December 23, 2022

Roche Diagnostics
Khoa Tran
Regulatory Affairs Program Manager
9115 Hague Road
Indianapolis, IN 46250

Re: K221765
Trade/Device Name: ONLINE DAT Benzodiazepines II
Regulation Number: 21 CFR 862.3170
Regulation Name: Benzodiazepine test system
Regulatory Class: Class II
Product Code: JXM
Dated: June 15, 2022
Received: June 17, 2022

Dear Khoa Tran:

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,

Paula Caposino -S
Digitally signed by Paula Caposino -S
Date: 2022.12.23 09:13:01 -05'00'

Paula Caposino, Ph.D.
Acting 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)*
K221765

Device Name
ONLINE DAT Benzodiazepines II

Indications for Use *(Describe)*
Benzodiazepines II (BNZ2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of benzodiazepines in human urine on cobas c systems at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 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), or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS).
Benzodiazepines 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. Gas chromatography/mass spectrometry (GC-MS) or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/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.

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ONLINE DAT Benzodiazepines II
K221765 - 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 ONLINE DAT Benzodiazepines II

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Khoa Tran Phone: (317) 946-7843 Email: khoa.tran@roche.com Secondary Contact Name: Leslie Patterson Phone: (317) 225-8563 Email: leslie.patterson@roche.com
Date Prepared	June 6, 2022
Proprietary Name	ONLINE DAT Benzodiazepines II
Common Name	Benzodiazepines Enzyme Immunoassay
Classification Name and Panel	Benzodiazepine Test System, 91 – Toxicology
Product Codes, Regulation Numbers	JXM, Class II, 21 CFR 862. 3170
Predicate Devices	ONLINE DAT Benzodiazepines Plus
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmBH Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis, IN United States: 1823260.

1. DEVICE DESCRIPTION

The Benzodiazepines II assay is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL and 300 ng/mL. The semi quantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.

1.1. ONLINE DAT Benzodiazepines II

The device consists of two wet reagents which contain the key components of the immunoassay; monoclonal/ polyclonal antibody against the drug, substrate, and enzyme-labeled drug (conjugate).

2. INDICATIONS FOR USE

Benzodiazepines II (BNZ2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of benzodiazepines in human urine on cobas c systems at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 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), or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS).

Benzodiazepines 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. Gas chromatography/mass spectrometry (GC-MS) or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/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.

3. TECHNOLOGICAL CHARACTERISTICS

The 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, free antibody binds to drug-microparticle conjugates causing the formation of particle aggregates that are photometrically detected by turbidity measurements. 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 particle-bound drug derivative for free 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.

The presence of β-glucuronidase enzyme enhances the Benzodiazepines II assay cross-reactivity to some of the glucuronidated metabolites. Enzymatic cleavage makes the benzodiazepine part of the glucuronides more accessible for the antibody.

The assay consists of two liquid reagents. Benzodiazepines antibody buffer and conjugated benzodiazepine derivative microparticles.

The following table compare the ONLINE DAT Benzodiazepines II with its predicate device, ONLINE DAT Benzodiazepines Plus (k043327).

Table 1: Technical Characteristics Comparison Table between ONLINE DAT Benzodiazepines II and ONLINE DAT Benzodiazepines Plus

Feature	Candidate Device ONLINE DAT Benzodiazepines II	Predicate Device ONLINE DAT Benzodiazepines Plus (k043327)
Intended Use	Benzodiazepines II (BNZ2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of benzodiazepines in human urine on Roche/Hitachi cobas c systems at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program. Benzodiazepines 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. Gas chromatography/mass spectrometry (GC-MS) or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/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.	The ONLINE DAT Benzodiazepines Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of benzodiazepines in human urine on automated clinical chemistry analyzers at cutoff concentrations of 100 ng/mL, 200 ng/mL, and 300 ng/mL. Semi-quantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.
Detection Method	KIMS, Kinetic interaction of microparticles in a solution	Same
Instrument Platform	cobas c 501	Mod P
Test Matrix	Urine	Same
Measured Analyte	Benzodiazepine and its metabolites	Benzodiazepine
Cutoff Levels	100 ng/mL, 200 ng/mL and 300 ng/mL	Same
Reagent Stability	2-8 °C until expiration date	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

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

- Precision according to CLSI EP5-A3
- Linearity according to CLSI EP6-A
- Analytical Specificity/Cross-Reactivity
- Endogenous Interferences
- Interference - Drugs
- Interference Testing of Specific Gravity and pH
- Method Comparison to Predicate
- Stability

All performance specifications were met.

4.1. Precision

4.1.1. Repeatability and Intermediate Precision

The precision study was performed using CLSI Guideline EP05-A3 as a guideline. Precision experiments were conducted using one reagent lot on one **cobas c** 501 instrument. Testing was carried out for 21 days with two runs per day, and two replicates per run in both Qualitative and Semi-quantitative modes, giving a total of 84 determinants (n = 84). Drug-free negative urine was spiked with Oxazepam to final concentrations of -50%, -25%, below cutoff and +25%, +50% above cutoff.

100 ng/mL SQ Repeatability	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Urine -50%	45.0	2.56	5.7
Urine -25%	68.8	2.44	3.6

DAT2N (control 75 ng/mL)	78.8	1.99	2.5
Cutoff Urine	99.7	2.38	2.4
Urine +25%	123	2.43	2.0
DAT2P (control 125 ng/mL)	127	2.24	1.8
Urine +50%	146	2.59	1.8
Intermediate Precision	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Urine -50%	45.0	2.79	6.2
Urine -25%	68.8	2.65	3.9
DAT2N (control 75 ng/mL)	78.8	2.79	3.5
Cutoff Urine	99.7	2.63	2.6
Urine +25%	123	2.92	2.4
DAT2P (control 125 ng/mL)	127	3.21	2.5
Urine +50%	146	2.94	2.0

100 ng/mL Qualitative	**Number Tested**	**Negative/Positive**	**Confidence Level**
Urine -50%	84	84/0	> 95 % negative reading
Urine -25%	84	84/0	> 95 % negative reading
DAT2N (control 75 ng/mL)	84	84/0	> 95 % negative reading

Cutoff Urine	84	73/11	N/A
Urine +25%	84	0/84	> 95 % positive reading
DAT2P (control 125 ng/mL)	84	0/84	> 95 % positive reading
Urine +50%	84	0/84	> 95 % positive reading

Repeatability 200 ng/mL SQ	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Urine -50%	98.2	2.50	2.5
Urine -25%	146	2.51	1.7
DAT3N (control 150 ng/mL)	150	1.91	1.3
Cutoff Urine	199	2.48	1.2
Urine +25%	242	3.15	1.3
DAT3P (control 250 ng/mL)	248	2.67	1.1
Urine +50%	279	2.34	0.8
Intermediate Precision	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Urine -50%	98.2	3.09	3.1
Urine -25%	146	2.87	2.0
DAT3N (control 150 ng/mL)	150	3.49	2.3
Cutoff Urine	199	3.33	1.7
Urine +25%	242	3.72	1.5

DAT3P (control 250 ng/mL)	248	5.68	2.3
Urine +50%	279	4.88	1.7

200 ng/mL Qualitative	Number Tested	Negative/Positive	Confidence Level
Urine -50%	84	84/0	> 95 % negative reading
Urine -25%	84	84/0	> 95 % negative reading
DAT3N (control 150 ng/mL)	84	84/0	> 95 % negative reading
Cutoff Urine	84	60/24	N/A
Urine +25%	84	0/84	> 95 % positive reading
DAT3P (control 250 ng/mL)	84	0/84	> 95 % positive reading
Urine +50%	84	0/84	> 95 % positive reading

300 ng/mL SQ Repeatability	Mean (ng/mL)	SD (ng/mL)	CV (%)
Urine -50%	151	4.41	2.9
Urine -25%	211	3.99	1.9
DAT1N (control 225 ng/mL)	223	5.50	2.5
Cutoff Urine	276	4.17	1.5
Urine +25%	354	5.21	1.5

DAT1P (control 375 ng/mL)	363	4.35	1.2
Urine +50%	432	5.14	1.2
Intermediate Precision	**Mean (ng/mL)**	**SD (ng/mL)**	**CV (%)**
Urine -50%	151	5.31	3.5
Urine -25%	211	5.40	2.6
DAT1N (control 225 ng/mL)	223	6.23	2.8
Cutoff Urine	276	6.07	2.2
Urine +25%	354	6.17	1.7
DAT1P (control 375 ng/mL)	363	7.35	2.0
Urine +50%	432	6.70	1.6

300 ng/mL Qualitative	**Number Tested**	**Negative/Positive**	**Confidence Level**
Urine -50%	84	84/0	> 95 % negative reading
Urine -25%	84	84/0	> 95 % negative reading
DAT1N (control 225 ng/mL)	84	84/0	> 95 % negative reading
Cutoff Urine	84	83/1	N/A
Urine +25%	84	0/84	> 95 % positive reading
DAT1P (control 375 ng/mL)	84	0/84	> 95 % positive reading

Urine +50%	84	0/84	> 95 % positive reading

4.2. Analytical Recovery and Linearity

The recovery study was evaluated on a single **cobas c** 501 in according to CLSI guideline EP06-A. The study protocol consisted of three reagent lots, the total number of samples was 17 levels per cutoff and ran in triplicate. The recovery study experiment was conducted using three reagent lots on one **cobas c** 501 instrument. Two series of samples were prepared for each cutoff to support that the recovery performance of the device is acceptable over the whole range between the lowest and the highest calibrator.

For each sample, the percentage recovery was calculated as the percent of the mean of the three results with regard to the target value. The average percent recovery is summarized in the table below.

Results for 0-200% of 100 ng/mL cutoff

100 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	1	N/A	0	N/A	4	N/A
25	27	108	29	116	29	115
50	54	107	53	105	52	105
75	76	102	76	101	75	100
100	99	99	99	99	100	100
125	122	98	122	98	121	97
150	146	97	145	97	148	99
175	169	97	168	96	172	98
200	188	94	189	95	193	97

Results for 0-1000% of 100 ng/mL cutoff

100 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	1	N/A	0	N/A	4	N/A
100	98	98	100	100	101	101
200	191	96	191	96	195	97
300	288	96	291	97	295	98
400	399	100	399	100	404	101
500	517	103	524	105	522	104
600	638	106	644	107	638	106
700	753	108	763	109	752	107
800	842	105	856	107	856	107
900	921	102	928	103	921	102
1000	982	98	978	98	988	99

Results for 0-200% of 200 ng/mL cutoff

200 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	1	N/A	0	N/A	1	N/A
50	52	104	54	107	52	103
100	97	97	100	100	99	99
150	142	95	144	96	143	96
200	191	95	190	95	192	96
250	243	97	238	95	242	97

300	292	97	289	96	295	98
350	351	100	347	99	349	100
400	408	102	403	101	406	101

Results for 0-1000% of 200 ng/mL cutoff

200 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	1	N/A	0	N/A	1	N/A
100	99	99	100	100	99	99
200	193	96	191	95	193	97
300	293	98	289	96	296	99
400	404	101	399	100	399	100
500	526	105	518	104	517	103
600	646	108	643	107	634	106
700	760	109	761	109	751	107
800	857	107	852	107	850	106
900	927	103	927	103	922	102
1000	986	99	982	98	986	99

Results for 0-200% of 300 ng/mL cutoff

300 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	0	N/A	0	N/A	9	N/A
75	89	119	84	112	87	116
150	155	104	154	103	160	106

225	216	96	220	98	224	99
300	281	94	283	94	300	100
375	349	93	348	93	351	94
450	416	92	418	93	432	96
525	482	92	487	93	491	94
600	550	92	556	93	561	93

Results for 0-1000% of 300 ng/mL cutoff

300 Cutoff Target (ng/mL)	Lot 1		Lot 2		Lot 3	
	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)	Mean (ng/mL)	Recovery (%)
0	0	N/A	0	N/A	9	N/A
300	284	95	281	94	288	96
600	554	92	557	93	561	93
900	869	97	888	99	869	97
1200	1253	104	1275	106	1228	102
1500	1687	112	1756	117	1639	109
1800	2096	116	2143	119	2069	115
2100	2422	115	2489	119	2424	115
2400	2679	112	2711	113	2674	111
2700	2837	105	2833	105	2831	105
3000	2903	97	2862	95	2907	97

4.3. Analytical Specificity/Cross-Reactivity

The determination of cross reactivity by common benzodiazepines was conducted on one **cobas c** 501, using one reagent lot. Concentration series were prepared for each cross reactant by spiking drug free urine. The percent cross-reactivity was calculated from the ratio of the cutoff concentration and the calculated equivalent concentration of the cross reactant. The study was conducted for the semi-quantitative application. Results are summarized below:

Cross Reactivity of Benzodiazepines and Metabolites for 100 ng/mL Cutoff

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Nordiazepam	101	99%
Alprazolam	92	109%
Diazepam	90	111%
Lorazepam	105	95%
Lorazepam glucuronide	178	56%
Oxazepam	89	113%
Oxazepam glucuronide	135	74%
Temazepam	94	106%
Temazepam glucuronide	160	63%
3-Hydroxybromazepam	153	66%
3-Hydroxyflubromazepam	130	77%
3-Hydroxyflunitrazepam	118	85%
4-Hydroxyalprazolam	63	160%
4-Hydroxytriazolam	98	102%
7-Acetamidonitrazepam	21421	0.5%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
7-Aminoclonazepam	124	80%
7-Aminoflunitrazepam	109	91%
7-Aminonimetazepam	87	115%
7-Aminonitrazepam	73	137%
Bentazepam	128	78%
Bromazepam	76	132%
Brotiazolam	138	73%
Chlordiazepoxide	109	92%
Clobazam	95	106%
Clonazepam	103	97%
Clonazolam	110	91%
Clorazepate	189	53%
Delorazepam	109	92%
Demoxepam	76	131%
Desalkylflurazepam	97	103%
Deschloretizolam	81	124%
Desmethylchlordiazepoxide	108	93%
Desmethylflunitrazepam	100	100%
Desmethylmedazepam	168	59%
Diclazepam	99	101%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Didesethylflurazepam	116	86%
Estazolam	88	114%
Etizolam	118	85%
Flubromazepam	132	76%
Flubromazolam	105	95%
Flunitrazepam	113	88%
Flurazepam	161	62%
Halazepam	132	76%
Hydroxyethylflurazepam	103	97%
Lormetazepam	107	94%
Meclonazepam	123	82%
Medazepam	138	72%
Midazolam	106	95%
Nifoxipam	129	78%
Nimetazepam	99	101%
Nitrazepam	96	105%
Phenazepam	124	81%
Pinazepam	110	91%
Prazepam	124	80%
Pyrazolam	103	97%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Tetrazepam	116	86%
Triazolam	103	97%
α-Hydroxyalprazolam	85	118%
α-Hydroxyalprazolam glucuronide	190	53%
α-Hydroxymidazolam	103	97%
α-Hydroxymidazolam glucuronide	179	56%
α-Hydroxytriazolam	96	105%

Cross Reactivity of Benzodiazepines and Benzodiazepines Metabolites for 200 ng/mL

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Nordiazepam	198	101%
Alprazolam	174	115%
Diazepam	175	115%
Lorazepam	208	96%
Lorazepam glucuronide	360	56%
Oxazepam	193	104%
Oxazepam glucuronide	282	71%
Temazepam	193	103%
Temazepam glucuronide	318	63%
3-Hydroxybromazepam	371	54%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
3-Hydroxyflubromazepam	256	78%
3-Hydroxyflunitrazepam	259	77%
4-Hydroxyalprazolam	119	169%
4-Hydroxytriazolam	203	99%
7-Acetamidonitrazepam	42005	0.5%
7-Aminoclonazepam	283	71%
7-Aminoflunitrazepam	219	91%
7-Aminonimetazepam	213	94%
7-Aminonitrazepam	177	113%
Bentazepam	288	69%
Bromazepam	154	130%
Brotiazolam	265	76%
Chlordiazepoxide	282	71%
Clobazam	185	108%
Clonazepam	208	96%
Clonazolam	226	89%
Clorazepate	396	50%
Delorazepam	217	92%
Demoxepam	182	110%
Desalkylflurazepam	194	103%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Deschloretizolam	159	126%
Desmethylchlordiazepoxide	304	66%
Desmethylflunitrazepam	196	102%
Desmethylmedazepam	399	50%
Diclazepam	202	99%
Didesethylflurazepam	231	87%
Estazolam	168	119%
Etizolam	236	85%
Flubromazepam	266	75%
Flubromazolam	203	98%
Flunitrazepam	212	94%
Flurazepam	312	64%
Halazepam	269	74%
Hydroxyethylflurazepam	206	97%
Lormetazepam	214	94%
Meclonazepam	306	65%
Medazepam	279	72%
Midazolam	206	97%
Nifoxipam	310	64%
Nimetazepam	201	99%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Nitrazepam	188	106%
Phenazepam	252	79%
Pinazepam	213	94%
Prazepam	240	83%
Pyrazolam	203	99%
Tetrazepam	233	86%
Triazolam	207	96%
α-Hydroxyalprazolam	168	119%
α-Hydroxyalprazolam glucuronide	399	50%
α-Hydroxymidazolam	201	100%
α-Hydroxymidazolam glucuronide	372	54%
α-Hydroxytriazolam	198	101%

Cross Reactivity of Benzodiazepines and Benzodiazepines Metabolites for 300 ng/mL Cutoffs

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Nordiazepam	305	98%
Alprazolam	275	109%
Diazepam	273	110%
Lorazepam	323	93%
Lorazepam glucuronide	519	58%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Oxazepam	275	109%
Oxazepam glucuronide	442	68%
Temazepam	272	110%
Temazepam glucuronide	496	61%
3-Hydroxybromazepam	504	59%
3-Hydroxyflubromazepam	401	75%
3-Hydroxyflunitrazepam	399	75%
4-Hydroxyalprazolam	192	156%
4-Hydroxytriazolam	319	94%
7-Acetamidonitrazepam	93148	0.3%
7-Aminoclonazepam	390	77%
7-Aminoflunitrazepam	343	87%
7-Aminonimetazepam	283	106%
7-Aminonitrazepam	230	131%
Bentazepam	393	76%
Bromazepam	229	131%
Brotiazolam	407	74%
Chlordiazepoxide	374	80%
Clobazam	277	108%
Clonazepam	317	95%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Clonazolam	338	89%
Clorazepate	601	50%
Delorazepam	334	90%
Demoxepam	256	117%
Desalkylflurazepam	307	98%
Deschloretizolam	257	117%
Desmethylchlordiazepoxide	370	81%
Desmethylflunitrazepam	301	100%
Desmethylmedazepam	549	55%
Diclazepam	317	95%
Didesethylflurazepam	352	85%
Estazolam	270	111%
Etizolam	362	83%
Flubromazepam	435	69%
Flubromazolam	327	92%
Flunitrazepam	329	91%
Flurazepam	487	62%
Halazepam	406	74%
Hydroxyethylflurazepam	324	92%
Lormetazepam	328	92%

Benzodiazepine and metabolites	Concentration Tested	Cross-reactivity (%)
Meclonazepam	409	73%
Medazepam	394	76%
Midazolam	332	90%
Nifoxipam	412	73%
Nimetazepam	309	97%
Nitrazepam	294	102%
Phenazepam	382	78%
Pinazepam	327	92%
Prazepam	363	83%
Pyrazolam	311	96%
Tetrazepam	360	83%
Triazolam	315	95%
α-Hydroxyalprazolam	275	109%
α-Hydroxyalprazolam glucuronide	567	53%
α-Hydroxymidazolam	326	92%
α-Hydroxymidazolam glucuronide	569	53%
α-Hydroxytriazolam	312	96%

4.4. Endogenous Interference Testing of Structurally Unrelated Compounds

Interference from structurally unrelated compounds was evaluated with two sets of samples were prepared and measured for the analysis of each individual interferent. One set of the samples

contained the interferent in the presence of a benzodiazepine at both target concentrations (75% and 125% of the cutoff of the assay), and one set of the samples contained the interferent in the presence of a glucuronidated benzodiazepine (oxazepam-glucuronide) at both target concentrations (75% or 125% of the cutoff of the assay). Testing was performed in both qualitative and semiquantitative modes. The compounds listed in the table below did not cause any positive or negative interference at the concentrations shown:

Compound Name	**Concentration in presence of benzodiazepine (mg/dL)**
Acetone	1000
Ascorbic Acid	1500
Calcium (as $CaCl_2$)	133
Citrate (K_3-Citrate x H_2O)	357
Creatinine	1000
Ethanol	1000
Glucose	7000
Hemoglobin	750
Human Albumin	250
Human IgG	110
Magnesium ($MgCl_2$)	238
Oxalate (Na_2-Oxalate)	20
Phosphate (NaH_2PO_4 x H_2O)	2028
Sodium chloride	5844
Urea	18000

Compound Name	Concentration in presence of benzodiazepine (mg/dL)
Uric Acid	100
Urobilinogen	15

4.5. Interference Testing of Specific Gravity and pH

Urine samples within a pH range from 4.0 to 9.0 and samples with specific gravities ranging from 1.001 to 1.034 containing benzodiazepine at the level of the negative control (75 ng/mL, 150 ng/mL or 225 ng/mL) and at the level of the positive control (125 ng/mL, 250 ng/mL or 375 ng/mL) corresponding respectively to the given cutoff (100 ng/mL, 200 ng/mL or 300 ng/mL) recovered properly in both semi-quantitative and qualitative modes.

4.6. Drug Interferences

The drug interference study was conducted using one reagent lot on the **cobas c** 501. Samples spiked with benzodiazepine were measured in the presence of potentially interfering drugs. The target concentration for the benzodiazepine was 75% or 125% of the cutoff of the assay. For all samples three replicates were recorded with the semi-quantitative applications and the qualitative applications. The test results were checked for exceeding the cutoff value. The maximum drug concentration which doesn't interfere is reported and established as interferent claim. For the tested drugs and drug concentrations compare table below.

For Oxaprozin, the interference was additionally evaluated following an alternative protocol. In a drug-free matrix, the approximate quantity of Oxaprozin that is equivalent in assay reactivity to the 100 ng/mL, 200 ng/mL, and 300 ng/mL cutoff was determined to be 790 ng/mL, 3091 ng/mL and 3049 ng/mL respectively. This equals to a cross reactivity of 13% (at cutoff 100 ng/mL), 6% (at cutoff 200 ng/mL), and 10% (at cutoff 300 ng/mL).

When oxaprozin was added pooled human urine containing benzodiazepine at the level of the negative control (75 ng/mL, 150 ng/mL or 225 ng/mL), positive results were observed at >100 ng/mL, >200 ng/mL, and >300 ng/mL for the 100 ng/mL cutoff, 200 ng/mL cutoff, and 300 ng/mL

cutoff, respectively. Patient samples containing benzodiazepines in the presence of oxaprozin may yield falsely elevated results. Results should always be assessed in conjunction with the patient's medical history, clinical examinations, and other clinicopathological findings.

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
Acetaminophen	3000000	3000000	3000000
Acetylsalicylic acid	100000	100000	100000
Amitryptyline	100000	100000	100000
Amobarbital	100000	100000	100000
d-Amphetamine	100000	100000	100000
l-Amphetamine	100000	100000	100000
Ampicillin	100000	100000	100000
Aspartame	100000	100000	100000
Atropine	100000	100000	100000
Benzocaine	100000	100000	100000
Benzoylecgonine	100000	100000	100000
Benzphetamine	100000	100000	100000
Buspirone	100000	100000	100000
Butabarbital	100000	100000	100000
Ca-dobesilate	1000000	1000000	1000000
Caffeine	100000	100000	100000
Calcium hypochlorite	100000	100000	100000

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
Cannabidiol	100000	100000	100000
Captopril	100000	100000	100000
Cefoxitin	2000000	4000000	6000000
Chloroquine	100000	100000	100000
Chlorpheniramine	40000	100000	100000
Chlorpromazine	100000	100000	100000
Cocaine	100000	100000	100000
Codeine	100000	100000	100000
Desipramine	100000	100000	100000
Dextromethorphan	100000	100000	100000
Dextropropoxyphene (d-Propoxyphene)	100000	100000	100000
Digoxin	100000	100000	100000
Diphenhydramine	40000	100000	100000
Doxepine	100000	100000	100000
Ecgonine	100000	100000	100000
Ecgonine methyl ester	100000	100000	100000
EDDP (2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine)	25000	50000	75000
EMDP (2-Ethyl-5-methyl-3,3-diphenylpyrroline)	25000	40000	80000
Enalapril	100000	100000	100000

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
d-Ephedrine	100000	100000	100000
l-Ephedrine	100000	100000	100000
Epinephrine	100000	100000	100000
Erythromycin	100000	100000	100000
Estriol	100000	100000	100000
Fenoprofen	40000	100000	100000
Flumazenil	100000	100000	100000
Furosemide	100000	100000	100000
Gentamicine sulfate	400000	400000	400000
Gentisic acid	100000	100000	100000
Glutethimide	100000	100000	100000
Guaiacol glycerol ether	100000	100000	100000
Hydrochlorothiazide	100000	100000	100000
Hydroxyindole acetic acid	100000	100000	100000
Hydroxyindole carboxylic acid	100000	100000	100000
Ibuprofen	4000000	4000000	4000000
Imipramine	100000	100000	100000
Isoproterenol	100000	100000	100000
Ketamine	100000	100000	100000

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
Levodopa	1000000	1000000	1000000
Lidocaine	100000	100000	100000
LSD	100000	100000	100000
Melanin	100000	100000	100000
Meperidine (Pethidin)	100000	100000	100000
Methadone	40000	40000	40000
d-Methamphetamine	100000	100000	100000
l-Methamphetamine	100000	100000	100000
Methaqualone	100000	100000	100000
Methyldopa	2000000	2000000	2000000
Methylenedioxyamphetamine (MDA)	100000	100000	100000
Methylenedioxymethamphetamine (MDMA)	100000	100000	100000
Methylphenidate	100000	100000	100000
Morphine	100000	100000	100000
N-acetyl cysteine	10000	10000	10000
Naloxone	100000	100000	100000
Naltrexone	100000	100000	100000
Naproxen	100000	100000	100000
Niacinamide	100000	100000	100000

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
Nicotine	100000	100000	100000
Norethindrone	100000	100000	100000
l-Norpseudoephedrine	100000	100000	100000
Ofloxacin	900000	900000	900000
Omeprazol	100000	100000	100000
Oxaprozin	100	200	300
Penicillin G	100000	100000	100000
Pentazocine	100000	100000	100000
Pentobarbital	100000	100000	100000
Phenazopyridine	300000	300000	300000
Phencyclidine	100000	100000	100000
Phenobarbital	100000	100000	100000
Phenothiazine	100000	100000	100000
Phenylbutazone	100000	100000	100000
Phenylpropanolamine	100000	100000	100000
Phenytoin	100000	100000	100000
Procaine	100000	100000	100000
Promethazine	100000	100000	100000
d-Pseudoephedrine	100000	100000	100000

Compounds	Concentration (ng/mL)		
	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
Quetiapine	5000	5000	5000
Quinidine	100000	100000	100000
Quinine	100000	100000	100000
Salicyluric acid	6000000	6000000	6000000
Secobarbital	100000	100000	100000
Sulindac	100000	100000	100000
Tetracycline	300000	300000	300000
Tetrahydrozoline	100000	100000	100000
Δ9 THC-9-carboxylic acid	100000	100000	100000
Thioridazine	100000	100000	100000
Tolmetin	100000	100000	100000
Trifluoperazine	100000	100000	100000
Trimipramine	100000	100000	100000
Tyramine	100000	100000	100000
Verapmil	100000	100000	100000
Zaleplone	100000	100000	100000
Zolpidem	50000	50000	50000
Zopiclone	100000	100000	100000

4.7. Method Comparison to Predicate

The method comparison study was performed in accordance with CLSI Guideline EP09-A3. A collection of 137 native human unaltered samples were purchased from clinical laboratories where they screened negative and preliminary positive flanking the cutoffs 100 ng/mL, 200 ng/mL and 300 ng/mL. The total of 117 of the 137 samples were measured with the assays with the cutoff 100 ng/mL, 134 samples were measured with the assays with cutoff 200 ng/mL and 114 samples were measured with the assays with cutoff 300 ng/mL. The results were compared to LC-MS/MS where samples were also treated with β-glucuronidase.

A total of 48 urine samples, obtained from a clinical laboratory, where they screened negative in a drug test panel, were evaluated with Benzodiazepines II. 100 % of these normal urines were negative relative to the 100 ng/mL cutoff.

A total of 54 urine samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed by Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS), were evaluated with the Benzodiazepines II assay. 100 % of these samples were positive relative to the 100 ng/mL cutoff.

In addition, 8 urine samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 50-100 % of the cutoff concentration and 7 samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 100-150 % of the cutoff concentration. The following results were obtained with the Benzodiazepines II assay on the **cobas c** 501 analyzer relative to the LC-MS/MS values. The results are summarized in the table below. Values in brackets represent the results for the two qualitative applications (Qualitative/Qualitative Clinical).

Benzodiazepines II Clinical Correlation (Cutoff = 100 ng/mL)					
		Negative Samples	LC-MS/MS values (ng/mL)		
			Near Cutoff		152-1558
			50-99	104-147	
cobas c 501 analyzer	+	0	2 (1/1)	7	54
	-	48	6 (7/7)	0	0

The correlation between the semi-quantitative and the qualitative applications is summarized in the tables below.

Correlation (100 ng/mL Cutoff)			
		Semi-Quantitative	
		-	+
Qualitative	+	0	62
	-	54	1

Correlation (100 ng/mL Cutoff)			
		Semi-Quantitative	
		-	+
Qualitative Clinical	+	0	62
	-	54	1

The samples found to be discrepant at the 100 ng/mL cutoff with one of the predicate device applications are listed below.

Sample	Semi-Quantitative		Qualitative	Qualitative Clinical	LC-MS Confirmation		Comment
ID#	Values [ng/mL]	Pos/Neg	Pos/Neg	Pos/Neg	Values [ng/mL]	Pos/Neg	
UR_065	104	POS	NEG	NEG	68	NEG	near cutoff
UR_131	150	POS	POS	POS	99	NEG	near cutoff

A total of 56 urine samples obtained from a clinical laboratory, where they screened negative in a drug test panel, were evaluated with the Benzodiazepines II assay. 100 % of these normal urines were negative relative to the 200 ng/mL cutoff.

A total of 57 urine samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed by Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS), were evaluated with the Benzodiazepines II assay. 100 % of these samples were positive relative to the 200 ng/mL cutoff. In addition, 12 urine samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 50-100 % of the cutoff concentration and 9 urine samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 100-150 % of the cutoff concentration. The following results were obtained with the Benzodiazepines II assay on the **cobas c** 501 analyzer relative to the LC-MS/MS values. The results are summarized in the table below. Values in brackets represent the results for the qualitative application.

Benzodiazepines II Clinical Correlation (Cutoff = 200 ng/mL)					
		Negative Samples	LC-MS/MS values (ng/mL)		
			Near Cutoff		304-2971
			137-196	211-295	
cobas c 501 analyzer	+	0	2 (3)	7	57
	-	56	10 (9)	2	0

The correlation between the semi-quantitative and the qualitative applications is summarized in table below.

Correlation (200 ng/mL Cutoff)			
		Semi-Quantitative	
		-	+
Qualitative	+	1	66
	-	67	0

The samples found to be discrepant at the 200 ng/mL cutoff with one of the predicate device applications are listed below.

Sample	Semi-Quantitative		Qualitative	LC-MS		Comment
ID#	Values [ng/mL]	Pos/Neg	Pos/Neg	Values [ng/mL]	Pos/Neg Confirmation	
UR_051	132	NEG	NEG	282	POS	near cutoff
UR_060	235	POS	POS	147	NEG	near cutoff
UR_073	197	NEG	POS	196	NEG	near cutoff
UR_134	249	POS	POS	142	NEG	near cutoff

A total of 40 urine samples obtained from a clinical laboratory, where they screened negative in a drug test panel, were evaluated with the Benzodiazepines II assay. 100 % of these normal urines were negative relative to the 300 ng/mL cutoff.

A total of 45 urine samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed by Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS), were evaluated with the Benzodiazepines II assay. 100 % of these samples were positive relative to the 300 ng/mL cutoff. In addition, 17 urine samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 50-100% of the cutoff concentration and 12 urine samples obtained from a clinical laboratory were found by LC-MS/MS in a concentration of 100-150 % of the cutoff concentration. The following results were obtained with the Benzodiazepines II assay on the **cobas c** 501 analyzer relative to the LC-MS/MS values. The results are summarized in the table below. Values in brackets represent the results for the qualitative application.

Benzodiazepines II Clinical Correlation (Cutoff = 300 ng/mL)					
		Negative Samples	LC-MS/MS values (ng/mL)		
			Near Cutoff		456-2971
			152-295	304-441	
cobas c 501 analyzer	+	0	1 (4)	11	45
	-	40	16 (13)	1	0

The samples found to be discrepant at the 300 ng/mL cutoff with one of the predicate device applications are listed below.

Sample	Semi-Quantitative	Qualitative	LC-MS	Comment

ID#	Values [ng/mL]	Pos/Neg	Pos/Neg	Values [ng/mL]	Pos/Neg Confirmation	
UR_062	276	NEG	NEG	304	POS	near cutoff
UR_076	297	NEG	POS	277	NEG	near cutoff
UR_077	296	NEG	POS	216	NEG	near cutoff
UR_078	295	NEG	POS	272	NEG	near cutoff
UR_083	348	POS	POS	295	NEG	near cutoff

4.8. Stability

The measurements to prove the on board stability of 12 weeks were carried out using one reagent lot on the **cobas c** 501 instrument. The reagent transport stress was simulated using the following incubation condition: ≥ 120 h at 35°C (± 2°C).

Two control samples, the cutoff calibrator and two clinical samples, were tested per each cutoff. The two clinical samples were prepared by pooling urine of individual donor samples in a way to achieve concentrations around 50% and 150% of the cutoff respectively.

Overview: samples for the on board stability experiment

Specimen	Cutoff 100 ng/mL	Cutoff 200 ng/mL	Cutoff 300 ng/mL
negative control (target value)	DAT2N, DATCN (75 ng/mL)	DAT3N (150 ng/mL)	DAT1N (225 ng/mL)
positive control (target value)	DAT2P, DATCP (125 ng/mL)	DAT3P (250 ng/mL)	DAT1P (375 ng/mL)
calibrator (target value)	Preciset DAT Plus II / S3 (100 ng/mL)	Preciset DAT Plus II / S4 (200 ng/mL)	Preciset DAT Plus I / S3 (300 ng/mL)
clinical neg	approx. 50 ng/mL	approx. 100 ng/mL	approx. 150 ng/mL
clinical pos	approx. 150 ng/mL	approx. 300 ng/mL	approx. 450 ng/mL

100 ng/mL for Semi-Quantitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	76.5	77.5	80.7	77.0
SD [ng/mL]	1.69	2.16	1.82	1.76

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
CV [%]	2	3	2	2
positive control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	125	126	129	124
SD [ng/mL]	2.32	1.64	2.02	2.16
CV [%]	2	1	2	2
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100
calibrator (n=3)				
mean [ng/mL]	100	101	106	101

200 ng/mL for Semi-Quantitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	151	152	151	147
SD [ng/mL]	1.51	2.55	2.80	1.63
CV [%]	1	2	2	1
positive control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	255	257	254	251
SD [ng/mL]	2.82	3.91	2.59	2.46
CV [%]	1	2	1	1
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100
calibrator (n=3)				
mean [ng/mL]	199	201	199	197

300 ng/mL for Semi-Quantitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard

negative control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	226.0	231.3	230.7	227.4
SD [ng/mL]	3.51	2.85	5.70	6.45
CV [%]	2	2	2	3
positive control (n=21)				
agreement [%]	100	100	100	100
mean [ng/mL]	363.0	371.4	370.0	364.0
SD [ng/mL]	4.85	5.42	5.61	6.20
CV [%]	1	1	2	2
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100
calibrator (n=3)				
mean [ng/mL]	291	301	296	287

100 ng/mL for Qualitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
positive control (n=21)				
agreement [%]	100	100	100	100
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100

200 ng/mL for Qualitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
positive control (n=21)				
agreement [%]	100	100	100	100
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100

300 ng/mL for Qualitative

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
positive control (n=21)				
agreement [%]	100	100	100	100
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100

100 ng/mL for Qualitative Clinical

time point Reagent Status:	1 start	2 transport stressed (≥120 h 35°C)	3 transport stressed + 84 days onboard	4 transport stressed + 91 days onboard
negative control (n=21)				
agreement [%]	100	100	100	100
positive control (n=21)				
agreement [%]	100	100	100	100
negative clinical sample (n=3)				
agreement [%]	100	100	100	100
positive clinical sample (n=3)				
agreement [%]	100	100	100	100

5. CONCLUSIONS

The information provided in this 510(k) Premarket Notification will support a determination of substantial equivalence for ONLINE DAT Benzodiazepines II. The data supports a safe and effective device, which performs as well or better than the predicate devices.