510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k121456

B. Purpose for Submission:

New device

C. Measurand:

Measurement of the following in urine samples: glucose, protein, bilirubin, urobilinogen, pH, blood, ketones, nitrite, leukocytes, specific gravity, turbidity, color and microscopic determination of RBC, WBC, epithelial cells, casts, bacteria, and flags the presence of the following: pathologic cast, crystal, sperm, small round cell, yeast like cell and mucus.

D. Type of Test:

Qualitative and semi-quantitative reagent strip testing and quantitative urine flow cytometry

E. Applicant:

Arkray, INC.

F. Proprietary and Established Names:

ARKRAY AUTION HYBRID AU-4050 Fully Automated Integrated Urine Analyzer

Uriflet S 9HA Urine Test Strips

AUTION Control Solution

G. Regulatory Information:

Name	Regulation	Product Code	Classification
Urinary glucose (non-quantitative) test system.	21 CFR §862.1340	JIL	II
Occult blood test	21 CFR §864.6550	JIO	II

Urinary urobilinogen (non-quantitative) test system	21 CFR §862.1785	CDM	I
Urinary bilirubin and its conjugates (non-quantitative) test system	21 CFR §862.1115	JJB	I
Ketones (non-quantitative) test system	21 CFR §862.1435	JIN	I
Urinary protein or albumin (non-quantitative) test system	21 CFR §862.1645	JIR	I
Nitrite (non-quantitative) test system	21 CFR §862.1510	JMT	I
Leukocyte peroxidase test	21 CFR §864.7675	LJX	I
Urinary pH (non-quantitative) test system	21 CFR §862.1550	CEN	I
Specific Gravity	21 CFR §862.2800	JRE	I
Automated Urinalysis System	21 CFR §862.2900	KQO	I
Automated cell counter	21 CFR 864.5200	LKM	II
Quality control material (assayed and unassayed)	21 CFR 862.1660	JJW	I

4. Panel:

   Chemistry (75)

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   See indications for use statements below.

2. Indication(s) for use:

   AUTION HYBRID™ AU-4050 Fully Automated Integrated Urine Analyzer System

   The AUTION HYBRID™ AU-4050 Fully Automated Integrated Urine Analyzer System contains a test strip chemistry urine analyzer and a flow cytometry urine particle analyzer together in a single integrated device. The test strip chemistry module (CHM) is an automated urine analyzer intended for the in vitro measurement of the following parameters: glucose, protein, bilirubin, urobilinogen, pH, blood, ketones, nitrite, leukocytes, specific gravity, turbidity, and color. The chemistry module is intended for use with the Uriflet™ S 9HA multi-parameter urine chemistry test strips.

The flow cytometry module (FCM) is an automated urine particle analyzer intended to analyze the following parameters in urine samples: Red Blood Cells, White Blood Cells, Epithelial Cells, Casts, and Bacteria and flags the presence of the following: Pathologic Casts, Crystals, Sperm, Small Round Cells, Yeast Like Cells, and Mucus. The AUTION HYBRID AU-4050 is intended for in vitro diagnostic use in screening patient populations found in clinical laboratories.

Uriflet™ S 9HA Urine Test Strips

Uriflet™ S 9HA is a urinalysis test strip with reagent pads for the determination of Glucose, Protein, Bilirubin, Urobilinogen, pH, Blood, Ketones, Nitrite, and Leukocytes. Uriflet S 9HA is for use with the AUTION HYBRID AU-4050 only.

AUTION™ Control Solution

The AUTION Control Solution is intended for in vitro diagnostic use only for performing quality control procedures with the AUTION HYBRID AU-4050 flow cytometry module.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

AUTION HYBRID Fully Automated Integrated Urine Analyzer (model AU- 4050)

I. Device Description:

The AUTION HYBRID™ AU-4050 Fully Automated Integrated Urine Analyzer contains a test strip chemistry urine analyzer for the measurement of glucose, protein, bilirubin, urobilinogen, pH, blood, ketones, nitrite, leukocytes, specific gravity, turbidity, and color using Uriflet 9HA test strips and a flow cytometry module that analyzes the following parameters: RBC, WBC, epithelial cells, casts, bacteria, and flags the presence of the following: pathologic cast, crystal, sperm, small round cell, yeast like cell and mucus.

Urine Chemistry Module (CHM)

The CHM consists of an automated urine analyzer, sampler, and accessories. The sampler automatically feeds sample racks to the analyzer. The sampler contains a bar code reader for urine specimen identification. The analyzer uses reflectance spectroscopy for the measurement of the urine parameters: glucose, protein,

bilirubin, urobilinogen, pH, blood, ketones, nitrite, leukocytes, specific gravity, turbidity, and color. Specific gravity is determined using the refractive index method, and turbidity is evaluated by measuring the transmission and scattering of light passing through the urine specimen. The CHM is designed to be used with Uriflet™ S 9HA multi-parameter test strips. The Uriflet™ S 9HA multi-parameter test strips contain reactive pads on a non-reactive plastic backing. The reactive pads are impregnated with reagents formulated to detect a specific urine analyte or characteristic. Each strip also contains a correction pad for urine color determination. The Uriflet™ S 9HA test strip (for use with the AU-4050) is identical to the AUTION Sticks 9EB test strip (for use with the AX-4030) which was cleared under k093098 with regard to specific urine analyte, reagent composition and performance. The only difference is the barcode on the bottom of the test strip which provides for exclusive use of the Uriflet™ S 9HA test strip on the AU-4050.

Flow Cytometry Module (FCM)

The FCM consists of an automated urine particle analyzer for the analysis of microscopic formed elements in urine specimens. The FCM consists of three principal units: (1) Main Unit which aspirates, dilutes, mixes and analyzes urine samples; (2) Auto Sampler Unit supplies samples to the Main Unit automatically; (3) IPU (Information Processing Unit) which processes data from the Main Unit and provides the operator interface with the system. The IPU also contains a modular work area management (WAM) system for data processing and acts as an independent data manager system that interfaces with the AU-4050 and the LIS (Laboratory Information System). This data manager has the capability for patient demographics, test orders, and test results. The FCM is equipped with a Sampler that provides continuous automated sampling for up to 50 tubes. The FCM uses flow cytometry using a red semiconductor laser for analyzing organized elements of urine. Particle characterization and identification is based on detection of forward scatter, fluorescence and adaptive cluster analysis. Using its own reagents, the FCM automatically classifies organized elements of urine and carries out all processes automatically from aspiration of the sample to yielding the results.

Test Strip Analysis (CHM) Methodology and Sample Flow

Specialized test strips are analyzed with the dual-wavelength reflectance method (one wavelength for BLD). Test strips set in the feeder are fed, one at a time, onto the test strip tray inside the instrument, and they are moved by the guide arms to the sample drop application position. After drop application, the test strip is moved to the light measurement area.

The test strip reacts within around 60 seconds of drop application, changing color, and its reflectivity is measured at that time. In the light measurement area, a 5-wavelength LED emits 2-wavelength light that shines onto the reagent pad. The light reflected from the pad is picked up by one sensor. Light from the color compensation pad of the test strip is also measured to compensate for variable factors such as the amount of reflected light and the coloration of the sample.

Specific gravity is measured by the transmission refractometry method. The turbidity/color hue measurement unit built into the instrument uses transmitted light to

measure color hue. For color hue measurement, R (635 nm), G (525 nm) and B (470 nm) light are shone onto the sample in the cylindrical cell, and the hue and shade of the sample are analyzed from the amounts of each color transmitted through the sample. The colors are YELLOW, ORANGE, BROWN, RED, VIOLET, BLUE, and GREEN, and these 7 colors each have LIGHT, normal, and DARK graduations. Additional color determinations are COLORLESS and OTHER, for a total of 23 colors. The turbidity/color hue measurement unit built into the instrument uses transmitted light and scattered light to measure turbidity.

Flow Cytometry (FCM) Methodology and Sample Flow

This analyzer uses the flow cytometry method to analyze elements contained in urine. After the staining reaction, laser light is shone onto the sample flow within sheath flow in the flow cell, generating a forward scattered light signal, a laterally scattered light signal and a fluorescent light signal from each urine particle. These are converted into electrical signals, which are detected and used to identify each particle. The fully automated integrated urine analyzer AU-4050 uses Flow Cytometry (FCM) technology to obtain the parameters of forward scattered and forward fluorescent light of urine cells. After specific substances in the cells are given fluorescent staining and placed in suspension, they are then covered in sheath fluid and ejected through a nozzle in a single row. Here each urine cell is illuminated by a tightly focused laser beam. The individual cells fluoresce and scatter light to varying degrees. It is the analysis of these electrical signals which allows each urine cell to be discriminated by generating a one dimensional histogram, based on fluorescent intensity, and a two-dimensional scatter gram, based on fluorescent intensity and scattered light intensity.

Controls :

CHM QC analysis

The sponsor recommends the use of commercially available controls intended for monitoring urine dipstick results for the following parameters: glucose, protein, bilirubin, urobilinogen, pH, blood, ketones, nitrites, leukocytes, and specific gravity.

FCM QC analysis

- AUTION Control Solution (AUTION Control Solution (H)/AUTION Control Solution (L))

J. Substantial Equivalence Information:

1. Predicate device name(s):

AUTION MAX AX-4030 Urinalysis System

Sysmex UF-1000i Urine Particle Analyzer with Urinalysis WAM software

2. Predicate k number(s):

   k093098, k080887

3. Comparison with predicate:

Category	AX-4030 (k090398)	AU-4050 (candidate device)
Intended Use	Automated urine chemistry analyzer for the in vitro measurement of urine chemistry analytes.	Same
Sample Type	Human Urine	Same
Sample Volume	2mL	5mL
Measurement Wavelength	430,500,565,635,760 nm	Same
Measurement Method	Spectrophotometry Test Strip: Dual -wavelength reflectance measurement (single wavelength for BLD) S.G.: reflection refractometry. Color tone: Light-transmission measurement. Turbidity: Light-scattering measurement.	Same
Measurands	GLU, PRO, BIL, URO, PH, BLD, KET, NIT, LEU, S.G., turbidity and color-tone.	Same

Category	UF-1000i (k080887)	AU-4050 (candidate device)
Intended Use	Automated urine particle analyzer for the in vitro measurement of urine sediment	Same
Sample Type	Human Urine	Same
Sample Volume	3mL	5mL
Measurement Method	The device utilizes flow cytometry using a red semiconductor laser for analyzing organized elements of urine. Particle characterization and identification is based on detection of forward scatter, fluorescence, and adaptive cluster analysis.	Same
Measurands	RBC, WBC, Epithelial Cells, Cast, and Bacteria and flags the presence of the following: Pathogenic Cast, Crystal, Sperm, Small Round Cell, Yeast like cell and Mucus.	Same

Category	Sysmex UF-II Control (Predicate device-k070910)	AUTION Control Solution (Candidate device)
Intended Use	contains control particles for use in quality control mode of the analyzer	Same
Form	Liquid, ready to use	Same
Levels	2	Same
Storage	2°C-10°C until expiration date	Same
Open Vial	30 days at 2°C-10°C	Same
Matrix	Liquid matrix solution	Same
Analytes	Red Blood Cells, White Blood Cells, Epithelial Cells, Casts, and Bacteria	Same

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

- EN ISO 13485: Medical devices-Quality management systems-Requirements for regulatory purposes.

- NCCLS Guideline EP17: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

- CLSI EP5-A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline Second Edition (2002)

- CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach, Approved Guideline

- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." (May 11, 2005)

L. Test Principle:

The AU-4050 uses flow cytometry (FCM) to detect and characterize formed elements in the urine through the use of forward scattered and forward fluorescent light of urine cells. Chemical testing is performed with urine reagent test strips which use dual-wavelength reflectance photometry. Specific gravity is measured by transmission refractometry. Color hue of the urine is measured using the reflectivity of transmitted light. Turbidity is measured using transmitted and scattered light.

M. Performance Characteristics (if/when applicable):

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

   a. Precision/Reproducibility:

   The precision of the urine chemistry (CHM) and the flow cytometry (FCM) portions of the AU-4050 were assessed by a 15- day precision study performed at 3 clinical laboratory sites. The CHM precision samples consisted of a high-positive control; a mid-positive control, and a negative control. Precision samples for the FCM portion of the instrument included a high and low control. Each precision sample was run in duplicate during 2 runs per day; each run was separated by at least 4 hours. Repeatability and reproducibility were calculated across 3 clinical sites, 3 users (1 per site), 3 instruments (1 per site), and 3 lots of reagents (1 per site). The data were analyzed according to CLSI EP5-A2 guidelines, *Evaluation of Precision Performance of Quantitative Measurement Methods*. The tables below present the combined Precision results for the urine chemistry analytes (CHM) and urine sediments/flow cytometry (FCM).

Precision - Urine Chemistry Analytes (CHM)

Level 1 CHM Semi-Quantitative Precision Summary

Level 1 Control- Negative					
		Repeatability N=90		Reproducibility (within device) N=180	
Analyte	Control Limits (mg/dL)	Exact Agreement (%)	Agreement within ± 1 grading difference (%)	Exact Agreement (%)	Agreement within ± 1 grading difference (%)
Glucose	Neg (-)	100 (neg)	100	100 (neg)	100
Protein	Neg (-)	100 (neg)	100	100 (neg)	100
Bilirubin	Neg (-)	100 (neg)	100	100 (neg)	100
Urobilinogen	Normal	100 (normal)	100	100 (normal)	100
pH	5.0-6.0	100	100	100	100
Blood	Neg (-)	100 (neg)	100	100 (neg)	100
Ketones	Neg (-)	100 (neg)	100	100 (neg)	100
Nitrite	Neg (-)	100 (neg)	100	100 (neg)	100
Leukocytes	Neg (-)	100 (neg)	100	100 (neg)	100
Color	N/A	100 (colorless)	100	100 (colorless)	100
Tubidity	N/A	100 (neg)	100	100 (neg)	100
Specific Gravitiy	1.000-1.015	93 (1.004)	100 (± 0.005 SG units)	57 (1.004)	100 (± 0.005 SG units)

Level 2 CHM Semi-Quantitative Precision Summary

Level 2 Control- High Positive					
		Repeatability N=90		Reproducibility (within device) N=180	
Analyte	Control Limits (mg/dL)	Exact Agreement (%)	Agreement within ± 1 grading difference (%)	Exact Agreement (%)	Agreement within ± 1 grading difference (%)
Glucose	30(+)-≥1000(4+)	100 (3+)	100	100 (3+)	100
Protein	30(+)-≥600(4+)	100 (3+)	100	100 (3+)	100
Bilirubin	0.5(+)->10(4+)	74 (3+)	100	83 (3+)	100
Urobilinogen	(2+)- (4+)	91 (4+)	100	92 (4+)	100
pH	6.5-9.0	100 (8.5)	100	100 (8.5)	100
Blood	0.06(+)->1.0 (3+)	100 (3+)	100	100 (3+)	100
Ketones	10(+)->150 (4+)	94 (4+)	100	96 (4+)	100
Nitrite	1(+)-2(+)	100 (2+)	100	100 (2+)	100
Leukocytes	25-500 Leuk/µL	100 (500)	100	100 (500)	100
Color	N/A	100 (dark orange)	100	100 (dark orange)	100
Tubidity	N/A	100 (neg)	100	100 (neg)	100
Specific Gravity	1.010-1.030	55 (1.025)	100 (± 0.005 SG units)	40 (1.025)	100 (± 0.005 SG units)

Level 3 CHM Semi-Quantitative Precision Summary

Level 3 Control- Mid Positive			
		Repeatability N=90	Reproducibility (within device) N=180

Analyte		Exact Agreement (%)	Agreement within ± 1 grading difference (%)	Exact Agreement (%)	Agreement within ± 1 grading difference (%)
Glucose		100 (1+)	100	100 (1+)	100
Protein		79 (2+)	100	77 (2+)	100
Bilirubin		100 (2+)	100	100 (2+)	100
Urobilinogen		86 (2+)	100	55 (2+)	100
pH		86 (7.5)	100	76 (7.5)	100
Blood		99 (3+)	100	99 (3+)	100
Ketones		100 (2+)	100	100 (2+)	100
Nitrite		100 (2+)	100	100 (2+)	100
Leukocytes		100 (250)	100	94 (250)	100
Color		100 (yellow)	100	100 (yellow)	100
Tubidity		100 (neg)	100	100 (neg)	100
Specific Gravity		86 (1.008)	100 (± 0.005 SG units)	47 (1.008)	100 (± 0.005 SG units)

Precision - Urine Sediment/Flow Cytometry (FCM)
Between Run Precision- Control Level 1

Cell Type	N (runs)	N data points	Site	Mean cells/µL	SD	%CV
RBC	30	60	1	41.04	1.75	4.26
RBC	30	60	2	41.65	1.50	3.61
RBC	30	60	3	43.65	0.00	0.00
WBC	30	60	1	40.18	1.26	3.14
WBC	30	60	2	41.87	1.20	2.88
WBC	30	60	3	43.52	0.54	1.23
EC	30	60	1	10.23	0.44	4.32
EC	30	60	2	10.25	0.60	5.83
EC	30	60	3	9.79	0.55	5.62
Cast	30	60	1	6.09	0.29	4.82
Cast	30	60	2	4.03	0.00	0.00
Cast	30	60	3	5.43	0.57	10.49
Bacteria	30	60	1	192.93	0.00	0.00
Bacteria	30	60	2	201.56	0.00	0.00
Bacteria	30	60	3	198.29	5.62	2.83

Between Run Precision- Control Level 2

Cell Type	N (runs)	N data points	Site	Mean cells/µL	SD	%CV
RBC	30	60	1	189.24	1.46	0.77
RBC	30	60	2	196.07	0.00	0.00
RBC	30	60	3	194.48	0.00	0.00
WBC	30	60	1	745.01	0.00	0.00
WBC	30	60	2	763.36	8.77	1.15
WBC	30	60	3	822.25	0.00	0.00
EC	30	60	1	68.35	0.92	1.35
EC	30	60	2	74.89	0.00	0.00
EC	30	60	3	74.87	2.28	3.05
Cast	30	60	1	17.07	0.32	1.89
Cast	30	60	2	15.65	0.99	6.35
Cast	30	60	3	18.83	0.38	2.04
Bacteria	30	60	1	712.67	18.90	2.65
Bacteria	30	60	2	730.70	20.57	2.81
Bacteria	30	60	3	799.00	0.00	0.00

Between Day Precision- Control Level 1

Cell Type	N (days)	N data points	Site	Mean cells/µL	SD	%CV
RBC	15	60	1	41.04	0.00	0.00
RBC	15	60	2	41.65	0.00	0.00
RBC	15	60	3	43.65	1.12	2.57
WBC	15	60	1	40.18	0.00	0.00
WBC	15	60	2	41.87	0.00	0.00
WBC	15	60	3	43.52	0.00	0.00
EC	15	60	1	10.23	0.00	0.00
EC	15	60	2	10.25	0.00	0.00
EC	15	60	3	9.79	0.17	1.71
Cast	15	60	1	6.09	0.00	0.00
Cast	15	60	2	4.03	0.33	8.20
Cast	15	60	3	5.43	0.00	0.00
Bacteria	15	60	1	192.93	0.00	0.00
Bacteria	15	60	2	201.56	7.27	3.61
Bacteria	15	60	3	198.29	0.00	0.00

Between Day Precision- Control Level 2

Cell Type	N (days)	N data points	Site	Mean cells/µL	SD	%CV
RBC	15	60	1	189.24	2.27	1.20
RBC	15	60	2	196.07	1.14	0.58
RBC	15	60	3	194.48	0.77	0.40
WBC	15	60	1	745.01	1.65	0.22
WBC	15	60	2	763.36	0.00	0.00
WBC	15	60	3	822.25	2.73	0.33
EC	15	60	1	68.35	1.07	1.56
EC	15	60	2	74.89	2.02	2.70
EC	15	60	3	74.87	0.00	0.00
Cast	15	60	1	17.07	0.20	1.15
Cast	15	60	2	15.65	0.00	0.00
Cast	15	60	3	18.83	0.00	0.00
Bacteria	15	60	1	712.67	0.00	0.00
Bacteria	15	60	2	730.70	0.00	0.00
Bacteria	15	60	3	799.00	0.00	0.00

Total Imprecision- Control Level 1

Cell Type	N (days)	N (data points)	N data points	Site	Mean cells/µL	SD	%CV
RBC	15	30	60	1	41.04	2.70	5.85
RBC	15	30	60	2	41.65	2.30	5.53
RBC	15	30	60	3	43.65	2.53	5.79
WBC	15	30	60	1	40.18	2.62	6.52
WBC	15	30	60	2	41.87	2.29	5.46
WBC	15	30	60	3	43.52	2.14	4.92
EC	15	30	60	1	10.23	1.33	12.99
EC	15	30	60	2	10.25	1.45	14.10
EC	15	30	60	3	9.79	1.24	12.71
Cast	15	30	60	1	6.09	0.89	14.64
Cast	15	30	60	2	4.03	0.68	16.91
Cast	15	30	60	3	5.43	0.89	16.44
Bacteria	15	30	60	1	192.93	15.60	8.09
Bacteria	15	30	60	2	201.56	16.56	8.21
Bacteria	15	30	60	3	198.29	17.83	8.99

Total Imprecision- Control Level 2

Cell Type	N (days)	N (data points)	N data points	Site	Mean cells/µL	SD	%CV
RBC	15	30	60	1	189.24	6.57	3.47
RBC	15	30	60	2	196.07	5.43	2.77
RBC	15	30	60	3	194.48	5.61	2.88
WBC	15	30	60	1	745.01	17.90	2.00
WBC	15	30	60	2	763.36	12.83	1.68
WBC	15	30	60	3	822.25	12.47	1.52
EC	15	30	60	1	68.35	4.03	5.90
EC	15	30	60	2	74.89	4.35	5.81
EC	15	30	60	3	74.87	4.10	5.48
Cast	15	30	60	1	17.07	1.32	7.73
Cast	15	30	60	2	15.65	1.52	9.72
Cast	15	30	60	3	18.83	1.41	7.51
Bacteria	15	30	60	1	712.67	32.45	4.55
Bacteria	15	30	60	2	730.70	38.21	5.23
Bacteria	15	30	60	3	799.00	37.53	4.70

b. *Linearity/assay reportable range*:

Urine Chemistry Module (CHM)

The linear range of the AU-4050 chemistry module was evaluated by measuring negative urine and negative urine spiked with known concentrations covering the entire measuring range of each analyte present on the Uriflet S 9HA urine strip. Sample measurement was performed on 3 lots of reagent strips in replicates of 7 for a total of 21 measurements per sample tested. The spiked samples were also measured on the predicate device to confirm the results. A pH meter was used to confirm the pH results. Specific gravity samples were prepared by diluting sucrose in deionized water at 0.010 intervals from 1.000 to 1.060. Specific gravity measurements were tested in replicates of 20 on each of 3 AU-4050 analyzers. The specific gravity values were confirmed by a clinical, handheld refractometer. Color tone samples were designed and prepared in accordance with the International Commission of Illumination (CIE) XYZ color system. Color tone measurements were tested in singleton, performed over 3 separate runs on one AU-4050 analyzer for a total of 3 measurements per color tone sample. Turbidity samples were prepared at the negative, 1+, and 2+ ranks using a latex turbidity standard solution diluted with deionized water. Turbidity measurements were performed in replicates of 20 on one AU-4050 analyzer and one predicate analyzer. The linear range of the AU 4050 is summarized below:

Chemistry	Range of Results
GLU	Semi-quant: <30 to >1000 mg/dL Qual: neg to 4+
PRO	Semi-quant: <10 to >600 mg/dL Qual: neg to 4+
BIL	Semi-quant: <0.5 to >10mg/dL Qual: neg to 4+
URO	Semi-quant: <2 to >12 mg/dL Qual: normal to 4+
BLD	Semi-quant: <0.03 to >1.0 mg/dL Qual: neg to 3+
KET	Semi-quant: <10 to >150 mg/dL Qual: neg to 4+
NIT	Qual: neg to 2+
LEU	Semi-quant: <25 to 500 mg/dL
PH	5.0-9.0
SG	1.000-1.050
TURBIDITY	Neg to 2+
COLOR	Colorless, Yellow, Orange, Brown, Red, Violet, Blue, Green, Other. Light and Dark shades are indicated for each of the reported colors.

The linearity study has demonstrated that the device is able to detect the claimed measuring range stated in the above chart for each of the CHM analytes.

Flow Cytometry Module (FCM)

Linearity studies were performed to assess the performance of the Flow Cytometry Module (FCM) over a wide range of cell type concentrations. High and Low Pools were created by concentrating or diluting samples which spanned the full measuring range of RBC, WBC, Epithelial Cell, Cast and Bacteria parameters in accordance with CLSI EP6A approved guidelines. FCM dilution tubes were prepared by mixing low and high urine pools for each parameter to achieve a minimum of five dilution points that were evenly distributed across the measuring range for each parameter. Each tube was tested 2 to 5 times using manual mode for FCM analysis. Slope, intercept and Mean Replicate % differences were calculated for each FCM parameter. FCM Mean replicate percent difference values recovered within the maximum allowable % difference as shown below:

FCM Linearity Summary Results

Cell Type	AU-4050 Measuring Range (Cells/µL)	R^2	Slope	y-intercept	Sample results range (Cells/ µL)
RBC	1-5000	1.00	0.99	-1.07	1.0-5367
WBC	1-5000	1.00	1.00	-1.80	1.2-5154
EC	1-200	1.00	1.01	-0.76	1.1-283
BACT	5-10000	1.00	1.00	12.78	2.1-11520

The method for FCM has been demonstrated to be linear from the lower limit to upper limit of the analytical measuring range and within measured allowable maximum percent difference for each parameter.

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

Traceability- Control Value Assignment

The control value assignment was performed using 3 analyzers and 3 bottles of each of the two levels of control solutions (L and H). To determine the target value of each control, for each cell type measured, a mean result was calculated from the 15 replicate results from each of the 3 analyzers. A grand mean of replicates from all three analyzers (n=45) was then calculated. The %CV of each analyzer's 15 replicates was calculated and checked for acceptability against the predetermined acceptance criteria for each cell type.

Stability

AUTION Control Solution

Stability studies were performed to assess the open and closed bottle stability for the AU-4050 FCM controls, AUCTION Control Solutions L and H. The procedure used to evaluate open bottle stability was to assay three lots of AUCTION Control Solutions L and H stored at 12º C. Testing occurred at pre-determined time-points throughout the study. The procedure used to evaluate closed bottle stability was to assay a single lot of AUTION Control Solutions L and H stored at 12º C. Testing occurred at pre-determined time-points throughout the study. The stability testing results demonstrated opened urine controls used on the AUTION HYBRID™ AU-4050 are stable for 217 days.

Unopened controls used on the AUTION HYBRID™ AU-4050 are stable for 1 year. The labeling states that the open vial stability is 30 days at 2-10º C. Storage stability (closed vial) is until expiration date at 2-10º C.

Chemistry Module (CHM) Stability

Stability studies were performed to assess the open and closed bottle stability for the urine chemistry strips used on the AUTION HYBRID™ AU-4050. The procedure used to evaluate open bottle stability was to assay bi-level control materials using a single lot of ARKRAY urinalysis strips stored at room temperature in replicates of three and AUTION Check Strips in replicates of two at pre-determined time-points throughout the study. The procedure used to evaluate closed bottle stability was to assay spiked urine samples using three lots of ARKRAY urinalysis strips stored at room temperature in replicates of five at pre-determined time-points throughout the study. All testing was conducted in percent reflectance. The stability testing results revealed that opened ARKRAY urinalysis strips are stable for 31 days. Unopened ARKRAY urinalysis strips are stable for 2 years.

d. Detection limit:

AU-4050 CHM Strip Sensitivity Evaluation

Study 1: Sensitivity Study 1 was done to determine the concentration at which each analyte on the Uriflet S 9HA strip changed from negative to the lowest positive color block. Samples were prepared by spiking the specified analyte into negative urine to obtain the target concentrations to determine the sensitivity between the negative color block and the next lowest color block for each analyte on the Uriflet S9HA urinalysis strip. Each analyte tested a target concentration of the analyte, plus a concentration on each side of the target in order to determine the sensitivity concentration. Each pool was spiked with the specified analyte concentration, and then analyzed in replicates of 5 on each of 3 strip lots, for a total of 30 replicates. The analytical sensitivity for each color block for each analyte is defined as the lowest concentration at which >50% of the test results are positive between the negative color block and the first positive color block. The results are summarized in the following table:

Negative to Positive Sensitivities n=30		
Analyte	Sensitivity	% Sensitivity
GLU	30 mg/dL	100
PRO	10 mg/dL	53.3
BIL	0.5 mg/dL	93.3
URO	2 mg/dL	100

BLD	0.023 mg/dL	60.0
KET	3 mg/dL	96.7
NIT	0.075 mg/dL	50.0
LEU	25 Leu/uL	100

Study 2: Sensitivity Study 2 was done to demonstrate the point of change between the semi-quantitative values for each color block. A negative urine pool was spiked with the specified analyte concentration, and then analyzed in replicates of 7 on each of the 3 strip lots, for a total number of 21 replicates. The sensitivity for each semi-quantitative rank measured for each analyte is defined as stated in the table below.

Target Glucose Concentration per color block (mg/dL)	% Sensitivity
Negative	100
50 (+/-)	67
100 (1+) – 150 (2+)	100
200 (2+) – 300 (3+)	100
500 (3+)	100
1000 (4+) – Over (4+)	100
Target Protein Concentration per color block (mg/dL)	% Sensitivity
Negative	100
20 (+/-)	100
50 (1+)	100
200 (2+)	100
600 (3+)	67
Over (4+)	71
Target Bilirubin Concentration per color block (mg/dL)	% Sensitivity
Negative	100
0.5 (1+) -1.0 (1+)	100
2 (2+)	100
6 (3+) – 8 (3+)	95
Over (4+)	100
Target Urobilinogen Concentration per color block (mg/dL)	% Sensitivity
Normal	100
2 (1+) - 3 (1+)	100
4 (2+) - 6 (2+)	100
12 (3+) – Over (4+)	100
Over (4+)	100
Target Blood Concentration per color block (mg/dL)	% Sensitivity

Negative	100
0.03 (+/-)	100
0.06 (1+) – 0.1 (1+)	100
0.2 (2+) -0.5 (2+)	90
0.5 (2+) – 1 (3+)	95
1.0 (3+) – Over (3+)	100
Target Ketone Concentration per color block (mg/dL)	% Sensitivity
Negative	100
10 (1+) – 20 (1+)	100
20 (1+) – 40 (2+)	100
60 (2+)	100
150 (4+)	100
Target Nitrite Concentration per color block (mg/dL)	% Sensitivity
Negative	100
0.08 (1+)	90
0.16 (1+)	100
0.8 (2+)	100
Target Leukocyte Concentration per color block (mg/dL)	% Sensitivity
Negative	100
75	100
250	100
500	100

Flow Cytometry Module (FCM) Detection Limit

Limit of Blank (LoB) Flow Cytometry Module (FCM)

The LoB was determined by measuring 60 replicates of sheath solution (blank) in the FCM manual analysis mode. The mean, SD, and LoB were calculated for all measured reportable parameters. The estimated LoB equals the 95th percentile of the distribution of blank values.

LoB= Mean + (1.645 x SD)

Limit of Detection (LoD) Flow Cytometry Module (FCM)

The LoD for the AU-4050 was performed following CLSI EP17A. Three low concentration samples for each of the cell types measured by AU-4050 were prepared by diluting with normal saline to obtain the target concentrations. Each sample was measured 20 times on the AU-4050. Each sample was also measured 10 times on the predicate device to obtain a reference value. The

mean, SD, and LoD were calculated for each of the five cell types using the following equation: LoD=LoB + (1.645 x SD)

Limit of Quantitation (LoQ) Flow Cytometry Module (FCM)

The LoQ study was performed in accordance with CLSI EP17A. The study was performed by preparing three low concentration samples for each cell type measured by the AU-4050. Each sample was measured 15 times on the AU-4050 for a total of 45 replicates. A mean value was calculated for each sample. Each sample was also measured 5 times on the predicate device to obtain a reference value. The mean bias was calculated by averaging the individual sample bias. The LoQ was determined to be equal to the LoD for each of the 5 cell types measured by the FCM module of the AU-4050.

FCM LoB, LoD and LoQ Summary

Cell Type	LoB	LoD	LoQ
RBC	0.20	0.75	0.75
WBC	0.20	0.71	0.71
EC	0.40	0.77	0.77
Cast	0.10	0.53	0.53
Bacteria	0.30	1.25	1.25

The sponsor's claimed measuring range:

Cell Type	AU-4050 Measuring Range (Cells/µL)
RBC	1-5000
WBC	1-5000
EC	1-200
BACT	5-10000

e. Analytical specificity:

Chemistry Module (CHM) Interfering Substances

Interfering substance studies were performed to assess the interfering effect of various substances on the urine chemistry test strips used on the AUTION HYBRID™ AU-4050. Urine sample pools were prepared at 2 concentrations for each urine chemistry analyte; negative and positive. The negative sample pools had no analyte present while the positive sample pools were prepared by spiking each analyte into negative urine at the concentrations listed below:

Concentration of Samples Tested

Analyte	Concentrations to be Tested		
	Negative	Positive	Unit
GLU	0	200	mg/dL
PRO	0	300	mg/dL
BIL	0	4	mg/dL
URO	0	6	mg/dL
pH	6.5	8	-
BLD	0	0.3	mg/dL
KET	0	60	mg/dL
NIT	0	0.5	mg/dL
LEU	0	250	cell/µL

The sample pools were spiked with potential interfering substances at the concentrations listed below:

Concentrations at Which Interfering Substances Were Tested

Interfering Substance	Concentration to be Tested		
	Low	High	Unit
Acetoacetate	60	150	mg/dL
Albumin	300	1000	mg/dL
Ammonium chloride	100	400	mg/dL
Ascorbic acid	50	200	mg/dL
Calcium chloride	40	160	mg/dL
Citric acid	65	130	mg/dL
Creatinine	300	600	mg/dL
Fructose	100	300	mg/dL
Galactose	100	300	mg/dL
Glucose	200	500 and 2000	mg/dL
Glycine	450	900	mg/dL
Hemoglobin	0.3	50	mg/dL
Potassium chloride	500	1000	mg/dL
Lactose	100	300	mg/dL
MESNA	50	200	mg/dL
Sodium chloride	1000	2000	mg/dL
Oxalic acid	20	70	mg/dL
pH (Citric acid) pH (Sodium phosphate)	3, 4, 8, 9		-
Phenolphthalein	2	10	mg/dL
Riboflavin	2	5	mg/dL
Sodium acetate	300	1200	mg/dL
Sodium bicarbonate	500	1000	mg/dL
Sodium nitrate	0.5	10	mg/dL
Sodium nitrite	0.5	2	mg/dL

Sodium phosphate	500	1000	mg/dL
Specific gravity (Sucrose)	1.010	1.030	-
Tetracycline	20	100	mg/dL
Urea	1000	3000	mg/dL

Each sample was measured on the AU-4050 in replicates of 5 and a mean result was calculated. The mean result from samples with no interfering substance was compared against the mean result of the sample spiked with the interfering substance at the stated concentrations. Interference was determined based on the acceptance criteria stated below. Negative Samples: If sample results are 1+ (75 for Leukocytes) or greater, interference is considered positive. pH results will be considered positive for interference when the results differ by greater than +/- 2 ranks from the pH sample containing no interfering substance.
Positive Samples: If sample results differ by greater than +/- 1 color block between samples containing the interfering substance and samples without it, interference will be considered positive.

Based on the results of this testing the labeling includes the following interferences statement as shown below:

Summary of Results Causing Increased/Decreased Results

Item	Decreased Results	Increase Results
GLU	Ascorbic Acid (50mg/dL)	MESNA (200mg/dL)
PRO	-	Sodium acetate (1200mg/dL), Sodium
BIL	Ascorbic acid (200mg/dL), MESNA (200mg/dL), Sodium bicarbonate(1000mg/dL), Sodium nitrite (2mg/dL)	-
URO	Sodium nitrite (2mg/dL)	-
BLD	Ascorbic acid (200mg/dL), Sodium bicarbonate (500mg/dL), Sodium phosphate (500mg/dL)	-
NIT	Ascorbic acid (200mg/dL), pH 3	-
LEU	Albumin (1000mg/dL), Glucose (500mg/dL), Hemoglobin (50mg/dL),MESNA (200mg/dL), pH 3, Phenolphthalein (2mg/dL), Tetracycline (20mg/dL)	-

Summary of Results Causing Interference

Item	Substance Causing False Negative Results	Substance Causing False Positive Results
GLU	Ascorbic acid (200mg/dL)	pH 3
PRO	-	Hemoglobin (50mg/dL), pH 8
URO	-	Bilirubin (4mg/dL)
BLD	MESNA (200mg/dL)	-
KET	-	MESNA (50mg/dL)

Flow Cytometry Module (FCM) Interfering Substances:

The sponsor includes the following statement in the labeling:
Based on the technological characteristics of the flow cytometry method, when measuring the following sample types on the AUTION HYBRID™ AU-4050, there is a possibility that correct results will not be obtained.

(1) High viscosity sample containing pus	Samples with high viscosity may form blockages in the sample filter preventing sample aspiration which in turn may prevent output of correct measurement results.
(2) Samples with gross hematuria	Flow cytometry analysis is used to optically detect individual particles such as cells based on signal waveform characteristics . With gross hematuria, there are a great number of red blood cells and there is a possibility that multiple red blood cells or other substances in the urine may be detected at the same time (simultaneous flow-through). If simultaneous flow through occurs, the characteristics of the signal waveform may not match with the Operating Manual (10.2.4 FCM Measurement Particle Analysis Principle) and correct measurement may not be obtained.
(3) Samples with high numbers of indeterminate particles such as mucus strings.	Flow cytometry analysis is used to optically detect individual particles such as cells based on signal waveform characteristics. With indeterminate particles, there is a possibility that multiple indeterminate particles or other substances in the urine may be detected at the same time (simultaneous flow- through). If simultaneous flow through occurs, the characteristics of the signal waveform may not match with the Operating Manual (10.2.4 FCM Measurement Particle Analysis Principle) and correct measurement may not be obtained.

(4) Samples that contain preservative	Even if particulate preservative appears to have dissolved, it may not have completely dissolved on a micrometer scale. As specified in the Operating Manual (10.2.4 FCM Measurement Particle Analysis Principle), analysis is performed according to the size of the particle and the degree of luminescence that emanates from them as well as other factors. Where preservative particles are equivalent in size as red blood cells etc, misdetection may occur resulting in a failure to obtain correct measurement results.
(5) Stored urine	Cells in the presence of hypersthenuria or hyposthenuria may become deformed due to the osmotic potential. Red or white blood cells may lyse and the nucleus of epithelial cells may become exposed. It is known that red blood cells lyse easily in low osmotic potential environments and in the presence of alkaline urine. At room temperature, bacteria may proliferate which may increase the alkalinity of the urine. This may result in the detection or non-detection of crystals in urine or encourage the lysing of red blood cells. As such, where stored urine is used, correct measurement results may not be obtained.

Carryover

Chemistry Module (CHM) Carryover

Carryover studies were performed to assess the amount of sample carried over by the AUTION HYBRID™ AU-4050 CHM from one specimen reaction into subsequent specimen reactions. The procedure used to evaluate carryover was to create high and low concentrations of each analyte by spiking analytes into a negative urine pool. Testing consisted of two runs in the following order: Low 1, Low 2, High 1, High 2, Low 3, Low 4. Carryover (%) was calculated using the following formula:
Carryover (%) = [(Low 3) - (Low 4)] / [(High 1) - (Low 4)] × 100
Results of the carryover testing for the urine chemistry analytes demonstrated zero carryover by the AUTION HYBRID™ AU-4050

Flow Cytometry Module (FCM) Carryover

Carryover studies were performed to assess the amount of sample over by the AUTION HYBRID™ AU-4050 FCM from one specimen reaction into subsequent specimen reactions. The procedure used to evaluate carryover was to create high and low concentrations of each analyte by spiking analytes into a negative urine pool. Testing consisted of one run in the following order: High 1, High 2, High 3, Low 1, Low 2, Low 3. FCM Carryover (%) was calculated using the following formula:
Carryover % = [(Low 1 – Low 3)] / [(High 3 – Low 3)] x 100

Manufacturer acceptance criteria for FCM carryover are:
• Bacteria channel: ≤0.05% or L1 ≤5/μL
• Sediment Channel (WBC, RBC, EC, CAST): ≤0.1% or L1 ≤5/μL

Results of the FCM carryover testing meet the manufacturer's acceptance criteria specifications.

f. Assay cut-off:

See the Detection Limit section 1.d. above.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were conducted to evaluate the performance of the AUTION HYBRID™ AU-4050 for the measurement of urine chemistry analytes (CHM) and urine sediment/flow cytometry (FCM) in human urine specimens. Results from the AUTION HYBRID™ AU-4050 were compared to those from two commercially available systems, the ARKRAY AUTION MAX™ AX-4030 Automated Urine Chemistry Analyzer and the Sysmex UF-1000i™ Automated Urine Particle Analyzer.
Testing was performed at three external clinical sites in the United States. Each clinical site tested approximately 640 urine samples. The urine samples for analysis in these method comparison studies were provided by the external clinical sites. Samples were collected within 2 hours of testing if maintained at room temperature or were stored for up to 8 hours prior to testing if maintained at 2-8°C. In order to obtain the desired range of abnormal values, a pool of negative urine samples were spiked to elevated levels with the analytes to be evaluated. These spiked samples represent less than 15% of the total samples tested and are identified in the line data. A total of 1931urine samples (native urine samples + spiked samples) were tested in parallel using the AUTION HYBRID™ AU-4050 System, the AX-4030 and the UF-1000i. For each urine chemistry analyte and urine sediment type, the values obtained for the individual urine samples were referred to the respective cut-off values for each system to discriminate between the negative (normal) and positive (abnormal) findings, if applicable. Percent positive agreement (relative sensitivity) and percent negative agreement (relative specificity) were determined. The data are also presented in concordance charts showing percent exact agreement and percent agreement within 1 color block.
The tables below present the combined Method Comparison results for the urine chemistry analytes (CHM) and urine sediments/flow cytometry (FCM).

Urine Chemistry Method Comparison

Glucose

Positive % agreement	99.5%
Negative % agreement	99.7%
Overall % agreement	99.7%

Glucose		AX-4030		
		+	-	Total
AU-4050	+	401	4	405
	-	2	1524	1526
Total		403	1528	1931

GLUCOSE (mg/dL) n=1931							
REFERENCE: AX-4030							
		Neg	(±) 30-50	(+) 70-100	(++) 150-200	(+++) 300- 500	(++++) ≥1000
AU-4050	Neg	1524	2	0	0	0	0
	(±) 30-50	3	62	5	0	0	0
	(+) 70-100	0	1	49	1	0	0
	150-200 (++)	1	0	4	55	4	0
	300-500 (+++)	0	0	0	1	95	4
	(++++) ≥1000	0	0	0	0	3	117
TOTAL		1528	65	58	57	102	121
Exact Accuracy		100%	95%	84%	96%	93%	97%
Accuracy +/-1CB		100%	100%	100%	100%	100%	100%

Protein

Positive % agreement	98.1%
Negative % agreement	91.0%
Overall % agreement	95.7%

Protein		AX-4030		
		+	-	Total
AU-4050	+	1250	59	1309
	-	24	598	622
Total		1274	657	1931

PROTEIN (mg/dL) n=1931							
REFERENCE: AX-4030							
		Neg	±(10-20)	+(30-70)	++ (100-200)	+++ (300-600)	++++ (Over)
AU-4050	Negative	598	24	0	0	0	0
	±(10-20)	59	522	30	0	0	0
	+(30-70)	0	27	357	5	0	0
	++(100-200)	0	0	55	89	2	0
	+++(300-600)	0	0	1	39	73	0
	++++(Over)	0	0	0	0	12	38

TOTAL	657	573	443	133	87	38
Exact Accuracy	91%	91%	81%	67%	84%	100%
Accuracy +/-1CB	100%	100%	100%	100%	100%	100%

Urobilinogen

Positive % agreement 100.0%
Negative % agreement 95.8%
Overall % agreement 96.5 %

Urobilinogen		**AX-4030**		
		+	**-**	**Total**
AU-4050	**+**	**334**	**67**	**401**
	-	**0**	**1530**	**1530**
Total		**334**	**1597**	**1931**

UROBILINOGEN (mg/dL) n=1931						
REFERENCE: AX-4030						
AU-4050		**0.2-1mg/dL**	**2 - 3 (+)**	**4 - 6 (++)**	**8 - 12(+++)**	**OVER(++++)**
	Normal(0.2-1)	1530	0	0	0	0
	2 - 3 mg/dL (+)	67	176	0	0	0
	4 - 6 mg/dL (++)	0	15	59	0	0
	8 - 12 mg/dL(+++)	0	0	5	50	0
	OVER(++++)	0	0	0	7	22
TOTAL		1597	191	64	57	22
Exact Accuracy		**96%**	**83%**	**89%**	**88%**	**100%**
Accuracy +/-1CB		100%	100%	100%	100%	100%

Bilirubin

Positive % agreement 100.0%
Negative % agreement 99.1%
Overall % agreement 99.2%

Bilirubin		**AX-4030**		
		+	**-**	**Total**
AU-4050	**+**	**134**	**16**	**150**
	-	**0**	**1781**	**1781**
Total		**134**	**1797**	**1931**

BILIRUBIN (mg/dL) n=1931						
REFERENCE: AX-4030						
AU-4050		**Negative**	**0.5 - 1(+)**	**2 - 4 (++)**	**6 - 10(+++)**	**OVER(++++)**
	Negative	1781	0	0	0	0
	0.5 - 1(+)	16	33	0	0	0
	2 - 4 (++)	0	11	52	0	0
	6 - 10(+++)	0	0	13	20	0
	OVER(++++)	0	0	0	0	5
TOTAL		1797	44	65	20	5

Exact Accuracy	99%	75%	80%	100%	100%
Accuracy +/-1CB	100%	100%	100%	100%	100%

pH

Exact Accuracy 82% (95%CI = 79.5% to 85.1%) Accuracy +/-1CB 99%

pH										
REFERENCE: AX-4030										
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0
AU-4050	5.0	58	1							
	5.5	26	156							
	6.0	3	17	156						
	6.5			20	79	1				
	7.0				12	76				
	7.5					12	25			
	8.0						4	14		
	8.5							7	28	
	9.0							1	25	13
TOTAL		87	174	176	91	89	29	22	53	13
Exact Accuracy		67%	90%	89%	87%	85%	86%	64%	53%	100%
Accuracy +/-1CB		97%	100%	100%	100%	100%	100%	95%	100%	100%

Ketone

Positive % agreement	97.4%
Negative % agreement	97.4%
Overall % agreement	97.3%

Ketone		AX-4030		
		+	-	Total
AU-4050	+	426	39	465
	-	12	1454	1466
Total		438	1493	1931

KETONE (mg/dL) n=1931							
REFERENCE: AX-4030							
		Negative	± Trace(5)	(+) 10 -20	(++) 40 - 60	(+++) 80 - 100	(++++) ≥150
AU-4050	Negative	1454	12	0	0	0	0
	± Trace(5)	39	124	12	0	0	0
	(+) 10 - 20	0	5	107	5	0	0
	(++) 40 - 60	0	0	3	81	5	0
	(+++) 80 - 100	0	0	0	0	40	3
	(++++) ≥150	0	0	0	0	0	41

TOTAL	1493	141	122	86	45	44
Exact Accuracy	97%	88%	88%	94%	89%	93%
Accuracy +/-1CB	100%	100%	100%	100%	100%	100%

Blood

Positive % agreement 99.3%
Negative % agreement 97.5%
Overall % agreement 98.2%

Blood		**AX-4030**		
		+	**-**	**Total**
AU-4050	**+**	**709**	**30**	**739**
	-	**5**	**1187**	**1192**
Total		**714**	**1217**	**1931**

BLOOD (mg/dL) n=1931						
REFERENCE: AX-4030						
		Negative	**± (0.03)**	**1+(0.06-0.1)**	**2+(0.2-0.5)**	**3+ (≥1.0)**
AU-4050	**Negative**	1187	5	0	0	0
	± (0.03)	30	173	0	0	0
	1+(0.06-0.1)	0	50	172	0	0
	2+(0.2-0.5)	0	0	33	92	0
	3+ (≥1.0)	0	0	0	28	161
TOTAL		1217	228	205	120	161
Exact Accuracy		**98%**	**76%**	**84%**	**77%**	**100%**
Accuracy +/-1CB		100%	100%	100%	100%	100%

Nitrite

Positive % agreement 94.4%
Negative % agreement 99.4%
Overall % agreement 98.8%

Nitrite		**AX-4030**		
		+	**-**	**Total**
AU-4050	**+**	**221**	**11**	**232**
	-	**13**	**1686**	**1699**
Total		**234**	**1697**	**1931**

NITRITE (mg/dL) n=1931				
REFERENCE: AX-4030				
		Negative	**1+**	**2+**
AU-4050	**Negative**	1686	13	0
	1+	11	69	1
	2+	0	5	146
TOTAL		1697	87	147

Exact Accuracy	**99%**	**79%**	**99%**
Accuracy +/-1CB	100%	100%	100%

Leukocyte

Positive % agreement 94.4%
Negative % agreement 99.3%
Overall % agreement 97.5%

Leukocyte	**AX-4030**			
		+	**-**	**Total**
AU-4050	**+**	**690**	**8**	**698**
	-	**41**	**1192**	**1233**
Total		**731**	**1200**	**1931**

LEUKOCYTES (cells/µl) n=1931						
REFERENCE: AX-4030						
		Negative	**Trace(25)**	**1+ (75)**	**2+ (250)**	**3+ (500)**
AU-4050	**Negative**	1192	40	1	0	0
	Trace(25)	8	131	28	0	0
	1+ (75)	0	12	155	15	0
	2+ (250)	0	0	4	112	4
	3+ (500)	0	0	0	8	221
TOTAL		1200	183	188	135	225
Exact Accuracy		**99%**	**72%**	**82%**	**83%**	**98%**
Accuracy +/-1CB		100%	100%	99%	100%	100%

Specific gravity

n= 738 samples r= 0.99

y=1.0295x-0.0302 R^2 =0.984

Urine Sediment Method Comparison

Red blood cells

Positive % agreement 90%
Negative % agreement 95%
Range: 1-5367 cells/µL

Cell	Site	Equation	Slope	-95%	+95%	P-	R^2	R	N
RBC	Combine	1.019x +	1.019	1.012	1.026	<0.050	0.992	0.996	685

White blood cells

Positive % agreement 97%
Negative % agreement 98%
Range: 1-5154 cells/µL

Cell	Site	Equation	Slope	-95%	+95%	P-	R^2	R	N
WBC	Combine	y = 1.0039x +	1.004	1.000	1.008	<0.050	0.998	0.999	634

Epithelial cells

Positive % agreement 94%
Negative % agreement 98%
Range: 1-283 cells/µL

Cell	Site	Equation	Slope	-95%	+95%	P-	R^2	R	N
EC	Combine	y = 0.9961x +	1.00	0.98	1.01	<0.050	0.96	0.98	569

Casts

Positive % agreement 100%
Negative % agreement N/A
Range: 1-36 casts/ µL

Cell	Site	Equation	Slope	-95%	+95%	P-	R^2	R	N
CAST	Combine	y = 0.7783x +	0.778	0.729	0.828	<0.050	0.827	0.909	204

Bacteria

Positive % agreement 91%
Negative % agreement 97%
Range: 2-11520 cells/µL

Cell Type	Site	Equation	Slope	-95%	+95%	P-	R^2	R	N
BACT	Combine	y = 0.9736x +	0.974	0.948	0.999	<0.050	0.929	0.964	441

Flagging Parameters

Combined – 742 Samples	**Crystal**	**Yeast Like Cells**	**Small Round Cells**	**Pathological Casts**	**Mucus**	**Sperm**
Positive Agreement	74%	80%	97%	86%	82%	100%
Negative Agreement	51%	97%	47%	60%	74%	100%

b. Matrix comparison:

Not applicable. This device is for human urine only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical Sensitivity:

Not applicable

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

Not applicable.

4. Clinical cut-off**:**

Not applicable.

5. Expected values/Reference range:

The sponsor based the AU-4050 reference intervals on literature references

AU-4050 Chemistry Module Reference Intervals

Analyte	Expected Value
Glucose	Negative
Protein	Negative or Trace
Bilirubin	Negative
Urobilinogen	0.2-1 mg/dL
pH	4.6-8.0
Blood	Negative
Ketones	Negative
Nitrite	Negative
Leukocytes	Negative
Specific Gravity	1.001-1.035

AU- 4050 Flow Cytometer Reference Intervals

Analyte	Expected Value cells/ µL
Red Blood Cells	0-17
White Blood cells	0-44
Epitheal Cells	0-26
Casts	0-5
Bacteria	0-1200

Reference Interval Literature References:

1. Brunzel, N.A. Fundamentals of Urine and Body Fluid Analysis. 2nd ed. Philadelphia: Saunders. 2004.
2. Delanghe, JR, Kouri, TT, Huber AR, HAnnemann-Pohl K, Guder WG, Lun A, Sinha P,Stamminger G, Beier L: The role of automated urine particle flow cytometry in clinical practice. C. Chimica Acta. 2000; 301: 1-18.
3. Free, A. H., et al. Clinical Chemistry, 1957; 3 : 716
4. Henry, J.B. et al. Clinical Diagnosis and Management of Laboratory Methods, 21st ed. Philadelphia: Saunders; 2007.
5. Regeniter A, Haenni V, Risch L, Kochli HP, Colombo JP, Frei R, Huber AR: Urine analysis performed by flow cytometry: reference range determination and comparison to morphological findings, dipstick chemistry and bacterial culture results—a multicenter study. Clin Nephrol. 2001 May; 55(5): 384-92.
6. Tietz Fundementals of Clinical Chemistry, 4th ed. Philadelphia: Saunders. 1996.
7. Sysmex Corporation. Sysmex UF-1000*i* Instructions for Use. Japan. 2009.

N. Instrument Name:

AUTION HYBRID™ AU-4050 Fully Automated Integrated Urine Analyzer System

O. System Descriptions:

1. Modes of Operation:

   Single or continuous testing mode.

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:

   Manual sample identification or Barcode reader

4. Specimen Sampling and Handling:

Analysis of samples

Sampler analysis: Multiple samples are analyzed consecutively, using a sample rack. Using the Sampler Unit, sample racks can be transported automatically, and the samples analyzed sequentially. Up to ten samples can be set in one sample rack, and up to six racks (60 samples) can be set in one Sampler Unit at once. Analysis results are managed by sample number. Manual analysis (only compatible with FCM analysis parameters): Samples can be analyzed manually, without using sample racks, but only for FCM analysis. After inputting the information necessary for analysis into the IPU, the operator mixes one sample each and set the sample on the aspiration port of the Main Unit for analysis. Even when performing a sampler analysis, manual analysis can be performed by stopping the sampler analysis.

5. Calibration:

Automatic Background check

After the temperature has stabilized, the automatic rinsing/background check dialog box is displayed. A background check is performed. The analysis will be repeated a maximum of three times. The background analysis results will automatically be displayed in the automatic cleansing/background check dialog box. If the figure is below the allowable value, the dialog box will be closed and the Main Unit will enter stand-by status.

Specific gravity calibration

The instrument is calibrated using specific gravity standard solutions prepared by the customer (Low solution and High solution). The sponsor recommends performing specific gravity calibration once per month.

Check measurement

White Check Strips are provided by the manufacturer to verify calibration. The manufacture recommends to measure the check strips to verify that the CHM analyzer is working correctly any time CHM analysis results appear suspect.

6. Quality Control:

Recommendations for quality control are described in the labeling. Additionally, users should follow local, state and federal regulations.

CHM QC analysis

The sponsor recommends the use of commercially available controls intended for monitoring urine dipstick results for the following parameters: glucose, protein, bilirubin, urobilinogen, pH, blood, ketones, nitrites, leukocytes, and specific gravity.

FCM QC analysis
• AUTION Control Solution (AUTION Control Solution (H)/AUTION Control Solution (L))

The AU-4050 operator's manual reads as follows:
Perform QC analysis daily at start-up according to individual laboratory standard procedures. Quality control analysis is performed to verify accuracy of instrument. For QC analysis of CHM analysis parameters, the sample racks provided can be used to analyze three types or three concentrations of control material at once. Use manual analysis for QC analysis of FCM analysis parameters. There are two levels of quality control for FCM analysis: With X-Bar control, the control material is analyzed twice in succession, and the average is used as the control data. With L-J control, the control material is analyzed once and the value is used as the control data.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above: none

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

R. Conclusion:

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