February 12, 2026

Roche Diagnostics
Noel Mencias
Senior Regulatory Affairs Manager
9115 Hague Rd.
Indianapolos, Indiana 46250

Re: K253490
    Trade/Device Name: Glucose HK Gen.3; ONLINE DAT Methadone II; cobas pro integrated solutions
    Regulation Number: 21 CFR 862.1345
    Regulation Name: Glucose test system
    Regulatory Class: Class II
    Product Code: CFR, DJR, JJE
    Dated: November 14, 2025
    Received: November 14, 2025

Dear Noel Mencias:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13484 clause 8.3 (Nonconforming product), and ISO 13485 clause 8.5 (Corrective and preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

THOMAS C. MILLER -S

Date: 2026.02.12
14:43:07 -05'00'

for Paula Caposino, Ph.D.
Deputy Director
Division of Chemistry
 and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
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)*
K253490

Device Name
cobas pro integrated solutions;
Glucose HK Gen.3;
ONLINE DAT Methadone II

Indications for Use *(Describe)*
cobas pro integrated solutions is an automated analyzer, intended for running qualitative, semiquantitative, and quantitative clinical chemistry and immunochemistry assays as well as ion-selective measurements.

Glucose HK Gen.3 is an in vitro test for the quantitative determination of glucose in human serum, plasma, urine and CSF on cobas c systems. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and pancreatic islet cell tumors.

Methadone II (MDN2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of methadone in human urine on cobas c systems at a cutoff concentration of 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program. Semiquantitative assays are intended to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas chromatography/masspectrometry (GC-MS).

Methadone II provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. GC-MS is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

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.

510(k) Summary

cobas pro integrated solutions; Glucose HK Gen.3; ONLINE DAT Methadone II (K253490)

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

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Noel Mencias Phone: (463) 336-2546 Email: noel.mencias@roche.com
Date Prepared	October 24, 2025
Proprietary Name	Glucose HK Gen.3 ONLINE DAT Methadone II **cobas pro** integrated solutions
Common Name	Glucose HK Gen.3 ONLINE DAT Methadone II **cobas pro** integrated solutions
Classification Name	Hexokinase, Glucose Enzyme Immunoassay, Methadone Analyzer, Chemistry (photometric, discrete), for Clinical Use
Product Codes, Regulation Numbers	CFR, 21 CFR 862.1345 DJR 21 CFR 862.3620 JJE, 21 CFR 862.2160
Predicate Devices	Glucose HK Gen.3 ONLINE DAT Methadone II **cobas pro** integrated solutions
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmbH Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis, IN United States: 1823260

1.   DEVICE DESCRIPTION

cobas pro integrated solutions is an automated analyzer, intended for running qualitative, semiquantitative, and quantitative clinical chemistry and immunochemistry assays as well as ion-selective measurements**.**

The **cobas pro** integrated solutions consists of a high throughput core unit (sample supply unit and sample buffer unit) and can be configured with different analytical units for immunology, clinical chemistry, and electrolyte testing. The **cobas c** 703 analytical unit being added to **cobas pro** integrated solutions is a new clinical chemistry analyzer intended for the in-vitro quantitative/qualitative determination of analytes in body fluids.

Glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G-6-PDH) specifically oxidizes G-6-P to 6-phosphogluconate with the concurrent reduction of nicotinamide adenine dinucleotide (NAD) to nicotinamide adenine dinucleotide reduced (NADH). One micromole of NADH is produced for each micromole of glucose consumed. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance.

The Methadone assay is based on the kinetic interaction of microparticles in a solution (KIMS) as measured by changes in light transmission. In the absence of sample drug, soluble drug conjugates bind to antibody-bound microparticles, causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample drug, the absorbance increases.

When a urine sample contains the drug in question, this drug competes with the drug derivative conjugate for microparticle-bound antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample. Sample drug content is determined relative to the value obtained for a known cutoff concentration of drug.

2.   INDICATIONS FOR USE

cobas pro integrated solutions is an automated analyzer, intended for running qualitative, semiquantitative, and quantitative clinical chemistry and immunochemistry assays as well as ion-selective measurements.

Glucose HK Gen.3 is an in vitro test for the quantitative determination of glucose in human serum, plasma, urine and CSF on **cobas c** systems. Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and pancreatic islet cell tumors.

ONLINE DAT Methadone II (MDN2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of methadone in human urine on **cobas c** systems at a cutoff concentration of 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program. Semiquantitative assays are intended to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas chromatography/mass spectrometry (GC-MS).

3.   TECHNOLOGICAL CHARACTERISTICS

Table 1: Comparison of the cobas c 703 in cobas pro integrated solutions versus the predicate cobas c 503 in cobas pro integrated solutions

	Predicate cobas c 503 in cobas pro integrated solutions (K191899)	Candidate cobas c 703 in cobas pro integrated solutions (K253490)
Intended Use	Fully automated clinical chemistry analyzer intended for the in-vitro quantitative/qualitative determination of analytes in body fluids	Same
Measurement Principal	Absorbance Photometry (enzyme, substrate, proteins, DAT and TDM)	Same
Workflow Principle	Batch/random	Same
Throughput	1000 test/hr	2000 test/hr
Sample Handling		

	Predicate cobas c 503 in cobas pro integrated solutions (K191899)	Candidate cobas c 703 in cobas pro integrated solutions (K253490)
Typical Sample Volumes	1.0 – 25.0 µL	Same
Sample Types	Serum, plasma, urine, CSF and other depending on the chemistry test	Same
Sample Handling system	Input and transport of samples using universal sample racks, modular sample buffer (MSB) input, core/transportation unit and STAT port	Same
Sample Capacity Onboard	300	Same
Sample Identification	Barcode on the sample or position on the rack	Same
Reagent handling		
Reagent Volume	5-135 µL	Same
Reagent Container	**cobas c** pack green (plastic containers with conus screw caps)	Same
Reagent Access	Reagent cassette caps pierced onboard by the instrument	Same
Onboard Storage Temperature	10°C (Range 5-15°C)	Same
Reagent bottle/Cassette identification	RFID	Same
On board reagent storage capacity	60 positions	70 positions
System Cycle time measuring cell	3.6 seconds photometric	1.8 seconds photometric
Reagent Mix	Ultrasonic	Same
Automatic Rerun	Available	Same
Application information transfer to instrument	Via remote transfer (cobas Link) or CD	Same
Pipetting System		
Sample and Reagent Syringes	Rotation and Z robotic	Same
Reagent Probes	2 polished steel probes	4 polished steel probes
Sample Probes	Routine: 1 polished steel probe HbA1c in whole blood: 1 polished steel probe	2 polished steel probes, no HbA1c
Probe Cleaning	Automatic for all probes	Same

	Predicate **cobas c 503 in cobas pro** **integrated solutions** **(K191899)**	**Candidate** **cobas c 703 in cobas pro** **integrated solutions** **(K253490)**
Liquid Level Detection	Samples: capacitance Reagents: calculated level and counting	Same
Clot Detection	Yes	Same
Temperature Control	Circulating water bath at 37°C	Same
Reaction volume	Maximum 185 µL	Same
Volume ratios	Defined by master applications	Same
Sample and Reagent Syringes	Rotation and Z robotic	Same
Detection Information		
Spectrophotometer	Gradient photometer with discrete photodiodes in fixed array	Same
Detection Unit	Photometric/Turbidimetric/Fluorescence and Potentiometric	Same
Light source	Tungsten/halogen	LED
Light path	5.0 mm	Same
Measuring unit	1	1
Wavelengths (in nm)	340,376, 415, 450, 480, 505, 546, 570, 600, 660, 700, 800	Same
Calibration and Quality Control		
Calibrators & Control	CalSets and Controls	Same
Calibration Modes	linear and non-linear full calibration, 1- and 2-point recalibration, automatic lot calibration	Same
Calibration Stability	up to the shelf life of the reagent	Same
On-board QC	Optional	Same
Interfaces		
Host Interface	Ethernet (HL7)	Same
Printer	Laser	Same
Display	Touch screen without physical keyboard and mouse	Same
Software		
Software	**cobas pro** integrated solutions system software	Same
Configuration	Several analytical units with one PC and one core	Same

	Predicate cobas c 503 in cobas pro integrated solutions (K191899)	Candidate cobas c 703 in cobas pro integrated solutions (K253490)
Units Controlled	ISE, **c** 503, **e** 801	ISE, **c** 503, **c** 703, **e** 801
Function performed	Data Input, sample processing, result calculation, result reporting, quality control	Same
PC (Control Unit) Functions	Data input (keyboard, disc) data output (screen, printer, host)	Same
Core Unit Functions	**cobas pro** core with real time database, data input and output (via system software communication), control of sample conveyer	Same
Analytical Unit(s) Functions	Control of analytic processes (pipetting, incubation, detection) Primary Signal processing	Same
MSB Functions	Intermediate storage of sample racks	Same
Data Storage	Real time database in Core Unit (storage of System and Application parameters, Calibration Data, QC Data, Sample results, Alarm History)	Same
Software Controlled test countdown	Available	Same
Result Calculation	Automated measuring of signal for kinetic and endpoint methods according to cycle time and automated calculation of concentrations via calibration curve	Same
Flagging of Errors	Available	Same

Table 2: **Similarities and Differences between the Glucose HK Gen.3 on cobas c 703 and the Predicate Device**

	Predicate Glucose HK Gen. 3 on cobas c 503 (K191899)	Candidate Glucose HK Gen. 3 on cobas c 703 (K253490)
Proprietary name	Glucose HK Gen. 3	Glucose HK Gen. 3
Intended use	In vitro test for the quantitative determination of glucose in human serum, plasma, urine and CSF on **cobas c** systems.	In vitro test for the quantitative determination of glucose in human serum, plasma, urine and CSF on **cobas c** systems.
Technology	Photometric	Same
Test format	Enzymatic	Same
Test type	Quantitative	Same
Assay protocol	R1+R3+Diluent+Sample, incubation	Same
Pipetting volume sample	1.5 µL	Same
Pipetting volume R1	21 µL	Same
Pipetting volume R3	8 µL	Same
Sample types	Serum, plasma, urine and CSF	Same
Handling of R1 and R3	Liquid, ready to use	Same
Measuring Range	2 – 750 mg/dL (0.11 – 41.6 mmol/L)	Same

Table 3: **Similarities and Differences between the ONLINE DAT Methadone II on cobas c 703 and the Predicate Device**

	Predicate ONLINE DAT Methadone II on Roche/Hitachi Family (K021505)	Candidate ONLINE DAT Methadone II on cobas c 703 (K253490)
Methodology	KIMS, Kinetic interaction of microparticles in a solution	Same
Intended Use	Methadone II (MDN2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of methadone in human urine on automated clinical chemistry analyzers at a cutoff concentration of 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess	Methadone II (MDN2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of methadone in human urine on **cobas c** systems at a cutoff concentration of 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality

	Predicate ONLINE DAT Methadone II on Roche/Hitachi Family (K021505)	Candidate ONLINE DAT Methadone II on cobas c 703 (K253490)
	assay performance as part of a quality control program.	control program. Semiquantitative assays are intended to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas chromatography/mass spectrometry (GC-MS).
Sample Type	Urine	Urine
Reagents	Conjugate Working Solution: Conjugated methadone derivative in buffer with BSA and preservative. Antibody/Microparticle Working Solution: Microparticles coated with methadone monoclonal antibody (mouse) in buffer with BSA and preservative.	Same
Controls	Control Set DAT I: includes PreciPos DAT Set I and PreciNeg DAT Set I Control Set DAT Clinical: includes PreciPOS DAT Clinical and PreciNeg DAT Clinical	Same
Calibrators	Preciset DAT Plus I Calibrator Set	Preciset DAT Plus I calibrators C.f.a.s. DAT Qualitative Plus C.f.a.s. DAT Qualitative Plus Clinical
Qualitative and Semi-Quantitative cutoffs	300 ng/mL	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

The non-clinical performance studies for Glucose HK Gen.3 and ONLINE DAT Methadone II are summarized below.

4.1. Precision

4.1.1. Repeatability and Intermediate Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 703 analyzer.

Table 4: Summary of GLUC3 Precision Results – Serum/Plasma

Repeatability			
Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)
PCCC1	104	0.400	0.4
PCCC2	254	1.11	0.4
Serum 1	4.018	0.0948	2.4
Serum 2	67.9	0.371	0.5
Serum 3	112	0.568	0.5
Serum 4	389	1.48	0.4
Serum 5	741	3.84	0.5
Intermediate Precision			
Sample	Mean (mg/dL)	SD (mg/dL)	CV (%)
PCCC1	104	0.782	0.8
PCCC2	254	1.91	0.8
Serum 1	4.04	0.104	2.6
Serum 2	67.9	0.494	0.7
Serum 3	112	1.07	1.0
Serum 4	389	1.87	0.5
Serum 5	741	5.05	0.7

Table 5: Summary of GLUC3 Precision Results – Urine

Repeatability			
Sample	**Mean (mg/dL)**	**SD (mg/dL)**	**CV (%)**
LiQ_UR1	27.2	0.267	1.0
LiQ_UR2	290	1.75	0.6
Sample 1	3.80	0.263	6.9
Sample 2	13.8	0.207	1.5
Sample 3	69.7	0.407	0.6
Sample 4	375	1.802	0.5
Sample 5	730	3.32	0.5
Intermediate Precision			
Sample	**Mean (mg/dL)**	**SD (mg/dL)**	**CV (%)**
LiQ_UR1	27.2	0.297	1.1
LiQ_UR2	290	2.41	0.8
Sample 1	3.80	0.263	6.9
Sample 2	13.8	0.225	1.6
Sample 3	69.7	0.568	0.8
Sample 4	375	2.22	0.6
Sample 5	730	4.09	0.6

Table 6: Summary of GLUC3 Precision Results – CSF

Repeatability			
Sample	**Mean (mg/dL)**	**SD (mg/dL)**	**CV (%)**
LiQ_CSF1	57.3	0.303	0.5
LiQ_CSF2	29.6	0.231	0.8
Sample 1	4.47	0.254	5.7
Sample 2	37.8	0.234	0.6
Sample 3	70.8	0.335	0.5
Sample 4	375	1.75	0.5
Sample 5	726	3.08	0.4
Intermediate Precision			
Sample	**Mean (mg/dL)**	**SD (mg/dL)**	**CV (%)**
LiQ_CSF1	57.3	0.368	0.6
LiQ_CSF2	29.6	0.254	0.9
Sample 1	4.47	0.265	5.9
Sample 2	37.8	0.335	0.9
Sample 3	70.8	0.402	0.6
Sample 4	375	2.78	0.7
Sample 5	726	4.23	0.6

Table 7: Summary of MDN2 Precision Results, Repeatability and Intermediate Precision – Semi Quantitative

Repeatability			
Sample	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Sample -100% (zero)	15.1	13.7	90.6
Sample -75%	113	6.12	5.4
Sample -50%	170	5.94	3.5
DAT1N	238	6.82	2.9
DATCN	239	7.69	3.2
Cutoff	295	10.2	3.5
DAT1P	407	13.2	3.2
DATCP	393	12.1	3.1
Sample +50%	489	23.2	4.7
Sample +75%	579	20.3	3.5
Sample +100%	652	28.7	4.4
Intermediate Precision			
Sample	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Sample -100% (zero)	15.3	16.1	105.0
Sample -75%	113	9.97	8.8
Sample -50%	165	12.3	7.5
DAT1N	242	10.9	4.5
DATCN	239	11.4	4.8
Cutoff	296	22.5	7.6
DAT1P	407	18.4	4.5
DATCP	401	18.2	4.5
Sample +50%	505	31.5	6.2
Sample +75%	579	30.6	5.3
Sample +100%	635	36.7	5.8

Table 8: Summary of MDN2 Precision Results, Repeatability and Intermediate Precision – Qualitative

Reagent Lot: Lot 1	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 2	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 3	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100

Table 9: Summary of MDN2 Precision Results, Repeatability and Intermediate Precision – Qualitative Plus

Reagent Lot: Lot 1	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 2	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 3	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100

Table 10: Summary of MDN2 Precision Results, Repeatability and Intermediate Precision – Qualitative Plus Clinical

Reagent Lot: Lot 1	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 2	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100
Reagent Lot: Lot 3	21 Days	2 Runs	2 Aliquots		
Specimen	**N**	**NEG**	**POS**	**Crossover (N)**	**Agreement (%)**
Sample -100% (zero)	84	84	0	0	100
Sample -75%	84	84	0	0	100
Sample -50%	84	84	0	0	100
DAT1N	84	84	0	0	100
DATCN	84	84	0	0	100
Cutoff	84	n.a.	n.a.	n.a.	n.a.
DAT1P	84	0	84	0	100
DATCP	84	0	84	0	100
Sample +50%	84	0	84	0	100
Sample +75%	84	0	84	0	100
Sample +100%	84	0	84	0	100

4.2. Analytical Sensitivity

The Limit of Blank (LoB) of the Glucose HK Gen.3 assay on the **cobas c** 703 analyzer was determined according to CLSI EP17-A2. The LoB is the highest observed measurement value for an analyte-free sample. The Limit of Blank was determined as the 95th percentile of measurements of blank samples.

The Limit of Detection (LoD) of the Glucose HK Gen.3 assay on the **cobas c** 703 analyzer was determined according to CLSI EP17-A2. The LoD determines the lower limit for samples with analyte. The LoD was determined as the lowest amount of analyte in a sample that can be detected with a 95% probability.

The Limit of Quantitation (LoQ) of the Glucose HK Gen.3 assay was determined according to CLSI EP17-A2. LoQ determines the lowest amount of analyte that can be quantitatively determined with stated accuracy and stated experimental conditions. The LoQ was determined as the lowest concentration of analyte which can be quantified with a total error of no more than 20%.

Table 11: Summary of GLUC3 Analytical Sensitivity Results

Serum	
Limit of Blank	0.350 mg/dL (0.0194 mmol/L)
Limit of Detection	0.487 mg/dL (0.0270 mmol/L)
Limit of Quantitation	1.517 mg/dL (0.0842 mmol/L)
Urine	
Limit of Blank	0.777 mg/dL (0.0431 mmol/L)
Limit of Detection	1.160 mg/dL (0.0644 mmol/L)
Limit of Quantitation	1.160 mg/dL (0.0644 mmol/L)
CSF	
Limit of Blank	0.337 mg/dL (0.0187 mmol/L)
Limit of Detection	0.506 mg/dL (0.0281 mmol/L)
Limit of Quantitation	1.454 mg/dL (0.0807 mmol/L)

4.3. Linearity/Assay Reportable Range

Linearity studies were conducted to demonstrate that measurements across the claimed measuring range for each parameter are linear. The studies were performed according to CLSI guideline EP06-Ed2. Linearity was confirmed for the following measuring ranges:

GLUC3

Serum, plasma, urine and CSF

0.11-41.6 mmol/L (2-750 mg/dL)

MDN2

Urine

39.3 to 2081 ng/mL

Summary of MDN2 Linearity Results According to CLSI EP06-ED2:

Low end of linear range found:	37.0
High end of linear range found:	2255
Intercept:	0
Slope:	1.0040
Pearson's r:	0.9988
R^2:	0.991

4.4. Dilution

Post Dilution Check experiments were conducted to verify the automatic rerun function of the **cobas c** 703 analytical unit. Post Dilution studies for GLUC3 confirmed the 1:2 dilution of samples via rerun function.

4.5. Endogenous Interferences

The effects of interference by endogenous substances on Glucose HK Gen.3 and ONLINE DAT Methadone II were determined on the **cobas c** 703 analytical unit using, where applicable, human serum/plasma, urine, and CSF spiked with varying levels of interferent.

Table 12: Summary of GLUC3 Endogenous Interferences – Serum/Plasma

Potential Interferent	No Interference up to	Observed Sample Conc (mmol/L)
Albumin [Level 1]	63.3 [g/L]	2.17
Albumin [Level 2]	62.3 [g/L]	12.3
Conjugated Bilirubin [Level 1]	64 [Index]	2.17
Conjugated Bilirubin [Level 2]	79 [Index]	12.4
Hemolysis [Level 1]	1213 [Index]	2.14
Hemolysis [Level 2]	1228 [Index]	12.4
Immunoglobulin G [Level 1]	65.1 [g/L]	2.17
Immunoglobulin G [Level 2]	65.4 [g/L]	12.4
Lipemia [Level 1]	1134 [Index]	2.17
Lipemia [Level 2]	1102 [Index]	12.3
Unconjugated Bilirubin [Level 1]	77 [Index]	2.18
Unconjugated Bilirubin [Level 2]	90 [Index]	12.2

Table 13: Summary of GLUC3 Endogenous Interferences – Urine

Potential Interferent	No Interference up to	Observed Sample Conc (mmol/L)
Albumin [Level 1]	2.70 [g/L]	2.28
Albumin [Level 2]	3.10 [g/L]	12.5
Calcium [Level 1]	12.6 [mmol/L]	2.29
Calcium [Level 2]	13.5 [mmol/L]	12.5
Citrate [Level 1]	12.0 [mmol/L]	2.28
Citrate [Level 2]	12.2 [mmol/L]	12.5
Creatinine [Level 1]	91.9 [mmol/L]	2.28
Creatinine [Level 2]	89.7 [mmol/L]	12.5
Hemolysis [Level 1]	946 [Index]	2.31
Hemolysis [Level 2]	876 [Index]	12.1
Immunoglobulin G [Level 1]	1.10 [g/L]	2.29
Immunoglobulin G [Level 2]	1.30 [g/L]	12.4
Magnesium [Level 1]	27.3 [mmol/L]	2.29
Magnesium [Level 2]	28.9 [mmol/L]	12.5
Oxalate [Level 1]	2.70 [mmol/L]	2.27
Oxalate [Level 2]	2.70 [mmol/L]	12.5
Phosphate [Level 1]	139 [mmol/L]	2.29

Phosphate [Level 2]	137 [mmol/L]	12.5
Urea [Level 1]	1836 [mmol/L]	2.27
Urea [Level 2]	1825 [mmol/L]	12.5
Uric acid [Level 1]	6.00 [mmol/L]	2.30
Uric acid [Level 2]	7.50 [mmol/L]	12.5
Urobilinogen [Level 1]	0.250 [mmol/L]	2.30
Urobilinogen [Level 2]	0.250 [mmol/L]	12.3

Table 14: Summary of GLUC3 Endogenous Interferences – CSF

Potential Interferent	No Interference up to	Observed Sample Conc (mmol/L)
Conjugated Bilirubin [Level 1]	75 [Index]	2.21
Conjugated Bilirubin [Level 2]	66 [Index]	12.3
Hemolysis [Level 1]	1201 [Index]	2.21
Hemolysis [Level 2]	1259 [Index]	12.2

Table 15: Summary of MDN2 Endogenous Interferences – Urine

Compound	Concentration
Acetone	1000 mg/dL
Ascorbic acid	1500 mg/dL
Albumin	500 mg/dL
Bilirubin	25 mg/dL
Calcium	133 mg/dL
Creatinine	500 mg/dL
Ethanol	1000 mg/dL
Glucose	2000 mg/dL
Hemoglobin	750 mg/dL
IgG	110 mg/dL
Magnesium	238 mg/dL
NaCl	5800 mg/dL
Oxalate	200 mg/dL
pH	3.9–9.1
Phosphate	2028 mg/dL
Sodium citrate, dihydrate	323.51 mg/dL
Specific Gravity	1.001–1.035 g/mL
Urea	6000 mg/dL
Uric Acid	100.86 mg/dL
Urobilinogen	14.82 mg/dL

4.6. Exogenous Interferences – Drugs

Drug Interference studies were conducted to evaluate drugs for potential interference with Glucose HK Gen.3 and ONLINE TDM Methadone II measured on the **cobas c** 703 analytical unit. The following interference claims were verified:

Table 16: Drug Interferences GLUC3, Level 1 – Serum/Plasma

Drug	Drug Conc 1 [mg/L]	Analyte Mean Reference [mmol/L]	Analyte Mean Conc of Spiked Sample [mmol/L]	Recovery [%]
N-Acetylcysteine	150	2.21	2.22	100.5
Acetylsalicylic acid	30	2.21	2.21	100.0
Ampicillin-Na	75	2.21	2.21	100.0
Ascorbic acid	52.5	2.21	2.21	100.0
Cefoxitin	750	2.21	2.21	100.1
Doxycyclin	18	2.21	2.21	99.7
Heparin	3300 IU/L	2.21	2.22	100.2
Levodopa	7.5	2.21	2.22	100.3
Methyldopa	22.5	2.21	2.22	100.3
Metronidazole	123	2.21	2.23	100.6
Rifampicin	48	2.21	2.22	100.2
Acetaminophen	156	2.19	2.18	99.6
Cyclosporine	1.8	2.19	2.19	99.9
Ibuprofen	219	2.19	2.18	99.7
Theophylline	60	2.19	2.19	100.0
Phenylbutazone	321	2.15	2.16	100.4

Table 17: Drug Interferences GLUC3, Level 1 – Urine

Drug	Drug Conc 1 [mg/L]	Analyte Mean Reference [mmol/L]	Analyte Mean Conc of Spiked Sample [mmol/L]	Recovery [%]
Acetaminophen	3000	2.29	2.27	99.2
N-Acetylcysteine	10	2.29	2.27	99.5
Ascorbic acid	4000	2.29	2.28	99.7
Cefoxitin	12000	2.29	2.26	99.0
Gentamycine sulfate	400	2.29	2.26	99.0
Levodopa	1000	2.29	2.29	100.1
Methyldopa	2000	2.29	2.28	99.9
Ofloxacine	900	2.29	2.21	96.9

Ibuprofen	4000	2.13	2.19	103.1
Phenazopyridine	300	2.13	2.12	99.6
Salicyluric acid	6000	2.13	5.01	235.3
Tetracycline	300	2.26	1.98	87.9
Drug	**Drug Conc 2 [mg/L]**	**Analyte Mean Reference [mmol/L]**	**Analyte Mean Conc of Spiked Sample [mmol/L]**	**Recovery [%]**
Salicyluric acid	100	2.27	2.34	103.0
Tetracycline	100	2.21	2.21	100.0

Table 18: Drug Interferences GLUC3, Level 2 – Urine

Drug	**Drug Conc 1 [mg/L]**	**Analyte Mean Reference [mmol/L]**	**Analyte Mean Conc of Spiked Sample [mmol/L]**	**Recovery [%]**
Acetaminophen	3000	12.2	12.1	99.2
N-Acetylcysteine	10	12.2	12.2	99.7
Ascorbic acid	4000	12.2	12.2	99.8
Cefoxitin	12000	12.2	12.2	99.8
Gentamycine sulfate	400	12.2	12.2	100.2
Levodopa	1000	12.2	12.2	100.0
Methyldopa	2000	12.2	12.2	99.7
Ofloxacine	900	12.2	12.2	99.5
Ibuprofen	4000	11.3	11.8	103.9
Phenazopyridine	300	11.3	11.7	103.2
Salicyluric acid	6000	11.3	14.5	127.9
Tetracycline	300	11.6	11.5	99.7
Salicyluric acid	100	12.2	12.2	100.7

Table 19: Drug Interferences MDN2, Semi-Quantitative (MD3S0); Qualitative (MD3Q0); Qualitative Plus Clinical (MD3QC); Qualitative Plus (MD3QP) – Urine

Reagent Lot: Lot 1			
Compound	**Concentration (ng/mL)**	**Sample -25%**	**Sample +25%**
Acetaminophen	3000000	No crossover	No crossover
Acetyl cysteine	10000	No crossover	No crossover
Acetylsalicylic acid	100000	No crossover	No crossover
Aminopyrine	100000	No crossover	No crossover
Amitriptyline	100000	No crossover	No crossover
Ampicillin	100000	No crossover	No crossover
Ascorbic acid	4000000	No crossover	No crossover
Aspartame	100000	No crossover	No crossover
Atropine	100000	No crossover	No crossover
Benzocaine	100000	No crossover	No crossover
Caffeine	100000	No crossover	No crossover
Calcium dobesilate	100000	No crossover	No crossover
Calcium hypochlorite	100000	No crossover	No crossover
Carbamazepine	100000	No crossover	No crossover
Cefoxitin	12000000	No crossover	No crossover
Chloroquine	100000	No crossover	No crossover
Chlorpheniramine	100000	No crossover	No crossover
Cotinine	100000	No crossover	No crossover
Cyclobenzaprine	100000	No crossover	No crossover
Cyproheptadine	100000	No crossover	No crossover
d-Ephedrine	100000	No crossover	No crossover
Desipramine	100000	No crossover	No crossover
Diphenylhydantoin	100000	No crossover	No crossover
dl-Ephedrine	100000	No crossover	No crossover
Dopamine	100000	No crossover	No crossover
Doxepin	100000	No crossover	No crossover
Doxylamine	100000	No crossover	No crossover
d-Phenylpropanolamine	100000	No crossover	No crossover
d-Pseudoephedrine	100000	No crossover	No crossover
Erythromycin	100000	No crossover	No crossover
Estriol	100000	No crossover	No crossover
Fenoprofen	100000	No crossover	No crossover
Fluoxetine	100000	No crossover	No crossover
Furosemide	100000	No crossover	No crossover
Gentamicin sulfate	400000	No crossover	No crossover
Gentisic acid	100000	No crossover	No crossover
Guaiacol glycerol ether	100000	No crossover	No crossover
Haloperidol	100000	No crossover	No crossover
Hydrochlorothiazide	100000	No crossover	No crossover
Ibuprofen	4000000	No crossover	No crossover
Isoproterenol	100000	No crossover	No crossover
Ketamine	100000	No crossover	No crossover

Compound	Concentration (ng/mL)	Sample -25%	Sample +25%
l-Ephedrine	100000	No crossover	No crossover
Levodopa	1000000	No crossover	No crossover
Lidocaine	100000	No crossover	No crossover
l-Norpseudoephedrine	100000	No crossover	No crossover
Maprotiline	100000	No crossover	No crossover
Melanin	100000	No crossover	No crossover
Methyldopa	2000000	No crossover	No crossover
Mianserin	100000	No crossover	No crossover
Naloxone	100000	No crossover	No crossover
Naltrexone	100000	No crossover	No crossover
Naproxen	100000	No crossover	No crossover
Niacinamide	100000	No crossover	No crossover
Nicotine	100000	No crossover	No crossover
Nordoxepin	100000	No crossover	No crossover
Norethindrone	100000	No crossover	No crossover
Ofloxacine	90000	No crossover	No crossover
Penicillin G	100000	No crossover	No crossover
Phenazopyridine	300000	No crossover	No crossover
Phenetylamine	100000	No crossover	No crossover
Phenothiazine	100000	No crossover	No crossover
Phenylbutazone	100000	No crossover	No crossover
Phenylpropanolamine	100000	No crossover	No crossover
Procaine	100000	No crossover	No crossover
Quinidine	100000	No crossover	No crossover
Quinine	100000	No crossover	No crossover
Salicyluric acid	6000000	No crossover	No crossover
Sulindac	100000	No crossover	No crossover
Tetracycline	300000	No crossover	No crossover
Tetrahydrozoline	100000	No crossover	No crossover
Tramadol	20000	No crossover	No crossover
Trifluoperazine	100000	No crossover	No crossover
Tyramine	100000	No crossover	No crossover
Reagent Lot: Lot 2			
Compound	**Concentration (ng/mL)**	**Sample -25%**	**Sample +25%**
Amobarbital	100000	No crossover	No crossover
Benzoylecgonine	100000	No crossover	No crossover
Benzphetamine	100000	No crossover	No crossover
Butabarbital	100000	No crossover	No crossover
Chlordiazepoxide	100000	No crossover	No crossover
Cocaine	100000	No crossover	No crossover
Codeine	100000	No crossover	No crossover
d-Amphetamin	100000	No crossover	No crossover
Dextrometorphan	100000	No crossover	No crossover
Dextropropoxyphene	100000	No crossover	No crossover
Diazepam	100000	No crossover	No crossover
Diphenhydramine	100000	No crossover	No crossover
Disopyramide	100000	No crossover	No crossover
d-Methamphetamine	100000	No crossover	No crossover

Compound	Concentration (ng/mL)	Sample -25%	Sample +25%
Ecgonine	100000	No crossover	No crossover
Ecgonine methyl ester	100000	No crossover	No crossover
EDDP	100000	No crossover	No crossover
EMDP	100000	No crossover	No crossover
Epinephrine	100000	No crossover	No crossover
Glutethimide	100000	No crossover	No crossover
Imipramine	100000	No crossover	No crossover
l-Amphetamine	100000	No crossover	No crossover
l-Methamphetamine	100000	No crossover	No crossover
l-Pseudoephedrine	100000	No crossover	No crossover
LSD	100000	No crossover	No crossover
MDA	100000	No crossover	No crossover
MDMA	100000	No crossover	No crossover
Meperidine	100000	No crossover	No crossover
Methaqualone	100000	No crossover	No crossover
Methylphenidate	100000	No crossover	No crossover
Morphine	100000	No crossover	No crossover
Nordiazepam	100000	No crossover	No crossover
Nortriptyline	100000	No crossover	No crossover
Orphenadrine	100000	No crossover	No crossover
Oxazepam	100000	No crossover	No crossover
Pentobarbital	100000	No crossover	No crossover
Perphenazine	100000	No crossover	No crossover
Phencyclidine	100000	No crossover	No crossover
Phenobarbital	100000	No crossover	No crossover
Phentermine	100000	No crossover	No crossover
Protriptyline	100000	No crossover	No crossover
Quetiapine-Carboxylic acid	500000	No crossover	No crossover
Quetiapine-Fumarat	750000	No crossover	No crossover
Quetiapine-Sulfoxid	500000	No crossover	No crossover
Secobarbital	100000	No crossover	No crossover
THC-9-carboxylic acid	100000	No crossover	No crossover
Verapamil	100000	No crossover	No crossover
Reagent Lot: Lot 6			
Compound	**Concentration (ng/mL)**	**Sample -25%**	**Sample +25%**
Disopyramide	1000000	No crossover	No crossover

4.7. Cross Reactivity

The effects of interference by endogenous interferences were conducted on one **cobas c** 703 using one lot, one human sample per concentration level, in one run, ≥2 replicates per sample.

Table 20: Cross Reactivity Results MDN2

Cross Reactant	Cross Reactivity (%)
Lu AA34443	7.66
Vortioxetine	4.59
Cyamemazine	4.12
Methotrimeprazine (Levomepromazine)	3.47
Chlorpromazine	0.97
Thiothixene	0.39
Clomipramine	0.17
Thioridazine	0.15
Promazine	0.14
Promethazine	0.074
Trimipramine	0.052
Chlorprothixene	0.045

4.8. Sample Matrix Comparison

The recovery of analyte values in the presence of anticoagulants with the Glucose HK Gen.3 assay was determined on the **cobas c** 703 analytical unit by comparing values obtained from samples drawn into serum and plasma collection tubes. The following results were obtained.

Table 21: Summary of Matrix Comparison Passing/Bablok Results

Anticoagulant	Slope	Intercept (mg/dL)	Correlation Coefficient	Concentration of Samples (mg/dL)
Serum vs. Serum/gel separation tube	1.007	-0.432	1.000	3.17-737
Serum vs. K2-EDTA plasma	1.003	-0.0771	0.999	3.17-737

Anticoagulant	Slope	Intercept (mg/dL)	Correlation Coefficient	Concentration of Samples (mg/dL)
Serum vs. Li-Heparin plasma	1.031	-1.59	0.999	3.17-737
Serum vs. NaF/K-Oxalate plasma	1.025	-1.25	1.000	3.17-737
Serum vs. NaF/Na2-EDTA plasma	1.037	-1.78	0.999	3.17-737
Serum vs. KF/Na2-EDTA plasma	1.028	-0.587	0.999	3.17-737
Serum vs. NaF/Citrate/Na2-EDTA plasma	1.005	1.87	0.999	2.88-730

4.9.   Method Comparison to Predicate

Method Comparison experiments were performed for all sample types using the Glucose HK Gen.3 assay on the **cobas c** 703 versus the Glucose HK Gen.3 assay on the **cobas c** 503 to assess the bias between the two analytical units.

The results can be found below:

Table 22: Summary of GLUC3 Method Comparison Data – Serum/Plasma

Quality Characteristic	Result
Slope (Passing/Bablok)	0.995
Intercept (Passing/Bablok)	-0.0968
Bias (%) at medical decision point 1	-0.6
Coefficient of correlation (Pearson (r))	1.000
Slope (Linear Regression)	0.999
Intercept (Linear Regression)	-0.216
Coefficient of correlation (Kendall (Tau))	0.990
Sample concentration	3.60 - 724
Number of samples (n)	74

Table 23: Summary of GLUC3 Method Comparison Data – Urine

Quality Characteristic	Result
Slope (Passing/Bablok)	0.998
Intercept (Passing/Bablok)	0.209
Bias (%) at medical decision point 1	0.9
Coefficient of correlation (Pearson (r))	1.000
Slope (Linear Regression)	1.001
Intercept (Linear Regression)	0.214
Coefficient of correlation (Kendall (Tau))	0.950
Sample concentration	2.04 - 730
Number of samples (n)	67

Table 24: Summary of GLUC3 Method Comparison Data – CSF

Quality Characteristic	Result
Slope (Passing/Bablok)	0.987
Intercept (Passing/Bablok)	-0.234
Bias (%) at medical decision point 1	-1.9
Coefficient of correlation (Pearson (r))	1.000
Slope (Linear Regression)	0.989
Intercept (Linear Regression)	-0.259
Coefficient of correlation (Kendall (Tau))	0.984
Sample concentration	2.78 - 730
Number of samples (n)	75

87 urine samples, obtained from a clinical laboratory, where they screened negative in a drug test panel, were evaluated with the Methadone II assay. 97.7 % of these normal urines were negative relative to the 300 ng/mL cutoff. 79 urine samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay, were subsequently confirmed by GC-MS and were evaluated with the Methadone II assay. The following results were obtained with the Methadone II assay on the **cobas c** 703 analyzer relative to the GC-MS values.

Table 25: Summary of MDN2 Method Comparison versus GC/MS – Semi-Quantitative

		GC-MS values (ng/mL)			
		Negative samples	Near cutoff samples		Positive samples
		0-< 150	150-< 300	300-450	> 450
cobas c 703 analyzer	+	0	2	15	62
	-	59	26	2	0

Clinical samples were evaluated with this assay on a **cobas c** 703 analyzer and on a **cobas c** 503 analyzer. 50 urine samples screened negative for methadone on a **cobas c** 503 analyzer were evaluated with the Methadone II assay on a **cobas c** 703 analyzer. 100 % of these normal urines were negative on both the **cobas c** 703 analyzer and the **cobas c** 503 analyzer. 50 urine samples, obtained from a clinical laboratory where they screened preliminary positive with a commercially available immunoassay were subsequently confirmed by GC-MS and evaluated with the Methadone II assay on a **cobas c** 703 analyzer. 100 % of the samples were positive on both the **cobas c** 503 analyzer and the **cobas c** 703 analyzer.

Table 26: Summary of MDN2 Method Comparison cobas c 703 versus cobas c 503 – Semi-Quantitative

Methadone II correlation (cutoff = 300 ng/mL)		cobas c 503 analyzer	
		+	-
cobas c 703 analyzer	+	50	0
	-	0	50

4.10. Stability

The stability studies and acceptance criteria have been reviewed and found to be acceptable. The stability data supports Roche Diagnostic's claims as reported in the package labeling.

5. ADDITIONAL INFORMATION

The Glucose HK Gen.3 assay is intended to be used with the following:

- Calibrator f.a.s.
- PreciControl ClinChem Multi 1
- PreciControl ClinChem Multi 2
- Diluent NaCl 9 %

The ONLINE DAT Methadone II assay is intended to be used with the following:

- Preciset DAT Plus I
- C.f.a.s. DAT Qualitative Plus
- C.f.a.s. DAT Qualitative Plus Clinical
- Control Set DAT I
- Control Set DAT Clinical

6. CONCLUSIONS

The analytical performance data for Glucose HK Gen.3 and ONLINE DAT Methadone II on **cobas pro** integrated solutions support a substantial equivalence decision.