DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

May 27, 2016

Advanced Instruments, Inc.
Mr. Robert Mello
Vice President and Chief Operating Officer
Two Technology Way
Norwood, MA 02062

Re: K152776
Trade/Device Name: GloCyte® Automated Cell Counter System
GloCyte® Low and High Level Controls
Regulation Number: 21 CFR 864.5200
Regulation Name: Automated cell counter
Regulatory Class: Class II
Product Code: GKL, JPK
Dated: April 26, 2016
Received: April 27, 2016

Dear Mr. Mello:

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. 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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K152776

Device Name
GloCyte Automated Cell Counter System

GloCyte Low and High Level Controls

Indications for Use *(Describe)*

The GloCyte Automated Cell Counter System is intended for use by trained healthcare professionals in clinical laboratories to provide quantitative determination of fluorescence labeled total nucleated cells and erythrocytes in cerebrospinal fluid collected from adult and pediatric patients.

The GloCyte Low and High Level Controls are assayed hematology controls designed to monitor the performance of the GloCyte Automated Cell Counter System. Assayed parameters include total nucleated cells and erythrocytes.

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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510(k) Summary for
Glocyte® Automated Cell Counter System and Glocyte® Low and High Level Controls

5.1 Applicant

Advanced Instruments, Inc.
Two Technology Way
Norwood, MA 02062
USA
Phone: 781-320-9000
Fax: 617-845-9032

Date: September 24, 2015

Contact Person:
Robert Mello
Vice President and Chief Operating Officer
Phone: 781-471-2008
Fax: 781-320-8181

5.2 Device

Trade name: GloCyte® Automated Cell Counter System
Common Name: Automated Cell Counter
Panel: 81 Hematology
Regulation: 21 CFR 864.5200- Automated Cell Counter
Product Code: GKL
Class II

Trade name: GloCyte® Low and High Level Controls
Common Name: Hematology quality control mixture
Panel: 81 Hematology
21 CFR 864.8625 – Hematology quality control mixture
Product Code: JPK
Class II

5.3 Predicate Device

Sysmex XN-10, (K112605)

5.4 Device Description

The GloCyte® Automated Cell Counter System is intended for use by trained healthcare professionals in clinical laboratories to provide quantitative determination of fluorescence labeled total nucleated cells and erythrocytes in cerebrospinal fluid collected from adult and pediatric patients.

The GloCyte® Automated Cell Counter System is an automated cell counter that concentrates and enumerates total nucleated cells (TNCs) and red blood cells (RBCs) using fluorescent

microscopy and digital image analysis principles. The test method uses one of two reagents to stain TNCs (propidium iodide with detergent) or RBCs (fluorochrome labeled anti- human RBC antibody in buffer with stabilizers), and a digital imaging system to count the cells. The image is captured by a digital CCD camera, and the fluorescent stained cells are counted via digital image processing.

The GloCyte® Automated Cell Counter System includes the Instrument, Computer (hardware & software), Vacuum Station, Sample Preparation Tray, Barcode Reader, Pipettes (10 and 30 µL), Test Cartridge, TNC and RBC Reagents, Low and High Level Controls.

5.5 Intended Use

The GloCyte® Automated Cell Counter System is intended for use by trained healthcare professionals in clinical laboratories to provide quantitative determination of fluorescence labeled total nucleated cells and erythrocytes in cerebrospinal fluid collected from adult and pediatric patients.

The GloCyte® Low and High Level Controls are assayed hematology controls designed to monitor the performance of the GloCyte® Automated Cell Counter System. Assayed parameters include total nucleated cells and erythrocytes.

5.6 Substantial Equivalence

A comparison of similarities and differences between the GloCyte® Automated Cell Counter System and the predicate device is provided in table 5-1(Similarities) and 5-2 (Differences).

Table 5-1. Substantial Equivalence Table Comparing GloCyte® Automated Cell Counter System to Predicate Device: Similarities

Items	Predicate: Sysmex XN-10	GloCyte® Automated Cell Counter System
SIMILARITIES		
Sample Type	CSF (and other body fluids)	Cerebrospinal fluid (CSF)
Hardware	Flow system, semiconductor laser with optical components.	Semiconductor laser with optical components.
Parameter(s)	WBC-BF#, RBC-BF#	TNC, RBC

Table 5-2. Substantial Equivalence Table Comparing GloCyte® Automated Cell Counter System to Predicate Device: Differences

Items	Predicate: Sysmex XN-10	GloCyte® Automated Cell Counter System
DIFFERENCES		
Intended Use	The XN-Series modules (XN-10, XN-20) are quantitative multi-parameter automated hematology analyzers intended for in vitro diagnostic use in screening patient populations found in clinical laboratories. The XN-Series modules classify and enumerate the following parameters in whole blood: WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, NEUT%/#, LYMPH%/#, MONO%/#, EO%/#, BASO%/#, IG%/#, RDW-CV, RDW-SD, MPV, NRBC#/%, RET%/#, IPF, IRF, RET-He and has a Body Fluid mode for body fluids. The Body Fluid mode enumerates the WBC-BF, RBC-BF, MN%/#, PMN%/#, and TC-BF parameters in cerebrospinal fluid (CSF), serous fluids (peritoneal, pleural) and synovial fluids. Whole blood should be collected in K2 or K3EDTA anticoagulant and, Serous and Synovial fluids in K2EDTA anticoagulant to prevent clotting of fluid. The use of anticoagulants with CSF specimens is neither required nor recommended.	The GloCyte® Automated Cell Counter System is intended for use by trained healthcare professionals in clinical laboratories to provide quantitative determination of fluorescence labeled total nucleated cells and erythrocytes in cerebrospinal fluid collected from adult and pediatric patients.
Test Principles	Performs hematology analysis according to the Hydro Dynamic Focusing (DC Detection), flow cytometry method (using a semiconductor laser), and SLS-hemoglobin method.	Detection of fluorescence from stained RBCs/TNCs using semiconductor laser and optical system to analyze, calculate and display cell counts.
Reagents	LYSERCELL WDF (Lyse) FLUOROCELL WDF (Stain) CELLPACK™ DCL (Diluent) CELLPACKTM DFL (Diluent)	TNC Reagent (hemolysis of RBCs & stain nucleated cells) RBC Reagent (anti-human glycophorin A/B antibody fluorescent stain).
Calibrators	XN-10 Calibrator (XN CAL)	No external calibrator
Sample/Fluidic Pathway	Single fluidic pathway	No fluidic pathway

Dimensions of Main Unit	Width: 645mm Height: 855mm Depth: 755mm (Single Unit including Sampler)	Width: 153mm Height: 255mm Depth: 204mm (Instrument) Width: 121mm Height: 108mm Depth: 108mm (Vacuum Station)
Weight (kg)	78 (Single Unit including Sampler)	3.8 (Instrument) <1.0 (Vacuum Station)
Throughput	40 samples/hour maximum	6-15 samples/hour.
Sample Volume	88µL	30µL for TNC test 30µL for RBC test
Controls	XN Check BF – 2 Levels	GloCyte® Low and High Level Controls– 2 Levels

5.7 Performance Data

Accuracy

Accuracy was established according to CLSI EP09 *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Third Edition* (2013). Method comparison studies were performed at clinical sites and in-house using clinical and contrived CSF specimens. Results were shown to meet acceptance criteria.

Table 5-3. Hemocytometer vs. GloCyte TNC and RBC counts

Cell Type	Population	N	Range	Slope (95% CI)	Intercept (95% CI)	Constant Bias	Proportional Bias
TNC	Pediatric	129	0 – 7,672	0.963 (0.909, 1.000)	0.037 (0.000, 0.182)	none	none
	Adult	223	0 – 9,900	1.000 (1.000, 1.003)	0.000 (-0.003, 0.000)	none	none
RBC	Pediatric	196	0 – 817,500	0.910 (0.885, 0.935)	0.000 (-0.045, 0.058)	none	-9%
	Adult	267	0 – 901,250	1.000 (0.986, 1.007)	0.000 (0.000, 0.015)	none	none

Repeatability

A repeatability study was conducted at three clinical sites and in-house using clinical and manipulated CSF specimens as well as GloCyte® Low and High Level Controls. The results of the repeatability study met acceptance criteria.

Table 5-4. TNC and RBC Repeatability

Cell Type	Number of Samples	Range Tested [cells/µL]	%CV Results
TNC	26	4 – 10,313	2.5 – 18.0
RBC	29	5 – 727,800	2.7 – 16.3

Precision/Reproducibility

A reproducibility study was conducted at three clinical sites. The study involved testing a set of GloCyte® Low and High Level Controls for both RBC and TNC parameters, performed by two operators. Testing was done twice daily using the same lot of controls, for twenty non-consecutive days. The results of the precision study met acceptance criteria.

Table 5-5. TNC and RBC Reproducibility

Cell Type	Level	N	Mean [cells/µL]	%CV					
				Within-Run	Between-Run	Between-Day	Between-Site	Between-Operator	Total
TNC	Low	480	10.6	10.1	0.0	1.6	3.9	2.4	11.2
	High	480	122.9	5.9	0.0	0.0	3.1	1.5	6.9
RBC	Low	480	11.3	9.2	0.0	1.9	3.8	2.7	10.5
	High	480	130.0	5.3	0.0	0.7	1.7	1.0	5.7

Linearity

Linearity was established according to CLSI EP6-A *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline* (2003). The analytical method is linear when the observed values have a mathematically verified straight-line relationship with true concentrations of the analyte, *i.e.* they are directly proportional to each other.

Contrived RBC and TNC CSF samples, created by dilution of human blood cells into blank CSF, were used for linearity studies on three GloCyte® Automated Cell Counter Systems. Pooled data from the three GloCyte® Automated Cell Counter Systems demonstrate that there is a linear relationship between the measured GloCyte and the expected values for TNC and RBC counts in the ranges shown in table 5-6 below.

Table 5-6. Linearity

Cell Type	Range [cells/µL]
TNC	0 – 7,438
RBC	0 – 615,644

Determination of limit of blank, limit of detection, limit of quantitation and reportable range

Limit of Blank (LoB),Limit of Detection (LoD) and Limit of Quantitation (LoQ) were performed according to CLSI EP17-A2 *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline-Second Edition* (2012). The LoQ, combined with the linear range was used to determine the reportable range. See table 5-7 below:

Table 5-7 Reportable Range

Cell Type	Reportable Range [cells/µL)
TNC	3 – 6,500
RBC	2 – 615,644

Interfering Substances

Interference testing was conducted to determine if endogenous and external substances might interfere with results. Table 5-8 lists potential interferents tested and the test results.

Table 5-8. Interference Results Summary

Potential Interferent	GloCyte Assay	Highest Concentration at which No Interference was observed
Conjugated Bilirubin	TNC	307.8 µmol/L (18.0 mg/dL)
	RBC	307.8 µmol/L (18.0 mg/dL)
Unconjugated Bilirubin	TNC	323.2 µmol/L (18.9 mg/dL)
	RBC	323.2 µmol/L (18.9 mg/dL)
Hemolytic Hemoglobin	TNC	1.1 g/dL[1]
	RBC	NONE[2]
Protein	TNC	59.0 g/L
	RBC	59.0 g/L
Lactate	TNC	13.2 mmol/L
	RBC	13.2 mmol/L
Haemophilus influenzae	TNC	10^8 CFU/mL
	RBC	10^8 CFU/mL
Streptococcus pneumoniae	TNC	10^8CFU/mL
	RBC	10^8CFU/mL
Neisseria lactamica	TNC	10^7 CFU/mL
	RBC	10^8 CFU/mL
Escherichia coli	TNC	10^8 CFU/mL
	RBC	10^8 CFU/mL

Candida albicans	TNC	10^8 CFU/mL
	RBC	10^8 CFU/mL
Platelets	TNC	14.7 x 10^3 Platelets/µL
	RBC	14.7 x 10^3 Platelets/µL
Nonspecific FcR Binding (Monocytes)	RBC	1.7 x 10^3 Monocytes/µL
RBC Fragments	RBC	Could Not be Quantified[3].
Nucleated RBCs	TNC	None[4]

1. *Cellular debris in the hemolytic hemoglobin may cause interference for the GloCyte TNC Assay.*
2. *RBC fragments and cellular debris in hemolytic hemoglobin may cause interference for the GloCyte RBC Assay.*
3. *Quantitation of RBC fragment interference levels was not possible due to the enormous variety of RBC fragment sizes and RBC ghost cells present. RBC fragments, tested as part of the hemolytic hemoglobin, may cause interference for the RBC Assay.*
4. *Nucleated RBCs are counted by the GloCyte TNC Assay and are considered an interferent. Note nucleated RBCs are also counted by the GloCyte RBC Assay.*

Quality Control Stability

GloCyte® Low and High Level Controls closed vial (shelf life) stability study data support a preliminary stability claim of **7** months when stored at 2-8°C. This stability claim is based on the time point (Month 7) tested prior to the last time point that yielded test results within the acceptance criteria for all three (3) GloCyte® Low and High Level Control lots.

5.8 Conclusions

Data in this Premarket Notification for the GloCyte® Automated Cell Counter System meet the manufacturer's specifications and support a finding of substantial equivalence to the predicate device.