Microgenics Corporation
Thermo Fisher Scientific
Pranjali Shinde
Manager, Regulatory Affairs
46500 Kato Road
Fremont, California 94538

Re: K231020
Trade/Device Name: Alinity c Tricyclic Antidepressants Reagent Kit
Regulation Number: 21 CFR 862.3910
Regulation Name: Tricyclic Antidepressant Drugs Test System
Regulatory Class: Class II
Product Code: LFH
Dated: October 11, 2023
Received: October 13, 2023

Dear Pranjali Shinde:

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 System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 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 systems (QS) regulation (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.

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,

Joseph A. Kotarek -S

Digitally signed by Joseph A. Kotarek -S
Date: 2023.11.17 16:52:07 -05'00'

Joseph Kotarek
Branch Chief
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)*
K231020

Device Name
Alinity c Tricyclic Antidepressants Reagent Kit

Indications for Use *(Describe)*
The Alinity c Tricyclic Antidepressants Reagent Kit is a homogeneous enzyme immunoassay intended for use in the qualitative and/or semiquantitative determination of the presence of tricyclic antidepressants (TCAs) in human serum or plasma at a cutoff concentration of 300 ng/mL on the Alinity c system in patients suspected of drug overdose.

The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by confirmatory method such as Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS), or for permitting laboratories to establish control procedures.

The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method.

Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

For In Vitro Diagnostic Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

510(k) Number: K231020

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of Safe Medical Device Act of 1990 and 21 CFR 807.92.

A. Device Information

Sponsor:	Microgenics Corporation Thermo Fisher Scientific 46500 Kato Road Fremont, CA 94538 Phone: 510-979-5000 Fax: 510-979-5002
Correspondent Contact Information:	Pranjali Shinde Microgenics Corporation Thermo Fisher Scientific 46500 Kato Road Fremont, CA-94538 Email: Pranjali.Shinde@Thermofisher.com Phone: 510-979-5000 Fax: 510-979-5002
Device Common Name:	Alinity c Tricyclic Antidepressants Reagent Kit
Trade or Proprietary Name	Alinity c Tricyclic Antidepressants Reagent Kit
Brand Name	Alinity c Tricyclic Antidepressants Reagent Kit
Candidate Device Product Code, Classification, Classification Name & Panel	LFH, Class II, 21 CFR 862. 3910 – Tricyclic antidepressant drugs test system, 91 – Toxicology

Predicate Device Information:

Predicate Device:	DRI Tricyclics Serum Tox Assay
Predicate DeviceManufacturer:	Microgenics Corporation
Predicate Device Common Name	Tricyclics Serum Tox Assay
Predicate Device Premarket Notification #:	K213875
Predicate Device Product Code, Classification, Classification Name & Panel	LFH, Class II, 21 CFR 862. 3910 – Tricyclic antidepressant drugs test system, 91 – Toxicology

B. Date Summary Prepared

November 17, 2023

C. Description of Device

The Alinity c Tricyclic Antidepressants Reagent Kit is an automated clinical chemistry assay and a homogeneous enzyme immunoassay using ready-to-use liquid reagents. The assay uses polyclonal antibodies that detect most tricyclic antidepressants in serum or plasma. The assay is based on the competition between an enzyme-labeled drug and the drug from the serum or plasma for a fixed number of specific antibody binding sites. In the absence of drug from the sample, the specific antibody binds to the drug labeled with glucose-6-phosphate dehydrogenase (G6PDH) and the enzyme activity is inhibited. This phenomenon creates a direct relationship between the drug concentration in the serum or plasma and the enzyme activity. The G6PDH enzyme activity is determined spectrophotometrically at 340/416 nm by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH.

The Alinity c Tricyclic Antidepressants Reagent Kit is supplied as a two liquid reagent kit (R1 and R2). They are included within the same kit, see details below:

- **Antibody/Substrate Reagent (R1):** Contains polyclonal anti-tricyclics antibodies (sheep), glucose-6- phosphate (G6P), and nicotinamide adenine dinucleotide (NAD) in Tris buffer with sodium azide as a preservative.
- **Enzyme Conjugate Reagent (R2):** Contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with nortriptyline in Tris buffer with sodium azide as a preservative.

D. Intended Use

The Alinity c Tricyclic Antidepressants Reagent Kit is a homogeneous enzyme immunoassay intended for use in the qualitative and/or semiquantitative determination of the presence of tricyclic antidepressants (TCAs) in human serum or plasma at a cutoff concentration of 300 ng/mL on the Alinity c system in patients suspected of drug overdose.

The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by confirmatory method such as Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS), or for permitting laboratories to establish control procedures.

The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method.

Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

For In Vitro Diagnostic Use Only.

E. Comparison to Predicate Device

Characteristics	Candidate Device: Alinity c Tricyclic Antidepressants Reagent Kit	Predicate Device: DRI Tricyclics Serum Tox Assay (K213875)
Intended Use	The Alinity c Tricyclic Antidepressants Reagent Kit is a homogeneous enzyme immunoassay intended for use in the qualitative and/or semiquantitative determination of the presence of tricyclic antidepressants (TCAs) in human serum or plasma at a cutoff concentration of 300 ng/mL on the Alinity c system in patients suspected of drug overdose. The semiquantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by confirmatory method such as Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS), or for permitting laboratories to establish control procedures. The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method. Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used. For In Vitro Diagnostic Use Only.	The DRI ™ Tricyclics Serum Tox Assay is a homogeneous enzyme immunoassay intended for the qualitative and/or semiquantitative determination of the presence of tricyclic antidepressants (TCAs) in human serum, plasma, or urine of patients at a cutoff concentration of 300 ng/mL in patients suspected of drug overdose. The semi-quantitative mode is for the purpose of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS) or permitting laboratories to establish quality control procedures. The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Liquid Chromatography/Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method. Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used. For In Vitro Diagnostic Use Only.

Operating Principle (Technology)	DRI	Same
Measured Analyte	Nortriptyline	Same
Test Matrix	Serum, Plasma	Serum, Plasma, Urine
Cut-off Levels	300 ng/mL	Same
Methodology	Homogeneous Enzyme Immunoassay	Same
Reagents Form	Liquid ready-to-use.	Same
Antibody	Sheep polyclonal antibodies	Same
Storage	2–8 °C until expiration date.	Same
Principal Operator	Trained professionals	Same
Calibrator Levels for Semi-Quant	4-point Calibrator	5-point Calibrator

F. Test Principle

The Alinity c Tricyclic Antidepressants Reagent Kit is an automated clinical chemistry assay and a homogeneous enzyme immunoassay using ready-to-use liquid reagents. The assay uses polyclonal antibodies that detect most tricyclic antidepressants in serum or plasma. The assay is based on the competition between an enzyme-labeled drug and the drug from the serum or plasma for a fixed number of specific antibody binding sites. In the absence of drug from the sample, the specific antibody binds to the drug labeled with glucose-6-phosphate dehydrogenase (G6PDH) and the enzyme activity is inhibited. This phenomenon creates a direct relationship between the drug concentration in the serum or plasma and the enzyme activity. The G6PDH enzyme activity is determined spectrophotometrically at 340/416 nm by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH.

G. Summary of Supporting Data

Analytical Performance:
The performance was evaluated on Alinity c clinical chemistry analyzer.

a) Precision
Precision study is performed in accordance with CLSI Guideline *EP05-A3.*

Samples were prepared by spiking Nortriptyline in drug-free serum at final concentrations of -100%, -75%, -50%, -25% below cutoff, cutoff and +25%, +50% above cutoff. .

Repeatability:
The study was conducted for 20 days with 2 runs per day, 2 replicates per run in both qualitative and semi-quantitative modes with 1 lot of reagent, calibrators, and controls. There were 80 replicates for each level of precision samples. The results of the precision study (Repeatability) are presented in the table below.

Table 1: Precision study data (Repeatability) in qualitative and semi-quantitative mode for 300 ng/mL cutoff – Serum

Spiked Concentration (ng/mL)	% of Cutoff	Total Precision (n=80)		
		# of Determinants	Qualitative Immunoassay Results (Negative/Positive)	Semi-Quantitative Immunoassay Results (Negative/Positive)
0	-100	80	80/0	80/0
75	-75	80	80/0	80/0
150	-50	80	80/0	80/0
225	-25	80	80/0	80/0
300	100	80	54/26	56/24
375	+25	80	0/80	0/80
450	+50	80	0/80	0/80

Reproducibility:
The study was conducted for 5 days with 1 run per day, 5 replicates per run in both qualitative and semi-quantitative modes with 2 lots of reagents on 3 different instruments. The results of the precision study (Reproducibility) are presented in the table below.

Table 2: Precision study data (Reproducibility) in qualitative and semi-quantitative mode for
300 ng/mL cutoff – Serum

Spiked Concentration (ng/mL)	% of Cutoff	Total Precision (n=75) – Serum		
		# of Determinants	Qualitative Immunoassay Results (Negative/Positive)	Semi-quantitative Immunoassay Results (Negative/Positive)
0	-100	75	75/0	75/0
75	-75	75	75/0	75/0
150	-50	75	75/0	75/0
225	-25	75	75/0	75/0
300	100	75	40/35	49/26
375	+25	75	75/0	75/0
450	+50	75	75/0	75/0

b) Spike Recovery

The spike recovery study was performed using 20 replicates. Samples were prepared by spiking Nortriptyline in drug-free serum at 225 ng/mL, 300 ng/mL, 375 ng/mL. The study demonstrated the accuracy of spike recovery at low control (225 ng/mL) and high control (375 ng/mL) in both qualitative and semi-quantitative mode. The results of the study are presented in the table below.

Table 3: Spike Recovery in qualitative and semi-quantitative mode for 300 ng/mL cutoff – Serum

Replicates	Low Control: 225 ng/mL (-25% of cutoff) (n=20)	High Control: 375 ng/mL (+25% of cutoff) (n=20)
1	Negative	Positive
2	Negative	Positive
3	Negative	Positive
4	Negative	Positive
5	Negative	Positive
6	Negative	Positive
7	Negative	Positive
8	Negative	Positive
9	Negative	Positive
10	Negative	Positive
11	Negative	Positive
12	Negative	Positive
13	Negative	Positive
14	Negative	Positive

Replicates	Low Control: 225 ng/mL (-25% of cutoff) (n=20)	High Control: 375 ng/mL (+25% of cutoff) (n=20)
15	Negative	Positive
16	Negative	Positive
17	Negative	Positive
18	Negative	Positive
19	Negative	Positive
20	Negative	Positive
Overlap	No	No
Relative to C/O	All 20 below C/O	All 20 above C/O

c) Dilution Linearity

The Dilution Linearity study is performed in accordance with CLSI Guideline *EP06-Ed2.*

To demonstrate the dilution linearity for purposes of sample dilution and quality control of the entire assay range, drug-free serum was spiked using Nortriptyline and diluted with drug-free serum to generate 9 levels between 0 and 500 ng/mL. Each sample was run in replicates of 5 in semi-quantitative mode and the average was used to determine percent recovery compared to the expected target value. The study results are presented in the table below.

Table 4: Dilution linearity data in Serum

Level	Expected concentration (ng/mL)	Average of observed concentration (ng/mL) (N=5)	Mean Recovery (%)
1	0	5	N/A
2	62.5	74	118
3	125.0	144	115
4	187.5	210	112
5	250.0	260	104
6	312.5	310	99
7	375.0	393	105
8	437.5	453	104
9	500	492	98

d) Method Comparison and Accuracy

The method comparison study is performed in accordance with CLSI guideline *EP07-A3, EP09c-A3* & *EP12-A.*

One (1) replicate of each of the 50 negative and 50 positive patient specimens were analyzed in both qualitative and semi-quantitative modes. Results were compared to LC-MS/MS lab testing. The results of the study are presented in the tables below.

Table 5: Stratified data comparing immunoassay in qualitative mode with LC-MS/MS – Serum

Alinity TCA Assay Results	Negative by LC-MS/MS	< 50% of Cutoff concentration by LC-MS/MS (< 150 ng/mL)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration as determined by LC-MS/MS) (150-299 ng/mL)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration as determined by LC-MS/MS) (300-450 ng/mL)	High Positives (Greater than 50% above cutoff concentration (> 450 ng/mL)
Positive	0	2[1]	0	38	12
Negative	0	19	29	0	0
% Negative Sample Agreement			96% or (48/50)		
% Positive Sample Agreement			100% or (50/50)		
% Total Sample Agreement			98% or (98/100)		

[1] Refer to Table 7 for discordant samples of serum.

Table 6: Stratified data comparing immunoassay in semi-quantitative mode with LC MS/MS – Serum

Alinity TCA Assay Results	Negative by LC-MS/MS	< 50% of Cutoff concentration by LC-MS/MS (< 150 ng/mL)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration as determined by LC-MS/MS) (150-299 ng/mL)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration as determined by LC-MS/MS) (300-450 ng/mL)	High Positives (Greater than 50% above cutoff concentration (> 450 ng/mL)
Positive	0	2 [1]	0	38	12
Negative	0	19	29	0	0
% Negative Sample Agreement			96% or (48/50)		
% Positive Sample Agreement			100% or (50/50)		
% Total Sample Agreement			98% or (98/100)		

[1] Refer to Table 7 for discordant samples of serum.

[1]Table 7: Discordant Samples – Serum

Sample ID	Qualitative ([8]Δ mA/min) Result	Semi-Quantitative Observed concentration (ng/mL)	LC-MS/MS Value (ng/mL)
APP9489-2 [2]	Positive	332 (Positive)	104
APP9474-2 [3]	Positive	323 (Positive)	113

[2] Sample APP9489-2 contains Amitriptyline at 8.08 ng/mL, Imipramine at 18.35 ng/mL, Desipramine at 46.35 ng/mL, and Nortriptyline at 17 ng/mL by LC-MS/MS and cross-reacts at 100%, 158%, 107%, and 100% by immunoassay respectively.

[3] Sample APP9474-2 contains Amitriptyline at 9.08 ng/mL, Imipramine at 19.9 ng/mL, Desipramine at 49.8 ng/mL, and Nortriptyline at 19.65 ng/mL by LC-MS/MS and cross-reacts at 100%, 158%, 107%, and 100% by immunoassay respectively.

Additional Testing of discordant samples: Additional LC-MS analysis was performed on these two samples to assess root cause for the discordant result. In the final LC-MS/MS result, both samples, APP9489-2 and APP9474-2, detected positive by immunoassay contain Carbamazepine with concentrations of 4275 ng/mL and 595 ng/mL, respectively. Carbamazepine has been shown to cross-react in multiple antibody-based TCA immunoassays as documented in independent scientific literature (Section 22, References 19, 20, 21). In addition, this effect was demonstrated as part

of cross-reactivity studies reported in CDD-FR-REC-7208 Alinity c Tricyclic Antidepressants Serum Tox Assay Non-Critical Cross Reactivity Report. Both discordant samples contain carbamazepine with concentration above 3000 ng/mL, which is sufficient to cause the unconfirmed positive result seen for these two samples. The cross-reactivity with carbamazepine is a limitation of the immunoassay.

e) Matrix equivalency

Matrix Equivalency is performed in accordance with CLSI Guideline *EP12-A2, EP35 & EP39* Ed-1.

Two (2) replicates of 50 patient samples were run in both qualitative and semi-quantitative modes to demonstrate Nortriptyline concentrations obtained in different test plasma matrices with different anticoagulants are equivalent to those measured in the primary or control matrix, serum. The results of the matrix equivalency study are presented in the table below.

Table 8: Matrix Equivalency results in qualitative and semi-quantitative mode

Serum Matrix		Qualitative		Semi- Quantitative	
		Positive	Negative	Positive	Negative
K_2 EDTA Plasma	Positive	25	0	25	0
	Negative	0	25	0	25
K_3 EDTA plasma	Positive	25	0	25	0
	Negative	0	25	0	25
Lithium Heparin Plasma	Positive	25	0	25	0
	Negative	0	25	0	25
Sodium Citrate Plasma	Positive	25	0	25	0
	Negative	0	25	0	25
Potassium Oxalate Plasma	Positive	25	0	25	0
	Negative	0	25	0	25
Sodium Heparin Plasma	Positive	25	0	25	0
	Negative	0	25	0	25

f) Specificity

Cross-Reactivity to structurally related compounds (Critical Cross-Reactivity):
The cross-reactivity of Tricyclic compounds and other structurally related compounds were evaluated by adding known amount of each compound into drug-free serum at concentrations indicated. The results are summarized in the tables below.

Table 9: Cross Reactivity to structurally related compounds in Serum (TCA and its metabolites)

Structurally Related Compounds	Tested Concentration (ng/mL)	Positive/Negative	Cross Reactivity (%)
2-Hydroxy imipramine	1300	Positive	23.1%
7-Hydroxy quetiapine	100000	Negative	< 0.3%
7-Hydroxy amoxapine solution	100000	Negative	< 0.3%
8-Hydroxy amoxapine solution	100000	Negative	< 0.3%
10-Hydroxyamitriptyline	1100	Positive	27.3%
Amitriptyline	300	Positive	100%
Amoxapine	200000	Positive	0.15%
Clomipramine	325	Positive	92.3%
Desipramine	280	Positive	107.1%
Dosulepin	500	Positive	60.0%
Doxepin	600	Positive	50.0%
Imipramine	190	Positive	157.9%
Lofepramine	440	Positive	68.1%
N-Desmethyltrimipramine	325	Positive	92.3%
Norclomipramine hydrochloride	375	Positive	80.0%
Nordoxepin hydrochloride	2000	Positive	15.0%
Nortriptyline	300	Positive	100.0%
Opipramol HCl	350	Positive	85.7%
Protriptyline	500	Positive	60.0%
Quetiapine fumarate	55000	Positive	0.54%
Trimipramine	400	Positive	75.0%

Table 10: Cross Reactivity to structurally related compounds in Serum (other drugs)

Structurally Related Compounds	Tested Concentration (ng/mL)	Positive/Negative	Cross-reactivity (%)
Alimemazine	10000	Positive	3.0%
Blonanserin	100000	Negative	< 0.3%
Chlorpromazine	500	Positive	60.0%
Clozapine	100000	Negative	< 0.3%
Cyclobenzaprine	375	Positive	80.0%
Desloratadine	100000	Negative	< 0.3%
Diphenhydramine	60000	Positive	0.5%
Fluoxetine	100000	Negative	< 0.3%
Fluphenazine	2000	Positive	15.0%
Haloperidol	100000	Negative	< 0.3%
Loratadine	100000	Negative	< 0.3%
Loxapine succinate	100000	Negative	< 0.3%
Maprotiline	100000	Positive	0.3%
Mianserin	100000	Negative	< 0.3%
Mirtazapine	100000	Negative	< 0.3%
N-desmethylclozapine	100000	Negative	< 0.3%
N-Desmethylmirtazapine	100000	Negative	< 0.3%
Nefazodone	100000	Negative	< 0.3%
Normaprotiline	100000	Positive	0.3%
Olanzapine	100000	Negative	< 0.3%
Paroxetine	100000	Negative	< 0.3%
Perphenazine	450	Positive	66.7%
Phenoxybenzamine	100000	Negative	< 0.3%
Promazine	450	Positive	66.7%
Promethazine	20000	Positive	1.5%
Risperidone	100000	Negative	< 0.3%
Sertraline	100000	Negative	< 0.3%
Thioridazine	5000	Positive	6.0%
Thiothixene	100000	Negative	< 0.3%
Tianeptine	100000	Negative	< 0.3%
Trazodone	100000	Negative	< 0.3%
Ziprasidone	100000	Negative	< 0.3%

Cross-reactivity to structurally unrelated compounds (Non-Critical Cross-Reactivity):
Structurally unrelated compounds and/or concurrently used drugs were spiked at the concentration listed below into low and high controls (225 and 375 ng/mL) in serum. As shown in the table below the controls were detected accurately, with the low control as negative and the high control as positive, indicating that all the compounds evaluated exhibited minimal cross-reactivity at the concentration tested. The study results are presented in the table below:

Table 11: Cross Reactivity to structurally unrelated compounds in Serum

Structurally Unrelated Compounds	Tested Concentration (ng/mL)	Compound Spiked into Low Sample (225 ng/mL)	Compound Spiked into High Sample (375 ng/mL)
11-nor-Δ9-THC-COOH	100000	Negative	Positive
6-Acetyl morphine	75000	Negative	Positive
Acetaminophen	100000	Negative	Positive
Acetylsalicylic acid	100000	Negative	Positive
Amisulpride	100000	Negative	Positive
Amoxicillin	100000	Negative	Positive
Amphetamine	100000	Negative	Positive
Benzotropine Methane Sulfonate	3000	Negative	Positive
Benzoylecgonine	100000	Negative	Positive
Brompheniramine	3000	Negative	Positive
Caffeine	100000	Negative	Positive
Carbamazepine	3000	Negative	Positive
Carbamazepine Epoxide	10000	Negative	Positive
Chloroquine phosphate	100000	Negative	Positive
Cimetidine	100000	Negative	Positive
Cocaine	75000	Negative	Positive
Codeine	100000	Negative	Positive
Dextromethorphan	100000	Negative	Positive
Diacetylmorphine (Heroin)	100000	Negative	Positive
Diazepam	100000	Negative	Positive
Digoxin	100000	Negative	Positive
Dihydrocodeine	100000	Negative	Positive
EDDP Perchlorate	100000	Negative	Positive
EMDP-HCL	100000	Negative	Positive
Fentanyl	25000	Negative	Positive
Glutethimide	100000	Negative	Positive
Hydrocodone	100000	Negative	Positive
Hydrocortisone	100000	Negative	Positive
Hydromorphone	100000	Negative	Positive
Hydroxyzine	3000	Negative	Positive
Ibuprofen	100000	Negative	Positive
Levorphanol	100000	Negative	Positive
Levothyroxine	100000	Negative	Positive

Structurally Unrelated Compounds	Tested Concentration (ng/mL)	Compound Spiked into Low Sample (225 ng/mL)	Compound Spiked into High Sample (375 ng/mL)
Meperidine	25000	Negative	Positive
Methadone	75000	Negative	Positive
Methamphetamine	100000	Negative	Positive
Methaqualone	500	Negative	Positive
Methsuximide	75000	Negative	Positive
Methylphenidate	100000	Negative	Positive
Morphine	100000	Negative	Positive
Morphine-3β-glucuronide	100000	Negative	Positive
Morphine-6β-glucuronide	100000	Negative	Positive
Nalbuphine	100000	Negative	Positive
Nalorphine	100000	Negative	Positive
Naloxone	100000	Negative	Positive
Naltrexone	100000	Negative	Positive
Naproxen	100000	Negative	Positive
Norcodeine	100000	Negative	Positive
Nordiazepam	100000	Negative	Positive
Norethindrone	100000	Negative	Positive
Norhydrocodone	100000	Negative	Positive
Noroxycodone	100000	Negative	Positive
Noroxymorphone	100000	Negative	Positive
Norpropoxyphene	75000	Negative	Positive
Oxaprozin	100000	Negative	Positive
Oxazepam	100000	Negative	Positive
Oxycodone	100000	Negative	Positive
Oxymorphone	100000	Negative	Positive
PCP	25000	Negative	Positive
Phenobarbital	100000	Negative	Positive
Phenytoin	100000	Negative	Positive
Primidone	100000	Negative	Positive
Procyclidine	100000	Negative	Positive
Propoxyphene	100000	Negative	Positive
Secobarbital	100000	Negative	Positive
Tapentadol	100000	Negative	Positive
Temazepam	100000	Negative	Positive
Triprolidine	100000	Negative	Positive
Valproic Acid	100000	Negative	Positive
Venlafaxine	100000	Negative	Positive
Verapamil	100000	Negative	Positive

g) Interference

The interference s study is performed in accordance with CLSI Guideline *CLSI EP07-*A3*& EP37*_ED1*.*

The potential interference of endogenous and exogenous substances on the recovery of nortriptyline using Alinity TCA Reagent Kit was assessed. Potentially interfering substances were spiked into the low control, 225ng/mL (-25% of the cutoff concentration of 300 ng/mL) and high controls, 375 ng/mL (+25% of the cutoff concentration of 300 ng/mL).

In the presence of the compounds listed below, the controls were detected accurately, indicating that these compounds did not show interference in the assay.

Table 12: Results of Interfering Substances Testing – Serum

Compounds	Tested Concentrations (mg/dL)	Low Control (225 ng/mL)	High Control (375 ng/mL)
Bilirubin (Conjugated)	40	Negative	Positive
Bilirubin (Unconjugated)	40	Negative	Positive
Hemoglobin	1000	Negative	Positive
Human Serum Albumin (HSA)	7500	Negative	Positive
γ-globulin	5000	Negative	Positive
Rh Factor	1300 IU	Negative	Positive
Triglycerides	1500	Negative	Positive
Cholesterol	1400	Negative	Positive

H. Conclusion

The information supports a determination of substantial equivalence between Alinity c Tricyclic Antidepressants Reagent kit and DRI Tricyclics Serum Tox Assay (K213875).