November 6, 2020

Roche Diagnostics
Teresa Carrow
Regulatory Affairs Principal
9115 Hague Road
Indianapolis, Indiana 46256

Re: K200811
Trade/Device Name: cobas u 701 microscopy analyzer
Regulation Number: 21 CFR 864.5200
Regulation Name: Automated Cell Counter
Regulatory Class: Class II
Product Code: LKM
Dated: March 26, 2020
Received: March 27, 2020

Dear Teresa Carrow:

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,

Lea Carrington
Division Director
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: 06/30/2023
*See PRA Statement below.*

510(k) Number *(if known)*
K200811

Device Name
cobas u 701 microscopy analyzer

Indications for Use *(Describe)*
The cobas u 701 microscopy analyzer is a fully automated urine microscopy system intended for the in vitro quantitative determination of erythrocytes and leukocytes, the semi-quantitative determination of squamous epithelial cells, bacteria, and hyaline casts and the qualitative determination of non-squamous epithelial cells, crystals, yeasts, pathological casts, mucus and sperm in urine.

This system is intended to be used by trained operators in clinical laboratories. All instrument analyte image decisions may be reviewed and reclassified by a trained operator.

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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# **cobas u** 701 microscopy analyzer
# 510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the **cobas u** 701 microscopy analyzer.

| | |
|---|---|
| **Submitter Name** | Roche Diagnostics |
| **Address** | 9115 Hague Road<br>P.O. Box 50416<br>Indianapolis, IN 46250-0457 |
| **Contact** | Teresa Carrow<br>Phone: (317) 521-2963<br>FAX: (317) 521-2324<br>Email: teresa.carrow@roche.com<br><br>Kelli Turner<br>Phone: (317) 521-4515<br>FAX: (317) 521-2324<br>Email: kelli.turner@roche.com |
| **Date Prepared** | September 2, 2020 |
| **Proprietary Name** | **cobas u** 701 microscopy analyzer<br>**cobas u** cuvette |
| **Common Name** | Automated urine microscopy system<br>cuvette for urine microscopy |
| **Classification Name** | Automated urine microscopy system<br>cuvette |
| **Product Codes, Regulation Numbers** | See Table 1 |
| **Predicate Devices** | IRIS IQ 200 (k022774) |
| **Establishment Registration** | For the **cobas u** 701 microscopy analyzer the establishment registration number for<br>Roche Diagnostics GmbH Mannheim, Germany: 9610126<br>Roche Diagnostics GmBH Penzberg, Germany: 9610529<br>Roche Diagnostics Indianapolis, IN United States: 1823260. |

### Table 1: Product Code and Regulation Number

The Urine Particle Counter is a Class II device under 21 CFR 864.5200.

| Device/Analyte | Product Code | Classification | Regulation | Panel |
|---|---|---|---|---|
| Urine Particle Counter | LKM | II | §864.5200 | Hematology |

## 1. DEVICE DESCRIPTION

The **cobas u** 701 microscopy analyzer consists of the following components:

| Component | Description |
|---|---|
| **cobas u** 701 microscopy analyzer | Instrument with external color touch panel |
| **cobas u** cuvette (400 cuvettes) | Cuvette cassette with 400 microscopy cuvettes |
| Racks | Standard rack, different types |
| **Optional** | |
| Waste box carton | Carton for easy disposal of used test strips |
| **Connectivity** | |
| Mouse | Alternative for touch screen input |
| Keyboard | Alternative for touch screen input |
| Printer | Commonly available laser printers |
| Host/LIS connectivity | ASTM standard |
| Data transfer | USB-stick |

### 1.1. cobas u 701 microscopy analyzer

The **cobas u** 701 microscopy analyzer is a fully automated urine analysis system. It is optimized for the high-volume professional laboratory market. The **cobas u** 701 microscopy analyzer performs a maximum theoretical throughput of up to 116 samples per hour.

The **cobas u** 701 microscopy analyzer consists of several major components:

- Rack transport system
- Liquid handling system
- Cuvette cassette compartment
- Centrifuge
- Built-in reverse microscope with movable objective lens for focusing procedure
- High resolution camera system
- Touch Screen
- Inbuilt Computer with the imaging and evaluation software for analyzing the sediment pictures

Key functions of the **cobas u** 701 microscopy analyzer include:

| **Key Functions** |
|---|
| Sample loading and transport |
| Sample identification |
| Sample homogenization |
| Sample pipetting into cuvettes |
| Centrifugation of cuvettes |
| Image acquisition with a camera |
| Image assessment |
| Automatic disposal of used cuvettes |
| Result readout |
| Result and image memory |
| Optional manual classification and / or re-classification of particles (manual entries are flagged) |
| Manual or Automatic validation of the result |
| Optional formats for data output including electronic result communication |
| **Additional Functions** |
| Data export |
| Remote Service |
| Quality Control (optional with RFID tagged controls) |
| Processing of diluted samples |
| Washing |
| Filling Water tank, Emptying liquid and solid waste |

The operating system will be Microsoft Windows 10. The system will use a Postgres/SQL database.

The **cobas u** 701 microscopy analyzer is a stand-alone system, and it is designed to be inter-connected mechanically and electronically with the **cobas u** 601 Urine Analyzer in order to create a urine work area (**cobas** 6500). The **cobas u** 601 System was previously FDA-cleared under k183432. The connectivity to the **cobas u** 701 microscopy analyzer to form the **cobas** 6500 is not the subject of this submission.

### 1.2. cobas u cuvette (400 cuvettes)

The **cobas u** cuvette is used by the **cobas u** 701 microscopy analyzer to transport, centrifuge and analyze patient and control samples. They are provided separately from the analyzer, in a box holding 400 disposable cuvettes.

### 1.3. Calibrator

No calibration of the device is necessary for its intended use. However, there is a microscope check, which is not a calibration of the device. This microscope check ensures proper functioning of the focusing mechanism of the microscope utilizing a reference cuvette.

The reference cuvette is a cuvette with the same dimensions as the sample cuvette, which contains a transparent material with a standardized number of erythrocyte like particles etched in it. For differentiation from the sample cuvettes, the reference cuvette is green and marked with the letter R on the top. This microscope check confirms that the instrument is able to focus accurately on the position of the particles and to count correctly the number of the cells. This microscope check needs to be performed every 4 weeks. A message from the instrument informs the operator when it is due.

## 2. INDICATIONS FOR USE

### 2.1. cobas u 701 microscopy analyzer

The **cobas u** 701 microscopy analyzer is a fully automated urine microscopy system intended for the in vitro quantitative determination of erythrocytes and leukocytes, the semi-quantitative determination of squamous epithelial cells, bacteria, and hyaline casts and the qualitative determination of non-squamous epithelial cells, crystals, yeasts, pathological casts, mucus and sperm in urine.

This system is intended to be used by trained operators in clinical laboratories. All instrument analyte image decisions may be reviewed and reclassified by a trained operator.

### 2.2. cobas u cuvette

The **cobas u** cuvette is a cassette, containing cuvettes for the in vitro quantitative determination of erythrocytes and leukocytes, the semi-quantitative determination of squamous epithelial cells,

bacteria, and hyaline casts and the qualitative determination of non-squamous epithelial cells, crystals, yeasts, pathological casts, mucus, and sperm in urine with the **cobas u** 701 microscopy analyzer. For professional use only.

***Note:*** *For convenience, erythrocytes are referred to as RBC and leukocytes are referred to as WBC throughout this submission.*

## 3. TECHNOLOGICAL CHARACTERISTICS

The following table compares the **cobas u** 701 microscopy analyzer with its predicate device, IRIS IQ 200 (k022774).

**Table 2: Technical Characteristics Comparison Table between cobas u 701 Microscopy Analyzer and the IRIS IQ 200**

| Feature | Predicate Device<br>IRIS IQ 200 (k022774) | Candidate Device<br>**cobas u** 701 microscopy analyzer |
|---|---|---|
| Intended Use | The iQ200 system is an *in-vitro* diagnostic device used to automate the complete urinalysis profile, including urine test strip chemistry panel and microscopic sediment analysis. Optionally, the iQ200 Analyzer can be used as a stand-alone unit, or the results from the iQ200 Analyzer can be combined with other urine chemistry results received from an LIS. It produces quantitative or qualitative counts of all formed sediment elements present in urine, including cells, casts, crystals and organisms. A competent human operator can set criteria for auto-reporting and flagging specimens for review.<br>All instrument analyte image decisions may be reviewed and overridden by a trained technologist. | The **cobas u** 701 microscopy analyzer is a fully automated urine microscopy system intended for the *in vitro* quantitative determination of erythrocytes and leukocytes, the semi-quantitative determination of squamous epithelial cells, bacteria, and hyaline casts and the qualitative determination of non-squamous epithelial cells, crystals, yeasts, pathological casts, mucus and sperm in urine. This system is intended to be used by trained operators in clinical laboratories. All instrument analyte image decisions may be reviewed and reclassified by a trained operator. |
| Submission | K022774 | N/A |
| Date Cleared | 21 October 2002 | N/A |
| Automation | Automated | Same |

| Feature | Predicate Device<br>IRIS IQ 200 (k022774) | Candidate Device<br>**cobas u** 701 microscopy analyzer |
|---|---|---|
| Specimen | Urine in barcode labeled tubes | Same |
| Change of machine assignment | All instrument analyte image decisions may be reviewed and overridden by a trained technologist. | An appropriately trained laboratory operator may manually re-classify or (sub-) sub-classify particles. |
| Principle of Operation | The iQ200 System auto-identifies and processes barcoded tube specimens in 10-position racks by mixing, sampling, and analyzing automatically. The iQ200 system incorporates an iQ200 Automated Urine Microscopy Analyzer, in which a sample is presented as a lamina sandwiched between enveloping layers of suspending fluid to a microscope coupled to a CCD (charge coupling device) video camera.<br>This lamination positions the specimen exactly within the depth of focus and field of view of the objective lens of the microscope. Lamination is the planar equivalent of axial hydrodynamic focusing, used to position cells in certain types of blood cell counters and flow cytometers. It has the added advantage of achieving orthoscopic particle orientation, thereby presenting asymmetric particles with their largest profile facing the direction of view.<br>A CCD digital camera captures five hundred frames per sample, as each microscopic field of view is illuminated by the flash of a strobe lamp. The resulting pictures are digitized and delivered to the Analysis Processor computer. A previously stored image of a blank background is subtracted from the individual fields of view, enhancing the morphology of the captured particle.<br>Individual particle images are isolated within each frame. The Auto- | The analyzer auto-identifies and processes barcoded tube specimens in 5-position racks by mixing, sampling, and analyzing automatically.<br>**cobas u** 701 microscopy analyzer incorporates a robotic liquid handling system that pipettes an aliquot of the specimen into a disposable cuvette. The filled cuvette is forwarded to the built-in centrifuge for centrifugation of the non-soluble particles. After the centrifugation, all particles are brought to one monolayer to ensure they are all at the same focal plane. A built in camera takes pictures through a built in microscope at several positions of the sediment. All images are evaluated by an image processing software which is able to detect and further classify the following urine particles<br>• Red blood cells<br>• White blood cells<br>• Squamous epithelial cells<br>• Bacteria<br>• Hyaline casts<br>• Non-squamous epithelial cells<br>• Crystals<br>• Yeast<br>• Pathological casts<br>• Mucus<br>• Sperm<br><br>An appropriately trained laboratory user may manually re-classify or sub-classify particles on the basis of the acquired pictures. |

| Feature | Predicate Device<br>IRIS IQ 200 (k022774) | Candidate Device<br>**cobas u** 701 microscopy analyzer |
|---|---|---|
| | Particle Recognition (APR™) software, a highly trained neural network, uses size, shape, contrast and texture features to classify each image into one of 12 categories: RBCs, WBCs, WBC Clumps, Hyaline Casts, Unclassified Casts, Squamous Epithelial Cells, Non-squamous Epithelial Cells, Bacteria, Yeast, Crystals, Mucus and Sperm. Particle concentration is calculated using the number of images and the volume scanned. User-defined release criteria are checked and results are sent to an operator review screen or directly uploaded to the LIS based on these criteria. Specimen results can be edited, archived, retrieved, imported, exported and formatted into custom reports. | Particle concentration is calculated using the average count from the assessed images. |
| Detected and counted particles present in a specimen | • Red Blood Cells<br>• White Blood Cells<br>• White Blood Cell Clumps<br>• Non-Squamous Epithelial Cells<br>• Squamous Epithelial Cells<br>• Hyaline Casts<br>• Bacteria<br>• Crystals<br>• Yeast<br>• Artifact<br>• Unclassified Casts<br><br>It is possible to manually sub classify Unclassified Crystals, Unclassified Casts, Yeast and Non-Squamous Epithelial Cells.<br><br>It is possible to manually identify the following particles<br>• Sperm | • Red blood cells<br>• White blood cells<br>• Squamous epithelial cells<br>• Bacteria<br>• Hyaline casts<br>• Non-squamous epithelial cells<br>• Crystals<br>• Yeast<br>• Pathological casts<br>• Mucus<br>• Sperm<br><br>Not proposed<br><br>It is possible to manually sub classify particles (e.g. RBC morphologies, CRY)<br><br>It is possible to manually identify further particles (e.g. trichomonas, red |

| Feature | Predicate Device<br>IRIS IQ 200 (k022774) | Candidate Device<br>**cobas u** 701 microscopy analyzer |
|---|---|---|
| | • Mucus<br>• Trichomonas<br>• Fat Red Blood Cell Clumps<br>• Oval Fat Bodies | blood cell clumps, oval fat bodies, artifacts.) |
| QC | IQ Control material | Recommendation of commercially available control solutions |
| Calibration | Monthly focus with **iQ Focus** and calibration with IQ® Calibrator Material (suspension of fixed human red blood cells in a particulate-free solution) | No calibration needed due to different particle detection technology |
| Maintenance | Daily and periodic maintenance | Same |
| Specimen Volume | Minimum volume 3 mL of un-spun urine. Aspiration volume approx. 1.3 mL. | Minimum volume 2 mL of un-spun urine. Aspiration volume < 0.8 mL |
| Measurement Principle | Flow digital imaging | Digital imaging after automated centrifugation |
| Workstation | Computer with monitor/keyboard/mouse | Integrated PC with external touch screen, optional keyboard/mouse |
| Weight | Microscopy module 100 lbs = 45.4 kgs | Microscopy module 176 lbs. = 80kg |
| Fluid Waste | Waste is pumped from the instrument to a sink, floor drain or suitable container. Drain must be below or at same height as bench and should be less than 10 feet (3 meters) from the back of the instrument. | Waste container capacity is 5L. This capacity is sufficient to run 400 tests. A direct waste discharge is possible (max. height = instrument level). |

## 4. NON-CLINICAL PERFORMANCE EVALUATION

The following performance data are provided in support of the substantial equivalence determination:

- Precision according to CLSI EP5-A3
- Detection Limit: LoB, LoD and LoQ according to CLSI EP17-A2
- Linearity according to CLSI EP6-A
- Interferences

- Method Comparison to Reference Method

All performance specifications were met.

## 4.1. Precision

Precision was comprised of experiments for Repeatability and Intermediate precision.

### 4.1.1. Repeatability and Intermediate Precision

#### *4.1.1.1. Repeatability*

To assess the repeatability (within-run precision) of the **cobas u** 701 microscopy analyzer, a within-run precision study was performed. For the experiment, control samples as well as human specimens (residual amounts from routine) were used. Depending on the parameter methodology (quantitative, semi-quantitative, qualitative) up to three controls and up to three sample concentrations were measured. All predefined acceptance criteria were met.

**Table 3: Repeatability for Quantitative Parameters Using Controls**

| | | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **Number of Runs** | **N Total** | **Control Level*** | **Target Range (p/µL)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 1 | RBC | 2 | 42 | 1 | 0-25 | 0.00 | 0.00 | NA | 0.00 | 0.00 | NA |
| Site 1 | RBC | 2 | 42 | 2 | 425-1280 | 803 | 39.4 | 4.91 | 764 | 54.2 | 7.10 |
| Site 1 | RBC | 2 | 42 | 3 | 50-120 | 70.6 | 9.19 | 13.0 | 53.8 | 7.94 | 14.8 |
| Site 1 | WBC | 2 | 42 | 1 | 0-25 | 0.00 | 0.00 | NA | 0.00 | 0.00 | NA |
| Site 1 | WBC | 2 | 42 | 2 | 75-240 | 138 | 15.0 | 10.9 | 133 | 11.6 | 8.71 |
| Site 1 | WBC | 2 | 42 | 3 | 50-70 | 59.1 | 5.37 | 9.09 | 51.5 | 7.57 | 14.7 |
| Site 2 | RBC | 2 | 42 | 1 | 0-25 | 0.04 | 0.19 | 458 | 0.08 | 0.26 | 316 |
| Site 2 | RBC | 2 | 42 | 2 | 425-1280 | 641 | 31.9 | 4.97 | 890 | 48.3 | 5.42 |
| Site 2 | RBC | 2 | 42 | 3 | 50-120 | 76.4 | 8.45 | 11.1 | 112 | 10.7 | 9.52 |
| Site 2 | WBC | 2 | 42 | 1 | 0-25 | 0.00 | 0.00 | NA | 0.00 | 0.00 | NA |
| Site 2 | WBC | 2 | 42 | 2 | 75-240 | 131 | 11.5 | 8.78 | 146 | 10.4 | 7.13 |
| Site 2 | WBC | 2 | 42 | 3 | 50-70 | 62.7 | 6.74 | 10.8 | 67.4 | 7.34 | 10.9 |

*BioRad Liquicheck control levels include: Level 1, Level 2, Level 3 (Low positive control prepared by diluting Bio-Rad Level 1 and Level 2; obtained values for low pos controls depend on dilution factor).

**NOTE:** CV (%) cannot be calculated when mean = 0; these instances are marked as NA.

**Table 4: Repeatability for Quantitative Parameters Using Human Samples**

| | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **No. of Runs** | **N Total** | **Concentration** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 1 | RBC | 2 | 42 | Neg | 0.75 | 0.98 | 129 | 1.17 | 1.05 | 89.8 |
| Site 1 | RBC | 2 | 42 | Low pos | 17.4 | 4.90 | 28.1 | 80.3 | 16.8 | 20.9 |

| | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **No. of Runs** | **N Total** | **Concentration** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 1 | RBC | 2 | 42 | Pos | 1336 | 155 | 11.6 | 899 | 48.0 | 5.34 |
| Site 1 | WBC | 2 | 42 | Neg | 2.26 | 1.26 | 55.8 | 2.58 | 2.38 | 92.3 |
| Site 1 | WBC | 2 | 42 | Low pos | 14.1 | 4.06 | 28.8 | 63.9 | 8.86 | 13.9 |
| Site 1 | WBC | 2 | 42 | Pos | 813 | 29.2 | 3.59 | 631 | 29.0 | 4.59 |
| Site 2 | RBC | 2 | 42 | Neg | 0.92 | 1.02 | 111 | 0.59 | 1.12 | 192 |
| Site 2 | RBC | 2 | 42 | Low pos | 125 | 11.3 | 9.03 | 13.0 | 4.48 | 34.4 |
| Site 2 | RBC | 2 | 42 | Pos | 989 | 74.4 | 7.52 | 1175 | 50.8 | 4.33 |
| Site 2 | WBC | 2 | 42 | Neg | 0.53 | 0.82 | 154 | 0.00 | 0.00 | NA |
| Site 2 | WBC | 2 | 42 | Low pos | 22.8 | 5.28 | 23.2 | 56.4 | 7.18 | 12.7 |
| Site 2 | WBC | 2 | 42 | Pos | 496 | 56.6 | 11.4 | 620 | 90.2 | 14.5 |

*BioRad Liquicheck control levels include: Level 1, Level 2, Level 3 (Low positive control prepared by diluting Bio-Rad Level 1 and Level 2; obtained values for low pos controls depend on dilution factor).

**NOTE:** CV (%) cannot be calculated when mean = 0; these instances are marked as NA.

**Table 5: Repeatability for Semi-Quantitative and Qualitative Parameters**

| | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **No. of Runs** | **N Total** | **Concentration** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 1 | BAC | 2 | 42 | Neg | 79.6 | 12.7 | 15.9 | 32.7 | 5.88 | 18.0 |
| Site 1 | BAC | 2 | 42 | Low pos | 107 | 8.83 | 8.23 | 176 | 10.1 | 5.73 |
| Site 1 | BAC | 2 | 42 | Pos | 2380 | 169 | 7.10 | 1175 | 38.3 | 3.26 |
| Site 1 | CRY | 2 | 42 | Neg | 0.21 | 0.58 | 279 | 0.61 | 0.87 | 144 |
| Site 1 | CRY | 2 | 42 | Pos | 22.5 | 7.07 | 31.5 | 81.7 | 19.1 | 23.4 |
| Site 1 | HYA | 2 | 42 | Neg | 0.08 | 0.18 | 211 | 0.10 | 0.24 | 226 |

| | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **No. of Runs** | **N Total** | **Concentration** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 1 | HYA | 2 | 42 | Low pos | 4.00 | 1.16 | 29.1 | 6.81 | 2.09 | 30.6 |
| Site 1 | HYA | 2 | 42 | Pos | 14.4 | 3.40 | 23.7 | 15.4 | 3.62 | 23.5 |
| Site 1 | MUC | 2 | 42 | Neg | 26.5 | 8.63 | 32.5 | 4.44 | 2.55 | 57.5 |
| Site 1 | MUC | 2 | 42 | Pos | 298 | 41.1 | 13.8 | 618 | 88.1 | 14.3 |
| Site 1 | NEC | 2 | 42 | Neg | 0.21 | 0.30 | 143 | 0.00 | 0.00 | NA |
| Site 1 | NEC | 2 | 42 | Pos | 27.7 | 3.89 | 14.1 | 7.08 | 2.23 | 31.5 |
| Site 1 | PAT | 2 | 42 | Neg | 0.08 | 0.30 | 357 | 0.02 | 0.10 | 458 |
| Site 1 | PAT | 2 | 42 | Pos | 2.10 | 0.90 | 43.0 | 3.25 | 1.05 | 32.5 |
| Site 1 | SEC | 2 | 42 | Neg | 0.21 | 0.58 | 279 | 0.00 | 0.00 | NA |
| Site 1 | SEC | 2 | 42 | Low pos | 14.4 | 2.49 | 17.4 | 15.9 | 4.25 | 26.7 |
| Site 1 | SEC | 2 | 42 | Pos | 44.4 | 14.3 | 32.2 | 67.2 | 14.9 | 22.1 |
| Site 1 | SPRM | 2 | 42 | Neg | 0.04 | 0.13 | 316 | 0.00 | 0.00 | NA |
| Site 1 | SPRM | 2 | 42 | Pos | 17.7 | 5.87 | 33.1 | 36.7 | 5.98 | 16.3 |
| Site 1 | YEA | 2 | 42 | Neg | 0.06 | 0.16 | 251 | 0.00 | 0.00 | NA |
| Site 1 | YEA | 2 | 42 | Pos | 16.6 | 4.98 | 30.1 | 14.9 | 3.87 | 26.1 |
| Site 2 | BAC | 2 | 42 | Neg | 26.9 | 4.22 | 15.7 | 21.4 | 2.04 | 9.55 |
| Site 2 | BAC | 2 | 42 | Low pos | 117 | 8.11 | 6.95 | 151 | 8.32 | 5.51 |
| Site 2 | BAC | 2 | 42 | Pos (2+) | 239 | 13.8 | 5.80 | 250 | 10.4 | 4.17 |
| Site 2 | BAC | 2 | 42 | Pos | 1612 | 30.1 | 1.87 | 845 | 55.0 | 6.52 |
| Site 2 | CRY | 2 | 42 | Neg | 0.59 | 0.49 | 83.3 | 0.82 | 0.73 | 88.9 |
| Site 2 | CRY | 2 | 42 | Pos | 62.2 | 7.13 | 11.5 | 26.5 | 4.89 | 18.5 |
| Site 2 | HYA | 2 | 42 | Neg | 0.00 | 0.00 | NA | 0.02 | 0.10 | 458 |
| Site 2 | HYA | 2 | 42 | Low pos | 2.89 | 1.33 | 46.0 | 3.86 | 1.32 | 34.2 |

| | | | | | Run 1 | | | Run 2 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Site** | **Parameter** | **No. of Runs** | **N Total** | **Concentration** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** | **Mean (p/µL)** | **SD (p/µL)** | **CV (%)** |
| Site 2 | HYA | 2 | 42 | Pos | 20.9 | 3.51 | 16.8 | 17.0 | 4.10 | 24.1 |
| Site 2 | MUC | 2 | 42 | Neg | 0.63 | 1.21 | 192 | 9.32 | 4.72 | 50.6 |
| Site 2 | MUC | 2 | 42 | Pos | 491 | 34.8 | 7.08 | 426 | 52.9 | 12.4 |
| Site 2 | NEC | 2 | 42 | Neg | 0.04 | 0.13 | 316 | 0.02 | 0.10 | 458 |
| Site 2 | NEC | 2 | 42 | Pos | 7.50 | 1.97 | 26.2 | 8.21 | 1.96 | 23.9 |
| Site 2 | PAT | 2 | 42 | Neg | 0.00 | 0.00 | NA | 0.02 | 0.10 | 458 |
| Site 2 | PAT | 2 | 42 | Pos | 10.9 | 2.29 | 21.0 | 7.56 | 1.72 | 22.8 |
| Site 2 | SEC | 2 | 42 | Neg | 0.00 | 0.00 | NA | 0.02 | 0.10 | 458 |
| Site 2 | SEC | 2 | 42 | Low pos | 10.5 | 3.07 | 29.1 | 14.8 | 3.21 | 21.7 |
| Site 2 | SEC | 2 | 42 | Pos | 53.9 | 9.09 | 16.9 | 63.8 | 6.40 | 10.0 |
| Site 2 | SPRM | 2 | 42 | Neg | 0.00 | 0.00 | NA | 0.00 | 0.00 | NA |
| Site 2 | SPRM | 2 | 42 | Pos | 16.7 | 3.08 | 18.4 | 8.65 | 2.00 | 23.1 |
| Site 2 | YEA | 2 | 42 | Neg | 0.00 | 0.00 | NA | 0.00 | 0.00 | NA |
| Site 2 | YEA | 2 | 42 | Pos | 268 | 19.6 | 7.31 | 236 | 33.0 | 14.0 |

NOTE: CV (%) cannot be calculated when mean = 0; these instances are marked as NA.

#### *4.1.1.2. Intermediate Precision*

To assess long-term precision of the **cobas u** 701 microscopy analyzer an intermediate precision according to CLSI EP5-A3 was performed. Due to the instability of the human urine samples, only control samples were measured for the intermediate precision study. This assessment was limited to the parameter included in the control material (RBC, WBC). All predefined acceptance criteria were met.

**Table 6: Intermediate Precision for Controls at Site 2**

| Site 2 | | | | | | Repeatability | | Between-Run | | Between-Day | | Intermediate (Within-site) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Number of runs** | **N Total** | **Control Level** | **Mean (p/µL)** | **Target Value** | **SD** | **%CV** | **SD** | **%CV** | **SD** | **%CV** | **SD** | **%CV** |
| RBC | 2 | 84 | 1 | 0.15 | 0 - 25 p/µL | 0.49 | 334 | 0.00 | 0.00 | 0.27 | 187 | 0.56 | 383 |
| RBC | 2 | 84 | 2 | 813 | 425 - 1280 p/µL | 42.8 | 5.26 | 20.3 | 2.50 | 30.0 | 3.69 | 56.1 | 6.90 |
| RBC | 2 | 84 | 3 | 69.5 | 50 - 70 p/µL | 8.32 | 12.0 | 0.41 | 0.59 | 3.35 | 4.82 | 8.98 | 12.9 |
| WBC | 2 | 84 | 1 | 0.00 | 0 - 25 p/µL | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| WBC | 2 | 84 | 2 | 140 | 75 - 240 p/µL | 9.36 | 6.69 | 2.31 | 1.65 | 8.17 | 5.84 | 12.6 | 9.03 |
| WBC | 2 | 84 | 3 | 62.8 | 50 - 70 p/µL | 8.09 | 12.9 | 2.17 | 3.46 | 2.47 | 3.93 | 8.74 | 13.9 |

Note:

BioRad Liquicheck control levels include: Level 1, Level 2, Level 3 (Low positive control prepared by diluting Bio-Rad Level 1 and Level 2);

For Liquichek control Level 1 and Level 2 samples, Target Values are from package insert;

For prepared low positive control samples, Target Values will be affected by the variability of the control material.

**Table 7: Intermediate Precision for Controls at Site 1**

| Site 1 | | | | | | Repeatability | | Between-Run | | Between-Day | | Intermediate (Within-site) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parameter | Number of runs | N Total | Control Level | Mean (p/µL) | Target Value | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| RBC | 2 | 84 | 1 | 0.105 | 0 - 25 p/µL | 0.33 | 317 | 0.14 | 130 | 0.00 | 0.00 | 0.36 | 343 |
| RBC | 2 | 84 | 2 | 751 | 425 - 1280 p/µL | 47.1 | 6.26 | 18.5 | 2.46 | 33.6 | 4.47 | 60.7 | 8.08 |
| RBC | 2 | 84 | 3 | 54.3 | 50 - 70 p/µL | 6.64 | 12.2 | 4.37 | 8.03 | 6.14 | 11.3 | 10.0 | 18.5 |
| WBC | 2 | 84 | 1 | 0.000 | 0 - 25 p/µL | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| WBC | 2 | 84 | 2 | 139 | 75 - 240 p/µL | 14.2 | 10.2 | 5.06 | 3.65 | 8.23 | 5.93 | 17.1 | 12.3 |
| WBC | 2 | 84 | 3 | 58.5 | 50 - 70 p/µL | 8.43 | 14.4 | 0.00 | 0.00 | 6.93 | 11.8 | 10.9 | 18.7 |

Note:

BioRad Liquicheck control levels include: Level 1, Level 2, Level 3 (Low positive control prepared by diluting Bio-Rad Level 1and Level 2);

For Liquichek control Level 1 and Level 2 samples, Target Values are from package insert;

For prepared low positive control samples, Target Values will be affected by the variability of the control material.

**Table 8: Intermediate Precision for Controls at Site 4**

| Site 4 | | | | | | Repeatability (Within-Run) | | Between-Run | | Between-Day | | Intermediate (Within-Site) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parameter | Number of Runs | N Total | Control Level | Mean (p/µL) | Target Value | SD (p/µL) | CV (%)* | SD (p/µL) | CV (%)* | SD (p/µL) | CV (%)* | SD (p/µL) | CV (%)* |
| RBC | 2 | 84 | 1 | 0.23 | 0 - 25 p/µL | 0.65 | 283 | 0.00 | 0.00 | 0.00 | 0.00 | 0.65 | 283 |
| RBC | 2 | 84 | 2 | 375 | 160 - 495 p/µL** | 18.7 | 5.00 | 15.3 | 4.09 | 21.5 | 5.75 | 32.4 | 8.65 |
| RBC | 2 | 84 | 3 | 63.4 | 50 - 70 p/µL | 6.99 | 11.0 | 4.01 | 6.32 | 0.00 | 0.00 | 8.05 | 12.7 |
| WBC | 2 | 84 | 1 | 0.00 | 0 - 25 p/µL | 0.00 | NA | 0.00 | NA | 0.00 | NA | 0.00 | NA |
| WBC | 2 | 84 | 2 | 170 | 75 - 240 p/µL | 13.8 | 8.13 | 0.00 | 0.00 | 6.90 | 4.05 | 15.5 | 9.09 |
| WBC | 2 | 84 | 3 | 58.8 | 50 - 70 p/µL | 6.56 | 11.1 | 1.85 | 3.14 | 0.00 | 0.00 | 6.81 | 11.6 |

*CV(%) cannot be calculated when mean = 0; these instances are marked as NA.

BioRad Liquicheck control levels include: Level 1, Level 2, Level 3 (Low positive control prepared by diluting Bio-Rad Level 1 and Level 2).

For Liquichek control Level 1 and Level 2 samples, Target Values are from package insert.

**This lot had a lower claim for the RBC in Level 2 than the two external sites

For prepared low positive control samples, Target Values will be affected by the variability of the control material.

### 4.1.2. Reproducibility

Reproducibility measurements for quantitative parameters WBC and RBC were performed based on the compiled intermediate precision datasets for the three study sites each using one **cobas u** 701 microscopy analyzer.

**Table 9: Reproducibility for Combined Data from Three Sites**

| | | | | | Repeatability (Within-Run) | | Between-Run | | Between-Day | | Reproducibility (Within-Site) | | Between-Site | | Reproducibility (Within-System) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Parameter** | **N Total** | **Concentration Level** | **Mean (p/µL)** | **Target Value** | **SD (p/µL)** | **CV (%)*** | **SD (p/µL)** | **CV (%)*** | **SD (p/µL)** | **CV (%)*** | **SD (p/µL)** | **CV (%)*** | **SD (p/µL)** | **CV (%)*** | **SD (p/µL)** | **CV (%)*** |
| RBC | 252 | 1 | 0.16 | 0 - 25 p/µL | **0.51** | 316 | **0.00** | 0.00 | **0.09** | 56.4 | **0.52** | 321 | **0.03** | 21.1 | **0.52** | 322 |
| RBC | 252 | 2 | 846 | 425 - 1280 p/µL** | 46.2 | **5.46** | 27.9 | **3.30** | 41.5 | **4.90** | 68.1 | **8.05** | 113 | **13.4** | 132 | **15.6** |
| RBC | 252 | 3 | 62.4 | 50 - 70 p/µL | 7.35 | **11.8** | 3.43 | **5.50** | 4.03 | **6.45** | 9.06 | **14.5** | 7.50 | **12.0** | 11.8 | **18.8** |
| WBC | 252 | 1 | 0.00 | 0 - 25 p/µL | **0.00** | NA | **0.00** | NA | **0.00** | NA | **0.00** | NA | **0.00** | NA | **0.00** | NA |
| WBC | 252 | 2 | 150 | 75 - 240 p/µL | 12.6 | **8.45** | 0.00 | **0.00** | 7.79 | **5.21** | 14.9 | **9.92** | 17.6 | **11.8** | 23.0 | **15.4** |
| WBC | 252 | 3 | 60.0 | 50 - 70 p/µL | 7.74 | **12.9** | 0.00 | **0.00** | 4.20 | **6.99** | 8.80 | **14.7** | 2.09 | **3.48** | 9.05 | **15.1** |

Method Used: SAS 9.4 proc mixed method=type1 covtest; model result=; random site site*day site*day*run; by parameter concentration_level;

*CV(%) cannot be calculated when mean = 0; these instances are marked as NA.

SAS NOTE: When the estimated G matrix is not positive definite, some variance components have negative estimates - these will be reported as 0.

**Mannheim data fix added: Result for RBC Concentration Level 2 Multiplied by a factor of 2.595

### 4.1.3. Recovery

Recovery measurements for semi-quantitative parameters BAC, HYA, and SEC were performed in triplicate on the **cobas u** 701 microscopy analyzer at two sites each using one **cobas u** 701 microscopy analyzer. Additionally, one measurement was performed using the manual KOVA counting method. All predefined acceptance criteria were met.

**Table 10: Recovery for Semi-quantitative Parameters at Site 2**

| Parameter | Target Value | N | cobas u 701 | | | | | | KOVA | Exact Agreement | 2 of 3 results within the specified concentration block | Agreement within 2 adjacent concentration ranges |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Raw Count (bacteria or p/µL) | | | Result | | | Result | [%] | [Yes/No] | [%] |
| | | | 1st | 2nd | 3rd | 1st | 2nd | 3rd | | | | |
| BAC | Negative (NaCl) | 3 | 2.64 | 4.84 | 1.76 | neg | neg | neg | neg | 100 | Yes | 100 |
| | 1+ | 3 | 169 | 157 | 170 | 1+ | 1+ | 1+ | 1+ | 100 | Yes | 100 |
| | 2+ | 3 | 496 | 565 | 533 | 2+ | 2+ | 2+ | 2+ | 100 | Yes | 100 |
| | 3+ | 3 | 1066 | 1280 | 1253 | 3+ | 3+ | 3+ | 3+ | 100 | Yes | 100 |
| HYA | Negative (Urine) | 3 | 0.00 | 0.00 | 0.00 | neg | neg | neg | 0.00 | 100 | Yes | 100 |
| | 5 p/µL | 3 | 6.16 | 4.40 | 8.80 | 5 | 5 | 15 | 5.50 | 66.7 | Yes | 100 |
| | 15 p/µL | 3 | 15.4 | 8.80 | 15.4 | 15 | 15 | 15 | 18.7 | 100 | Yes | 100 |
| SEC | Negative (Urine) | 3 | 0.88 | 0.88 | 0.44 | neg | neg | neg | 1.10 | 100 | Yes | 100 |
| | 15 p/µL | 3 | 20.7 | 11.4 | 13.6 | 15 | 15 | 15 | 17.6 | 100 | Yes | 100 |
| | 40 p/µL | 3 | 49.3 | 36.5 | 47.1 | 40 | 40 | 40 | 56.1 | 100 | Yes | 100 |

**Table 11: Recovery for Semi-quantitative Parameters at Site 1**

| Parameter | Target Value | N | cobas u 701 | | | | | | KOVA | Exact Agreement | 2 of 3 results within the specified concentration block | Agreement within 2 adjacent concentration ranges |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Raw Count (bacteria or p/µL) | | | Result | | | Result | [%] | [Yes/No] | [%] |
| | | | 1st | 2nd | 3rd | 1st | 2nd | 3rd | | | | |
| BAC | Negative (NaCl) | 3 | 0.44 | 11.9 | 5.72 | neg | neg | neg | neg | 100 | Yes | 100 |
| | 1+ | 3 | 134 | 123 | 130 | 1+ | 1+ | 1+ | 1+ | 100 | Yes | 100 |
| | 2+ | 3 | 407 | 413 | 394 | 2+ | 2+ | 2+ | 2+ | 100 | Yes | 100 |
| | 3+ | 3 | 896 | 888 | 891 | 3+ | 3+ | 3+ | 3+ | 100 | Yes | 100 |
| HYA | Negative (Urine) | 3 | 0.00 | 0.00 | 0.00 | neg | neg | neg | 0.00 | 100 | Yes | 100 |
| | 5 p/µL | 3 | 3.96 | 3.52 | 8.36 | 5 | 5 | 15 | 2.75 | 66.7 | Yes | 100 |
| | 15 p/µL | 3 | 12.8 | 11.4 | 12.8 | 15 | 15 | 15 | 13.8 | 100 | Yes | 100 |
| SEC | Negative (Urine) | 3 | 0.00 | 0.00 | 0.00 | neg | neg | neg | 0.00 | 100 | Yes | 100 |
| | 15 p/µL | 3 | 11.0 | 16.3 | 13.6 | 15 | 15 | 15 | 13.2 | 100 | Yes | 100 |
| | 40 p/µL | 3 | 43.1 | 55.0 | 50.6 | 40 | 40 | 40 | 52.8 | 100 | Yes | 100 |

## 4.2. Analytical Sensitivity

### 4.2.1. Limit of Blank (LoB)

Limit of Blank (LoB) of the **cobas u** 701 microscopy analyzer was determined using one lot of **cobas u** cuvette and three **cobas u** 701 microscopy analyzers.

The Limit of Blank (LoB) is the highest observed measured value for samples free of analyte. The Limit of Blank was determined as the 95th percentile of the measurement of blank samples. All predefined acceptance criteria were met.

### 4.2.2. Limit of Detection (LoD)

Limit of Detection (LoD) of the **cobas u** 701 microscopy analyzer were determined using one lot of **cobas u** cuvette and three **cobas u** 701 microscopy analyzers.

Limit of Detection (LoD) determines the detection limit for samples with low analyte concentration. The LoD was determined as the lowest amount of analyte in a sample that can be detected with a 95% probability. All predefined acceptance criteria were met.

### 4.2.3. Limit of Quantitation (LoQ)

Limit of Quantitation (LoQ) of the **cobas u** 701 microscopy analyzer were determined using one lot of **cobas u** cuvette and three **cobas u** 701 microscopy analyzers.

Limit of Quantitation (LoQ) is defined as the lowest analyte concentration in a sample that can be reproducibly measured. All predefined acceptance criteria were met.

## 4.3. Linearity/Assay Reportable Range

### 4.3.1. Deviation to Higher Order Polynomial/Percentage for “Significant Level of Deviation”

Linearity of the **cobas u** 701 microscopy analyzer was determined for the two quantitative parameters Red Blood Cells (RBC) and White Blood Cells (WBC) using one lot of **cobas u** cuvette and one **cobas u** 701 microscopy analyzer. Linear regression was calculated according CLSI EP6-A.

### 4.4. Dilution

The dilution study assessed the performance of the **cobas u** 701 microscopy analyzer when diluted samples are evaluated.

Note: Dilution of urine is not advisable however, when sample dilution is performed using saline as the diluent, with immediate evaluation on the **cobas u** 701 microscopy analyzer, results will be obtained.

### 4.5. Interferences

The interference study assessed the potential interferences that may occur on the **cobas u** 701 microscopy analyzer due to its measurement technology; clinical samples were assessed for the individual interferents.

Native human urine samples containing the following interfering particles were measured on the **cobas u** 701 microscopy analyzer: high concentrations of mucus strands, artefacts, clumps, cell fragments, dysmorphic cells, shining particles, crowded samples, diluted samples, highly viscous samples and high turbidity (Intralipid) samples. Furthermore, challenging native urine samples including amorphous crystals and trichomonas were evaluated.

### 4.6. Assay Cut-Off Determination

For semi-quantitative and qualitative assay cut-off determination, range limits had to be set. Range limits were set using empirical and theoretical information from literature, knowledge from clinical practice and the available data from external performed studies.

## 5. EXTERNAL (CLINICAL) TESTING

The clinical evaluation included a total of 1310 samples, 689 for the method comparison study and 621 for the reference range study, which were used to execute 3 studies including method comparison for all parameters and reference value assessment for Red Blood Cells (RBC) and White Blood Cells (WBC), executed at two European sites (Site 1, Site 2) and one site located in the US (Site 3). In addition, those same samples were used for evaluation of interferences.

## 5.1. Method Comparison

### 5.1.1. Method Comparison versus Reference Method

To assess the accuracy of the **cobas u** 701 microscopy analyzer, the method comparison study was performed with manual microscopy using KOVA slides as the comparator method utilizing clinical samples.

The tables below (Table 13 – Table 15) summarize the results of the method comparison studies performed between **cobas u** 701 microscopy analyzer and visual counting using the Kova chamber. All obtained statistical results from the single sites as well as for the compiled data sets were within the defined specifications and confirmed the substantial equivalence of the automated **cobas u** 701 microscopy analyzer with the manual Kova counting method.

Below is the compiled demographics and information about the age range at the study sites. As there are no known differences related to race and ethnicity, this information was not taken into consideration in the demographic information.

**Table 12: Sample Size and Distribution Measured at the Different Sites**

| Site | Sample size | Age Range | Female | Male | Pediatrics |
|---|---|---|---|---|---|
| All sites | 689 | 1 month – 98 years | 355 | 334 | 91 |
| Site 3 | 208 | 1 month – 98 years | 112 | 96 | 59 |
| Site 2 | 235 | 1 month – 92 years | 121 | 114 | 17 |
| Site 1 | 246 | 1.5 years – 89 years | 122 | 124 | 15 |

**Table 13: Method Comparison – Passing-Bablok Regression Analysis for Quantitative Parameters**

| Site | Parameter | N* | Range of values | | Passing Bablok regression | | Pearson's | | | Agreement rates (%)** | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | cobas u 701 | KOVA | Slope (LCL, UCL) | Intercept (LCL, UCL) | r | $R^2$ | p=value (r=0) | Neg | Pos |
| All sites | RBC | 305 | 5 - 1746 | 5 - 1769 | 1.00 (0.99, 1.01) | -0.67 (-1.65, 0.16) | 0.99 | 0.97 | <0.001 | 99% | 92% |
| | WBC | 384 | 5 - 806 | 5 - 875 | 0.98 (0.97, 0.99) | -0.99 (-1.91, 0.04) | 0.98 | 0.97 | <0.001 | 98% | 98% |

*includes all data within the defined measuring range on **cobas u** 701

**negative agreement calculation includes results below measuring range for RBC / WBC

**Table 14: Method Comparison – Agreement Rates for Semi-quantitative Parameters**

| Parameter | All sites | | | |
|---|---|---|---|---|
| | N | NPA (LCL) | PPA (LCL) | Cohen's Kappa |
| BAC | 680 | 97% (95%) | 95% (93%) | 0.88 |
| SEC | 670 | 97% (95%) | 99% (96%) | 0.86 |
| HYA | 672 | 98% (97%) | 94% (89%) | 0.83 |

NPA = negative percentage agreement; PPA = positive percentage agreement; LCL = lower confidence limit

**Table 15: Method Comparison – Agreement Rates for Qualitative Parameters**

| Parameter | All sites | | | |
|---|---|---|---|---|
| | N | NPA (LCL) | PPA (LCL) | Cohen's Kappa |
| **CRY** | 670 | 97% (95%) | 98% (93%) | 0.95 |
| **MUC** | 670 | 99% (98%) | 94% (91%) | 0.93 |
| **NEC** | 675 | 90% (88%) | 94% (88%) | 0.84 |
| **PAT** | 670 | 93% (91%) | 89% (80%) | 0.82 |
| **SPRM** | 670 | 95% (93%) | 94% (85%) | 0.89 |
| **YEA** | 670 | 97% (95%) | 91% (82%) | 0.88 |

NPA = negative percentage agreement; PPA = positive percentage agreement; LCL = lower confidence limit

## 5.2. Reference range

To establish reference values for Red Blood cells (RBC) and White Blood cells (WBC) on the **cobas u** 701 microscopy analyzer, "urine healthy" residual samples were measured. Measurements were performed at the three sites, each using one **cobas u** 701 microscopy analyzer and a total of four **cobas u** cuvette lots.

**Table 16: Reference Range Study Results for RBC**

| Site | Gender | N | Min | Max | Mean | Median | 97.5th percentile (90% CI) | 99th percentile (90% CI) |
|---|---|---|---|---|---|---|---|---|
| All sites Combined | Female | 310 | 0.00 | 7.92 | 1.20 | 0.88 | 6.16 (5.28, 7.92) | 7.92 (6.16, 7.92) |
| | Male | 311 | 0.00 | 9.68 | 1.13 | 0.00 | 6.16 (5.28, 7.92) | 7.92 (6.16, 9.68) |
| | Total | 621 | 0.00 | 9.68 | 1.16 | 0.00 | 6.16 (5.28, 7.92) | 7.92 (7.04, 7.92) |

**Table 17: Reference Range Study Results for WBC**

| Site | Gender | N | Min | Max | Mean | Median | 97.5th percentile (90% CI) | 99th percentile (90% CI) |
|---|---|---|---|---|---|---|---|---|
| All sites Combined | Female | 310 | 0.00 | 17.8 | 1.72 | 0.66 | 10.6 (7.26, 13.9) | 13.2 (11.9, 17.8) |
| | Male | 311 | 0.00 | 15.8 | 1.02 | 0.00 | 5.94 (5.28, 12.5) | 9.90 (5.94, 15.8) |
| | Total | 621 | 0.00 | 17.8 | 1.37 | 0.66 | 7.92 (5.94, 11.9) | 12.5 (9.90, 16.5) |

## 6. CONCLUSIONS

The submitted information in this premarket notification 510(k) supports a substantial equivalence decision for the **cobas u** 701 microscopy analyzer as compared to the predicate device.