicate 1 NEUT%	Replicate 2 WBC	Replicate 2 NEUT%	WBC Average	CV WBC	NEUT Average	NEUT SD	NEUT% CV
1	5	57%	5.1	56%	5.1	1.4%	57%	**0.71%**	1%
2	6.1	63%	6.5	66%	6.3	4.5%	65%	**2.12%**	3%
3	7.1	59%	6.1	65%	6.6	10.7%	62%	**4.24%**	7%
4	5.5	57%	6	57%	5.8	6.1%	57%	**0.00%**	0%
5	1	32%	1.1	36%	1.1	6.7%	34%	**2.83%**	8%
6	7.2	75%	7.4	71%	7.3	1.9%	73%	**2.83%**	4%
7	1.4	31%	1.5	31%	1.5	4.9%	31%	**0.00%**	0%
8	2.6	79%	2.7	80%	2.7	2.7%	80%	**0.71%**	1%
9	5.6	66%	5.2	63%	5.4	5.2%	65%	**2.12%**	3%
10	5.7	63%	6.2	66%	6	5.9%	65%	**2.12%**	3%

11	5.4	62%	5.7	59%	5.6	3.8%	61%	**2.12%**	4%
12	6.6	61%	6.1	66%	6.4	5.6%	64%	**3.54%**	6%
13	4.7	58%	5.1	54%	4.9	5.8%	56%	**2.83%**	5%
14	6.2	45%	5.5	44%	5.9	8.5%	45%	**0.71%**	2%
15	4.2	27%	4.3	30%	4.3	1.7%	29%	**2.12%**	7%
16	6.1	33%	5.7	28%	5.9	4.8%	31%	**3.54%**	12%
17	7.4	37%	7.2	37%	7.3	1.9%	37%	**0.00%**	0%
18	3.3	31%	3.2	34%	3.3	2.2%	33%	**2.12%**	7%
19	5.1	63%	6.2	55%	5.7	13.8%	59%	5.66%	**10%**
20	7.3	55%	7.4	59%	7.4	1.0%	57%	**2.83%**	5%
21	5.2	45%	5.8	48%	5.5	7.7%	47%	**2.12%**	5%
22	7.1	52%	7.6	51%	7.4	4.8%	52%	**0.71%**	1%
23	12.5	72%	13.9	68%	13.2	7.5%	70%	**2.83%**	4%
24	9.8	65%	10.9	60%	10.4	7.5%	63%	**3.54%**	6%

Patient in-home QC Material Repeatability Self-Test

The in-home QC material repeatability study consisted of 10 patients, and 3 replicates per sample.

Replicate 1 WBC	Replicate 1 NEUT%	Replicate 2 WBC	Replicate 2 NEUT%	Replicate 3 WBC	Replicate 3 NEUT%	Average NEUT%	CV WBC	Average NEUT%	STD NEUT%
2.4	8.00%	2.6	11.00%	2.7	9.00%	2.6	6.0%	9.33%	**1.53%**
2.9	11.00%	2.9	12.00%	3.1	8.00%	3	3.9%	10.33%	**2.08%**
7.8	8.00%	7.2	6.00%	7.9	8.00%	7.6	5.0%	7.33%	**1.15%**
8	8.00%	8.3	8.00%	8.2	7.00%	8.2	1.9%	7.67%	**0.58%**
20	8.00%	23	9.00%	22	9.00%	21.7	7.1%	8.67%	**0.58%**
23.8	9.00%	23.8	6.00%	24.1	9.00%	23.9	0.7%	8.00%	**1.73%**
2.7	12.00%	2.8	11.00%	2.8	13.00%	2.8	2.1%	12.00%	**1.00%**
2.9	13.00%	2.9	14.00%	3	12.00%	2.9	2.0%	13.00%	**1.00%**
2	15.00%	3	18.00%	3.1	17.00%	2.7	22.5%	16.67%	**1.53%**
7.2	7.00%	7.6	9.00%	7.6	8.00%	7.5	3.1%	8.00%	**1.00%**

Results with Evaluation Criteria (see Specifications)

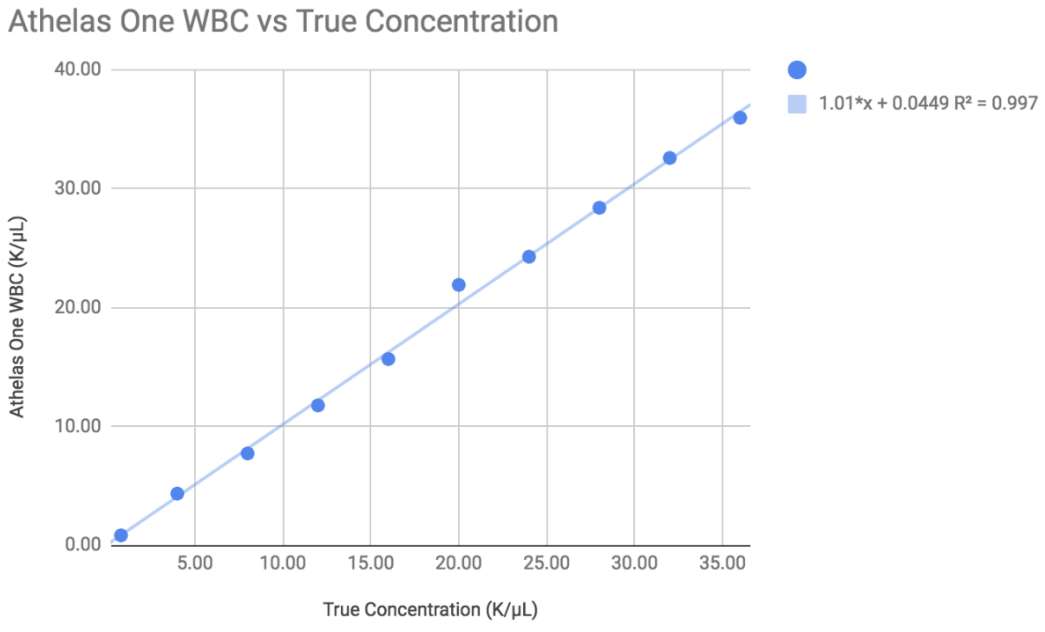
	Value	Eval Criteria	Pass/Fail
WBC CV%	5.4% CV	7.5% CV	Pass
NEUT% SD	1.2% SD	5% SD or 15% CV	Pass

Linearity

10 samples across the reporting range were run in 4 replicates across 4 devices and one test strip lot. The samples were obtained by pooling together one low WBC concentration fresh whole blood sample one high WBC concentration sample in different volumes which is a recommended option in CLSI EP6-A.

The method has been demonstrated to be linear from lower limit to upper limit and within measured allowable max % diff for each interval. The primary analyte (WBC) was analyzed in linearity as per CLSI EP06-A guidance. The CLSI recommended OLS regression of the linearity data is provided below:

Parameter	N	R^2	Slope	Intercept	CVr
WBC	10	0.997	1.013	0.0449	5.08%



Interfering Substances

Interference studies were performed taking sample abnormalities, drugs, metabolites, sample additives and dietary substances into consideration. A list of substances were tested and found naturally occurring in patient samples, or were spiked in whole blood. This list is included below (with highest concentration or percentages tested). None of the substances were found to interfere with the measurements of the Athelas One device. This was evaluated through analysis of interferon impact on bias and precision performance. All interferon spiked samples continued to perform within the evaluation criteria.

- Triglyceride Rich Lipoproteins
- Hemolysate
- Protein
- Levodopa
- Methyldopa
- Metronidazole
- Acetylsalicylic Acid
- Phenylbutazone
- Rifampicin
- Cyclosporine
- Acetaminophen
- Heparin
- Ibuprofin
- Bilirubin C
- Bilirubin F
- Reticulocytes
- Platelet Aggregates
- Nucleated Red Blood Cells
- Giant Platelets
- Myelodysplastic Syndrome
- Macrocytic Anemia
- Infectious Mononucleosis
- Bacterial Infections
- Chronic Myeloid Leukemia
- Patients on Chemotherapy
- Patients treated with GCSFs

Reference Intervals

Adult reference intervals for the Athelas One were verified across 120 healthy donors in comparison to pre-established reference intervals for the Sysmex XE-5000 utilizing whole blood samples.

Limit of Blank (LoB) – Whole Blood

The LoB was obtained from 120 total repeated measurements of blank samples analyzed in the sampling modes for whole blood. The mean, SD and LoB were calculated for the analyzer. The LoB for whole blood parameters WBC is zero (0) K/µL.

Limit of Detection (LoD) – Whole Blood

As per Agency recommendation, Limit of Detection was conducted using run as follows:

- 2 test strip lots (60 strips each)
- 2 instruments
- 3 days
- 5 low level samples
- 2 replicates per sample

Test Strip Lot 1 Summarized Data

N	LoB (from LoB section)	c_p	Pooled Standard Deviation (K/µL)	LoD (K/µL)
60	0	1.653	0.033	0.055

Test Strip Lot 2 Summarized Data

N	LoB (from LoB section)	c_p	Pooled Standard Deviation (K/µL)	LoD (K/µL)
60	0	1.653	0.048	0.079

As shown in the Limit of Blank section, the LoB was found to be 0.

The LoD of Lot 1 was 0.055 K/µL while the LoD of Lot 2 was 0.079 K/µL. The maximum LoD of the two lots was established as the final LoD. Hence, the LoD was set to be 0.079 K/µL.

The LoD was found to be 0.079 K/µL which is well below the LoQ of 0.44 K WBC/µL.

Limit of Quantification (LoQ) – Whole Blood

The Limit of Quantification study was designed to estimate the lowest measurement concentration that can be measured on the Athelas One and meet the predefined total error goals. **The study was conducted over two test-strip lots, 1 instrument, 3 days, 3 replicates per sample, and 4 independent low-level whole blood samples.** The samples were distinct whole blood samples acquired from patients in K_2EDTA tubes. The original concentrations were obtained from the predicate analyzer (Sysmex XE-5000). These samples were then diluted to reach an approximate concentration of 0.45 K WBC/µL. The original concentrations, the volume of diluent, and the final concentrations of the samples are shown in the table below.

Sample	WBC Initial (K/µL)	Volume of Sample in Aliquot (µL)	Volume of Diluent in Aliquot (µL)	Final Aliquot Concentration (K/µL)	Final Aliquot Volume (µL)
1	3.97	100	800	0.44	900
2	3.92	100	800	0.44	900
3	4.16	100	800	0.46	900
4	3.13	100	600	0.45	700

The Limit of Quantification of the Athelas One was determined to be **0.44 K WBC/µL** as per CLSI EP17-A2. This is below the lower limit of the Athelas One's reporting range of 1.0K WBC/µL.

Specimen Stability Studies

Whole blood stability - Room temperature vs Refrigerated temperature

Whole blood stability was evaluated on the Athelas One device by conducting a 48 hour stability study on nine different venous blood samples with low (0.5-3 K/µL, normal (4-10 K/µL), and high (>10 K/µL) WBC levels. The study was designed in accordance with recommendations from CLSI EP25-A.

Based on results evaluating deviation from pre-defined bias and precision criteria, the stability duration for all samples can be set to 24 hours with observed degradation at 48 hours for both the WBC and Neutrophil % parameters. Overall, all samples tested within 24 hours of collection time were found to meet the pre-set acceptance criteria of 7.5% CV for WBC precision, ± 7.5% Bias for WBC, 5% SD OR 15% CV for Neutrophils (updated based on Sysmex XW-100 Neut% CV criteria), and ± 10% Bias across the whole study.

Test Strip Stability over time

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 justify a 15 week expiration. 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, 4 analyzers, two replicates, and one lot of quality control materials. Each week, we performed two replicates per two lots of strips across 3 levels of control fluid.

From the study it can be observed that none of the analyzed test strips manifested statistically significant degradation/drift over the 105-day study ($p > 0.05$) as recommended by the CLSI EP25-A regression slope analysis. 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.

Clinical

Method Comparison

Method comparison studies were performed to assess the performance of the Athelas One analyzer when compared to the predicate Sysmex XE-5000 analyzer on a total of 312 patient samples taken at 3 point of care sites in the US. All samples were run in the Automated Sampling Modes in singlet on the XE-5000.

Samples covered clinical medical decision levels, and included normal and abnormal samples. The full reportable measuring ranges of the Athelas One analyzer were tested in method comparison. **All evaluation criteria (slope, r, bias at medical decision levels, overall bias, bland altman analysis, intercept) were met, and even more specifically: manufacture-defined criteria for equivalence between two predicate Sysmex XE-5000 devices was also met by the Athelas One.**

The overall results across three sites are shown in the table below.

Method Comparison Combined Site WBC and Neutrophil Results

Parameter	Interval	N	(r)	Slope			Intercept			Mean Bias	Mean % Bias
				Estimate	LCI (2.5%)	UCI (97.5%)	Estimate	LCI (2.5%)	UCI (97.5%)		
WBC	1.1 - 23 (K/µL)	312	0.99	0.978	0.958	1.000	-0.042	-0.159	0.086	-0.151	-2.31%
Neutrophil %	8 - 92.89 (%)	312	0.96	0.980	0.953	1.003	1.855	-0.530	3.677	0.636	1.18%

Flagging Comparison

As per Agency recommendation, a Flagging Comparison study was conducted to determine the ability for the Athelas One to successfully flag abnormal samples for manual review. The study design of a Sysmex XN series analyzer (FDA 510k K112605) was used, and a similar evaluation criteria of 90% flagging accuracy.

Morphological Flags

The results of the Athelas One morphological flagging compared to the XE-5000 flagging evaluation were divided into two categories: (1) No Flags, Negative Judgement (2) Patients with positive Morphology/Differential abnormalities - Flags present, Positive Judgement. The study was limited to WBC and DIFF related flags. The results obtained from the flagging comparison study met the specification of ≥ 90%.

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

% Positive Agreement (Sensitivity) = 100 * 90/(90 + 9) = 90.91%
% Negative Agreement (Specificity) = 100 * 206/(206 + 7) = 96.71%
% Overall Agreement = 100 * (90 + 206) / (90 + 206 + 9 + 7) = 94.87%

Evaluation criteria for morphological flagging accuracy was met, and a similar analysis was conducted for distributional flagging as well. The flagging study covered a variety of abnormal samples that are flagged by the predicate, with a breakdown as follows:

Predicate Flag	Count
PLT Clumps?	15
Abn Lympho/L_Blasts?	51
Blasts?	46
Immature Gran?	29
Left Shift?	14

Matrix Comparison

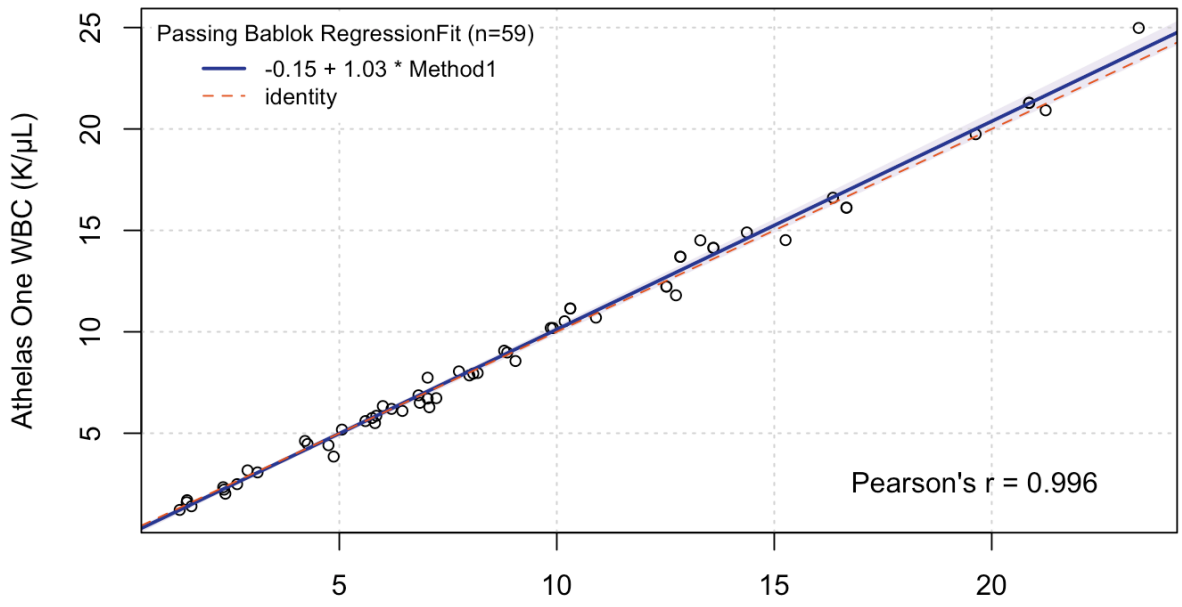
Experiments were conducted to determine the comparability of venous and capillary whole blood on the Athelas One device across 59 patients. These were in addition to the method comparison trials that used a combination of venous and capillary blood tested against venous samples run on the predicate device.

Capillary finger-prick blood samples were placed onto Athelas test strips from subjects. Venous whole blood samples were collected in K2EDTA vacutainer tubes for the same patients. The capillary whole blood and the venous whole blood samples were analyzed on Athelas One devices. It was concluded that there is no statistical difference between the systems when analyzing venous and capillary samples.

The regression parameters and 95% confidence interval of bias at the medical decision levels were calculated as per recommendation of CLSI EP5-A3 and H26-A2 and met all evaluation criteria. The information is summarized on the tables below:

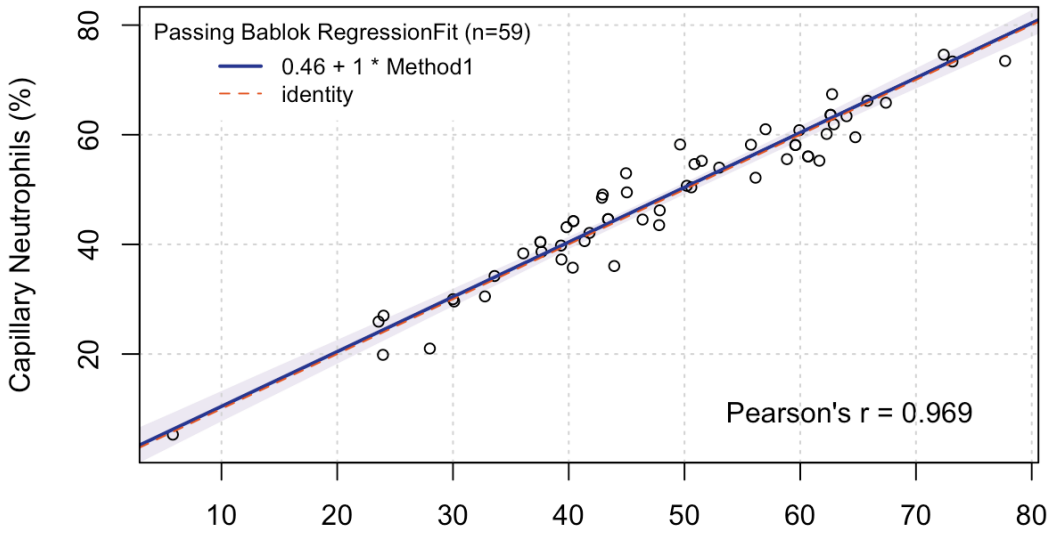
Parameter	Interval	N	(r)	Slope, 95% CI	Intercept	Mean Bias	Mean % Bias
WBC	1.33 - 23.38	59	0.996	1.026 (1.000, 1.055)	-0.145 (-0.319, 0.018)	0.056 (K/µL)	-0.588
Neutrophil %	5.8 - 74.6	59	0.969	0.999 (0.938, 1.058)	0.457 (-2.502, 3.614)	0.162 (Percentage Points)	-0.333

WBC Passing-Bablok Regression.



The 0.95-confidence bounds are calculated with the bootstrap(quantile) method.

Neutrophil % Passing-Bablok Regression.



The 0.95-confidence bounds are calculated with the bootstrap(quantile) method.

At-Home Method Comparison

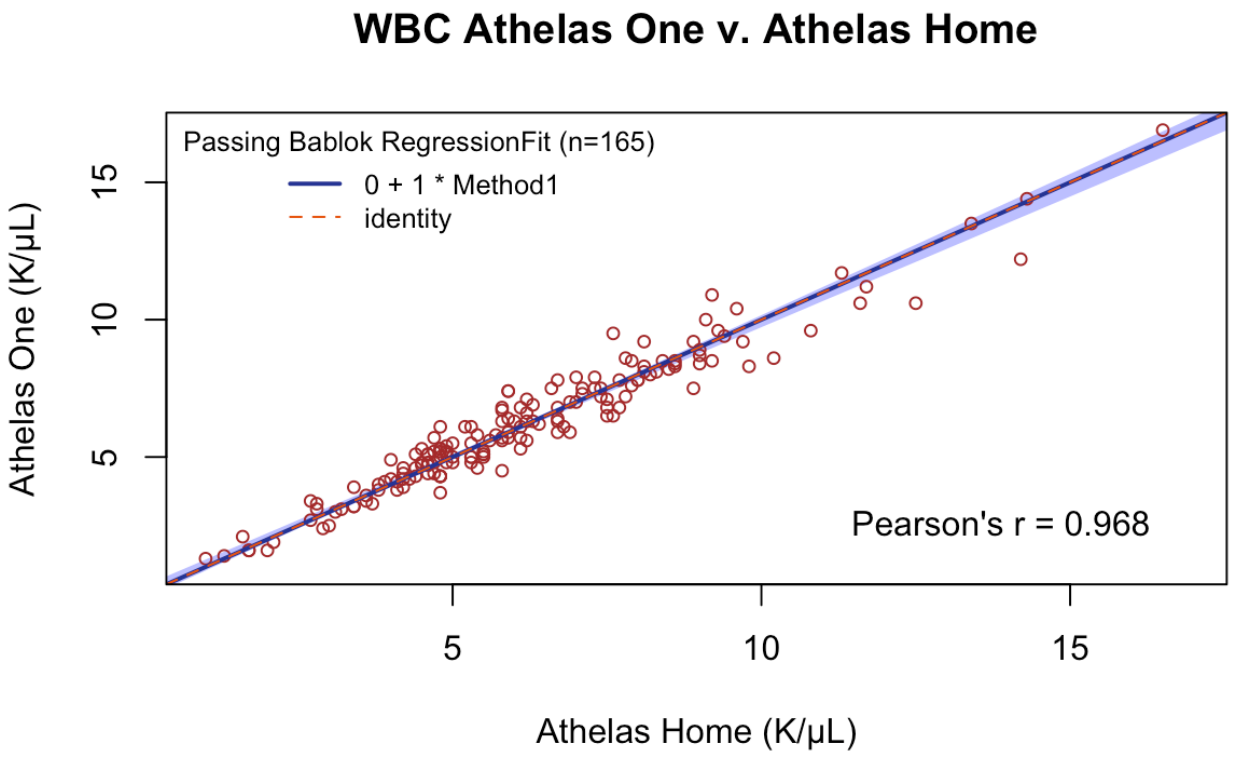
Method comparison studies were performed to assess the performance of the Athelas Home analyzer in at-home settings when compared to the predicate Athelas One analyzer on a total of 165 samples taken in at-home settings in the US.

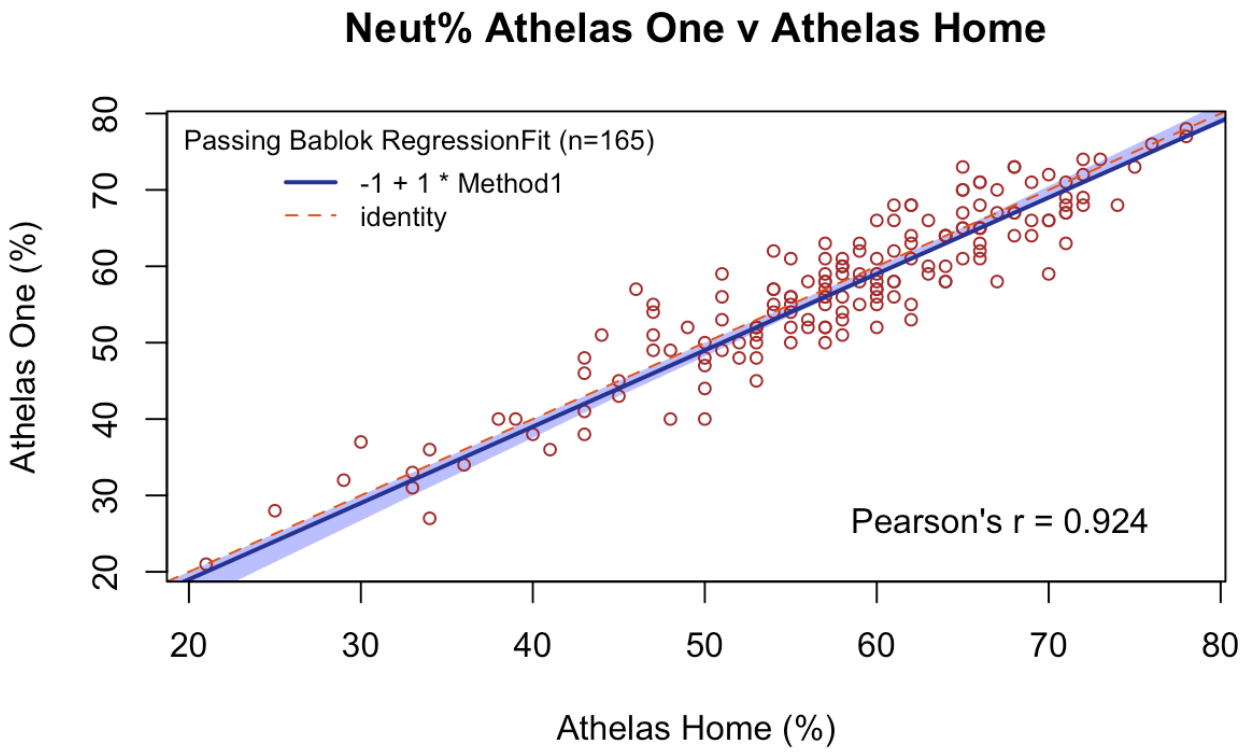
The full reportable measuring ranges of the Athelas Home analyzer were tested in method comparison. **All evaluation criteria (slope, r, bias at medical decision levels, overall bias, bland altman analysis, intercept) were met, and even more specifically: manufacture-defined criteria for equivalence between two predicate Sysmex XE-5000 devices was also met by the Athelas Home in home settings and the Athelas One.**

The overall results are shown in the table below.

Method Comparison WBC and Neutrophil Results

Parameter	Interval	N	(r)	Slope			Intercept			Mean Bias (K/µL)	Mean % Bias
				Estimate	LCI (2.5%)	UCI (97.5%)	Estimate	LCI (2.5%)	UCI (97.5%)		
WBC	1.0 - 16.9	165	0.97	1.0	0.95	1.03	0	-0.16	0.31	0	0.0
Neutrophil %	21-78	165	0.92	1.0	0.98	1.09	-1.0	-6.09	0.0	-0.5	1.3





At-Home Error Analysis

During At-Home testing, error analysis was conducted to verify the usability and ease of use of the Athelas Home when used by patients in the intended use settings. Over 94% of tests were run successfully with no errors. Errors that were found were resolved after running a single additional test-strip. The results are shown below:

Error Type	Number of Occurrences	Percent of Tests
No Error	76	94
Test-Strip/Optical Error	3	3.7
Incorrect Insertion Direction	2	2.5
HH! (shows as success to the patient)	1	1.2
LL! (shows as success to the patient)	1	1.2

At-Home Usability Analysis

During the first At-Home visits, study investigators were asked to conduct usability surveys to ensure at-home users had no difficulties in setting up and understanding how to run the test. The following questions were asked per user:

1. Was the user able to use the lancet correctly? Mark yes if the user was able to open the lancet, puncture the correct site on their finger, and dispose of the lancet correctly.
2. Did the user fill up the test-strip fully? Mark yes if the user placed enough blood such that the blood reached the end of the channel on the test-strip.
3. Did the user face any errors when running the test (not error codes)?
4. Did the user correctly know how to run the test using the application?
5. Was this test performed by the patient (yes) or caregiver (no)? (‘Yes’ if conducted by patient, ‘No’ if conducted by caregiver)

The results, shown below, indicate a large majority of patients found the Athelas Home easy to use and had very little difficulty running the test end to end.

Survey Question	“Yes” Responses	“No” Responses
1	32	0
2	30	2
3	31	1
4	32	0
5	10	22

Flex Testing

Fill-Volume Testing

A study was conducted to determine whether the Athelas Home correctly handles variable amounts of blood inserted into the test-strip. In particular, the study aimed to verify that should an at-home user place either too little or too much blood in the test-strip inlet, one of the following occurs:

1. An error code is returned with the appropriate message.
2. The results are accurate and meet the acceptance criteria.

The study found that the Athelas Home is robust to variable volumes of blood placed on the test-strip. The results for multiple fill volumes tested across different samples are shown below:

Sample	Fill-Volume (µL)	Mean WBC (K/µL)	Mean Neut (%)	Predicate WBC (K/µL)	Predicate Neut (%)	WBC Bias (%)	Neut% Bias (percentage points)	WBC bias criteria met	Neut % bias criteria met
1	0	error	error	2.7	42	N/A	N/A	Yes	Yes
1	1.4	2.7	39	2.7	42	0.00%	-3	Yes	Yes
1	3.4	2.8	43	2.7	42	3.70%	1	Yes	Yes
1	5.4	2.7	37.5	2.7	42	0.00%	-4.5	Yes	Yes
2	0	error	error	8.0	48	N/A	N/A	Yes	Yes
2	1.4	7.6	49.5	8.0	48	-5.00%	1.5	Yes	Yes
2	3.4	8.2	46	8.0	48	2.50%	-2	Yes	Yes
2	5.4	7.7	52.5	8.0	48	-3.75%	4.5	Yes	Yes
3	0	error	error	18.2	50	N/A	N/A	Yes	Yes
3	1.4	17.7	48	18.2	50	-2.75%	-2	Yes	Yes
3	3.4	18.4	49.5	18.2	50	1.10%	-0.5	Yes	Yes
3	5.4	17.6	45.5	18.2	50	-3.30%	-4.5	Yes	Yes

Device Tilt Testing

A study was conducted to determine whether the Athelas Home is robust against being placed on tilted surfaces in different orientations. In particular, the study aimed to verify that should an at-home user place place the device on some tilted surface and runs a test, one of the following occurs:

1. An error code is returned with the appropriate message.
2. OR The results are accurate and meet the acceptance criteria.

The study found that the Athelas Home is not affected by tilted placement of the device. The results indicating no significant bias in both parameters across tilt orientations and samples is shown below:

Sample	Condition	Average WBC (K/mL)	Average Neut (%)	Predicate WBC (K/µL)	Predicate Neut (%)	WBC Bias (%)	Neut% Bias (percentage points)	WBC Criteria Met	Neut% Criteria Met
1	1	3.0	40	2.9	42	1.72%	-2	Yes	Yes
1	2	3.1	42	2.9	42	6.90%	0	Yes	Yes

1	3	2.9	41.5	2.9	42	-1.72%	-0.5	Yes	Yes
1	4	3.1	40.5	2.9	42	6.90%	-1.5	Yes	Yes
2	1	6.8	46	7.2	47	-5.56%	-1	Yes	Yes
2	2	7.2	49	7.2	47	0.21%	2	Yes	Yes
2	3	6.9	45	7.2	47	-4.86%	-2	Yes	Yes
2	4	7.5	46	7.2	47	3.47%	-1	Yes	Yes
3	1	17.0	47	16.3	50	3.99%	-3	Yes	Yes
3	2	16.1	49	16.3	50	-1.07%	-1	Yes	Yes
3	3	16.0	49.5	16.3	50	-1.60%	-0.5	Yes	Yes
3	4	16.5	50.5	16.3	50	0.92%	0.5	Yes	Yes

Device Drop Testing

A study was conducted to determine whether the Athelas Home continues to return accurate results after being dropped from multiple orientations and heights. In particular, the study aimed to verify that should an at-home user drop the device, the following occurs:

1. An error code is returned with the appropriate message.
2. The results are accurate and meet the acceptance criteria.

The study was conducted in accordance with ASTM 1469 - D03 across 12 devices.

The study found that the Athelas Home is robust to the given drop and vibration schedules. The table below shows that all devices continued to pass functional tests after being subjected to the full testing schedules:

Device	Critical Physical Damage Present?	No functional defects?	Auto-Check WBC (K/μL)	Auto-Check Neut%	Reference WBC Range (K/μL)	Reference Neut% Range (%)	WBC in range?	Neut% In range?
1	No	Yes	3.4	41	2.9 - 3.4	35 - 45	Yes	Yes
2	No	Yes	3.1	38	2.9 - 3.4	35 - 45	Yes	Yes
3	No	Yes	3.3	42	2.9 - 3.4	35 - 45	Yes	Yes
4	No	Yes	3.3	41	2.9 - 3.4	35 - 45	Yes	Yes
5	No	Yes	3.3	41	2.9 - 3.4	35 - 45	Yes	Yes
6	No	Yes	3.3	39	2.9 - 3.4	35 - 45	Yes	Yes

7	No	Yes	3.3	41	2.9 - 3.4	35 - 45	Yes	Yes
8	No	Yes	2.9	42	2.9 - 3.4	35 - 45	Yes	Yes
9	No	Yes	3.0	40	2.9 - 3.4	35 - 45	Yes	Yes
10	No	Yes	3.1	45	2.9 - 3.4	35 - 45	Yes	Yes
11	No	Yes	3.0	42	2.9 - 3.4	35 - 45	Yes	Yes
12	No	Yes	3.1	38	2.9 - 3.4	35 - 45	Yes	Yes

Device and Test-Strip Temperature Testing

A study was conducted to verify the performance of the Athelas Home device and test-strips after extreme and varying temperature. The goal of the study was to confirm that the Athelas Home retains performance characteristics after prolonged exposure to such conditions. Flex temperatures may arise in home-use environments.

Both the Athelas Home device and Athelas Home test-strip were found to continue to meet performance specifications after exposure to extreme temperatures. The results are shown below.

Device Results

Environment Condition	Device	N	Average WBC Bias	Average Neut% Bias	WBC Meets Criteria	Neut% Meets Criteria
1	1	9	1.26%	1.70	Yes	Yes
1	2	9	-0.33%	1.48	Yes	Yes
1	3	9	2.34%	2.59	Yes	Yes
2	1	9	0.93%	-1.52	Yes	Yes
2	2	9	0.49%	-0.97	Yes	Yes
2	3	9	6.27%	0.81	Yes	Yes
3	1	9	6.15%	0.37	Yes	Yes
3	2	9	3.94%	-1.74	Yes	Yes
3	3	9	0.37%	-1.97	Yes	Yes

Test-Strip Results

Environment Condition	Test-Strip Lot	N	Average WBC Bias	Average Neut% Bias	WBC Meets Criteria	Neut% Meets Criteria
1	1	9	3.01%	1.26	Yes	Yes

1	2	9	3.08%	2.14	Yes	Yes
1	3	9	-2.69%	1.81	Yes	Yes
2	1	9	0.46%	0.59	Yes	Yes
2	2	9	-0.99%	0.14	Yes	Yes
2	3	9	-3.78%	0.70	Yes	Yes
3	1	9	6.01%	-2.52	Yes	Yes
3	2	9	5.58%	-1.08	Yes	Yes
3	3	9	-0.97%	-0.08	Yes	Yes

Vibration Testing

Vibration testing conducted to ensure that the Athelas Home device can continue to function or return appropriate error codes after exposure to extensive vibration in handling by a patient or shipping.

Vibration testing was conducted by third party ISTA certified test lab Quanta Testing. The system successfully met evaluation criteria post vibration test.

Conclusion

Through a range of CLSI recommended studies in clinical and bench settings, the Athelas Home has been shown to be safe and effective for at-home use and substantially equivalent to the POC Athelas One.

Humidity Flex Testing

Objective

Humidity Flex Testing was part of the final list of flex tests decided by Athelas and the Agency as part of the Athelas Home Presubmission (Q190305 Attachment B). A study was conducted to verify the performance of the Athelas Home test-strips under extreme humidity conditions.

Methodology

The study aimed to showcase functional performance of the Athelas Home Test-Strips after exposure of test-strips to the following humidity conditions:

Condition	Temperature (C)	Humidity (%)
X	38º	85

Y	-29	Uncontrolled

Each of eight test-strips were subject to the following test schedules based on the above conditions:

Test-Strip Number	Schedules
1	Condition X for 72 hrs
2	Condition X for 72 hrs
3	Condition X for 72 hrs
4	Condition X for 72 hrs
5	Condition X for 72 hrs followed by Y for 72 hrs
6	Condition X for 72 hrs followed by Y for 72 hrs
7	Condition X for 72 hrs followed by Y for 72 hrs
8	Condition X for 72 hrs followed by Y for 72 hrs

The conditions were implemented using humidity chambers at Quanta Laboratories, an ISTA certified environmental testing laboratory.

After exposure to the testing schedules, the following functional tests were conducted on the test-strips:

1. Change in Color
    a. Verify qualitatively that no change in test-strip color is present.
        i. This was conducted by comparing a reference test-strip that hadn't been placed into the testing conditions against the test-strip placed under the conditions.
2. Fill-Time
    a. Measurement of time for 3.4 µL of a single vial of Ath-Check control fluid to flow to the end of the channel.
    b. A stopwatch was started when a single drop of the fluid was placed on the channel inlet and stopped when the fluid met the side edges of the T channel on the test-strip.

These tests were chosen due to risk analyses which found that humidity primarily affects the test-strips by increasing fill-time through decreasing capillary pressure in the channel, and changing the test-strip color due to presence of condensation affecting stain color.

As such, verification of flow-time and color change were found to be sufficient checks for no performance degradation of the test-strip.

Results

The below table showcases the results of humidity related environment testing on the eight test-strips:

Test-Strip Number	Schedules	Fill Time (seconds)	Fill Time Criteria (seconds)	Fill Time Within Specification ?	No Color Change present?
1	X for 72 hrs	7.32	< 25	Yes	Yes
2	X for 72 hrs	7.72	< 25	Yes	Yes
3	X for 72 hrs	7.70	< 25	Yes	Yes
4	X for 72 hrs	7.58	< 25	Yes	Yes
5	X for 72 hrs followed by Y for 72 hrs	8.16	< 25	Yes	Yes
6	X for 72 hrs followed by Y for 72 hrs	7.66	< 25	Yes	Yes
7	X for 72 hrs followed by Y for 72 hrs	7.21	< 25	Yes	Yes
8	X for 72 hrs followed by Y for 72 hrs	7.08	< 25	Yes	Yes

Discussion

Based on the results, it was concluded that the Athelas Home test-strips continued to function within specifications after exposure to extreme humidity conditions. In particular, no evidence

was found of condensation in the test-strip which would be manifested in increased fill-time and changes in stain color.

All eight test-strips across all schedules were found to be within specifications for both fill time and color. This is due to specially designed packaging for the Athelas Home test-strips that ensure humidity resistance. The Athelas Home Test-Strip packaging includes three separate layers designed specifically to reduce humidity effects:

1. PET Layer
2. Aluminum Layer
3. Desiccant Layer

As such, the relative humidity within the package is consistently less than 10% in extreme conditions and ensures the test-strip is protected from humidity related effects.