DRI™ Tricyclics Serum Tox Assay

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Read Highlighted Changes: Revised February 2023

For In Vitro Diagnostic Use

REF 1128 (25 mL, 8 mL Kit)
10028827 (500 mL, 180 mL Kit)

Rx Only

Intended Use

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 [1]. 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.

Summary and Explanation of the Test

Amitriptyline, imipramine, and related compounds are TCAs that are widely used for the treatment of depression. Metabolites of amitriptyline and imipramine (nortriptyline and desimipramine, respectively) also possess antidepressant activity, but are less effective than the parent compounds. The most frequent side effects associated with the use of TCAs include dry mouth, constipation, dizziness, palpitations and urinary retention. Acute toxicity due to TCAs may lead to coma, cardiac arrhythmia, respiratory depression and death.[2,3] Tricyclics have become the most common drug overdose case admitted to intensive care units.[4] Detecting the presence of the drugs in serum, plasma, or urine from patients suspected of drug overdose can assist the physician in diagnosing and treating the patient.

The DRI Tricyclics Serum Tox Assay is a homogeneous enzyme immunoassay using ready-to-use liquid reagents. Specific tricyclic antibodies were used to detect TCAs in serum, plasma, or urine. The test is based on the competition of an enzyme, glucose-6-phosphate dehydrogenase (G6PDH), labeled-drug and the drug from the sample for a fixed amount of specific antibody binding sites. In the absence of the drug from the sample, the specific antibody binds the enzyme-labeled drug and the enzyme activity is inhibited. This phenomenon creates a direct relationship between drug concentration in the sample and the enzyme activity. The enzyme activity is determined spectrophotometrically at 340 nm by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH.

Reagents

Antibody/Substrate Reagent: 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: Contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with nortriptyline in Tris buffer with sodium azide as a preservative.

Additional Materials Required (sold separately):

REF	Kit Description
0962	Serum Tox Negative Calibrator, 10 mL
0963	Serum Tox Calibrator 1, 5 mL
0965	Serum Tox Calibrator 2, 5 mL
0967	Serum Tox Calibrator 3, 5 mL
0976	Serum Tox Calibrator 4, 5 mL
10011608	MAS Tox Control 1 and 2, 2 x 5 mL

⚠ Precautions and Warnings

The reagents are harmful if swallowed.

DANGER: DRI Tricyclics Serum Tox Assay contains ≤0.2% bovine serum albumin (BSA) and ≤0.5% drug-specific antibody.
H317 - May cause allergic skin reaction.
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Avoid breathing mist or vapor. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/eye protection/face protection. In case of inadequate ventilation wear respiratory protection. If on skin: Wash with plenty of soap and water. IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing. If skin irritation or rash occurs: Get medical advice/attention. If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. Wash contaminated clothing before reuse. Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Reagents used in the assay components contain ≤0.09% sodium azide. Avoid contact with skin and mucous membranes. Flush affected areas with copious amounts of water. Get immediate medical attention for eyes, or if ingested. Sodium azide may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with large volumes of water to prevent azide build-up. Clean exposed metal surfaces with 10% sodium hydroxide.

Do not use the reagents beyond their expiration dates.

Reagent Preparation and Storage

The reagents are ready for use. No reagent preparation is required. All assay components, when stored properly at 2-8°C, are stable until the expiration date indicated on the label.

Specimen Collection and Handling

Serum, plasma or urine can be used with the assay. Anticoagulants such as lithium heparin, sodium heparin, sodium citrate, potassium oxalate, K2 EDTA and K3 EDTA, were found not to interfere with the assay. Plasma samples collected with these anticoagulants may be used with the assay although a fresh serum sample is preferred. Store the samples refrigerated. An effort should be made to keep pipetted samples free of gross debris.

Analyte	Sample Type	Storage Temperature	Length of Storage
TCAs	Serum or Plasma	Room temperature (20°C - 25°C)	24 hours[5,6]
	Serum or Plasma	2°C - 8°C	4 weeks[5,6]
	Serum or Plasma	–20°C	> 1 year[5,6]
TCAs	Urine	Room temperature (20°C - 25°C)	24 hours[7]
	Urine	2°C - 8°C	4 weeks[8]
	Urine	–20°C	For longer storage prior to analysis or for sample retention after analysis[9].

Handle all serum, plasma or urine specimens as if they were potentially infectious.

Assay Procedure

Chemistry analyzers capable of maintaining a constant temperature, accurate pipetting of samples, mixing reagents, measuring enzymatic rates at 340 nm and timing the reaction accurately can be used to perform this assay. Before performing the assay refer to the analyzer-specific protocol sheet, which contains parameters and/or additional instructions for use.

Quality Control and Calibration

Good laboratory practice suggests the use of control specimens to ensure proper assay performance. Use controls near the cutoff calibrator to validate the calibration. Control results must fall within the established range. If results fall outside of the established range, assay results are invalid. All quality control requirements should be performed in conformance with local, state and/or federal regulations or accreditation requirements.

Qualitative analysis

For qualitative analysis of samples, use the 300 ng/mL calibrator as the cutoff level. The DRI Serum Tox Calibrator 2, which contains 300 ng/mL nortriptyline, is used as a cutoff for distinguishing "positive" from "negative" samples.

Semiquantitative analysis

For semiquantitative analysis, use all calibrators from 0-1000 ng/mL of nortriptyline to estimate the relative concentration of class of TCAs drugs.

Results and Expected Values

Qualitative results

A sample that exhibits a change in absorbance (ΔA) value equal to or greater than the cutoff calibrator is considered positive. A sample that exhibits a change in absorbance (ΔA) value lower than the cutoff calibrator is considered negative.

Semiquantitative results

A rough estimate of drug concentration in the samples can be obtained by running a standard curve with all calibrators and measuring samples off the standard curve.

Immunoassays that produce only a single result in the presence of a class of drugs, such as TCAs, cannot accurately measure the concentration of each individual component. For a qualitative application, a positive result indicates only the presence of TCAs. For a semiquantitative application, the assay gives an approximate, cumulative concentration of TCAs.

Limitations

1. A positive result from this assay indicates only the presence of TCAs and does not necessarily correlate with the extent of physiological and psychological effects.
2. A positive result by this assay should be confirmed by another non-immunological method. LC-MS/MS is the preferred method.
3. The test is designed for use with human serum, plasma or urine only.
4. Other substances and/or factors, (e.g.,technical or procedural) other than those investigated in the specificity study may interfere with the test and cause false results.
5. The assay is intended for use in clinical laboratories.
6. Patient samples containing tricyclic antidepressants in the presence of carbamazepine may yield falsely elevated results in the TCA immunoassay. Results should always be assessed in conjunction with the patient's medical history, clinical examinations, and other clinicopathological findings.

Specific Performance Characteristics

The following data were generated with a Architect c4000 clinical chemistry analyzer.

Precision

Precision is a combination of repeatability and reproducibility.

Repeatability

Samples were prepared by spiking nortriptyline into drug-free serum and drug-free urine at cutoff (100%), 25%, 50%, 75%, and 100% above and below the cutoff and tested in duplicate (n=2) twice per day for 20 days (total n=80 for each level), in both qualitative and semi-quantitative modes. The results are shown below.

Serum:

Spiked Concentration (ng/mL)	% of Cutoff	Total Precision (n=80) - Serum				
		# of Determinants	Qualitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Repeatability SD Results	Semi-quantitative Immunoassay Repeatability %CV Results
0	-100	80	80/0	80/0	N/A	N/A
75	-75	80	80/0	80/0	4.40	5.36%
150	-50	80	80/0	80/0	4.19	2.42%
225	-25	80	80/0	80/0	4.22	1.68%
300	100	80	10/70	19/61	17.29	5.34%
375	+25	80	0/80	0/80	16.59	3.92%
450	+50	80	0/80	0/80	19.15	3.94%
525	+75	80	0/80	0/80	47.37	8.25%
600	+100	80	0/80	0/80	43.10	6.28%

Urine:

Spiked Concentration (ng/mL)	% of Cutoff	Total Precision (n=80) - Urine				
		# of Determinants	Qualitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Repeatability SD Results	Semi-quantitative Immunoassay Repeatability %CV Results
0	-100	80	80/0	80/0	N/A	N/A
75	-75	80	80/0	80/0	4.62	5.96%
150	-50	80	80/0	80/0	7.19	4.45%
225	-25	80	80/0	80/0	9.62	4.08%
300	100	80	68/12	73/7	11.04	3.75%
375	+25	80	0/80	0/80	24.41	6.12%
450	+50	80	0/80	0/80	18.65	4.13%
525	+75	80	0/80	0/80	46.66	8.89%
600	+100	80	0/80	0/80	45.15	7.63%

Reproducibility

Samples were prepared by spiking nortriptyline into drug-free serum and drug-free urine at cutoff (100%), 25%, 50%, 75%, and 100% above and below the cutoff. Spiked samples were tested as 1 run per day, 5 replicates per run for a total of 5 days in qualitative and semi-quantitative modes on 3 different instruments of the same model. The results of the reproducibility precision study are shown below:

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)	Semi-quantitative Immunoassay Reproducibility SD Results	Semi-quantitative Immunoassay Reproducibility %CV Results
0	-100	75	75/0	75/0	N/A	N/A
75	-75	75	75/0	75/0	5.26	6.66%
150	-50	75	75/0	75/0	4.00	2.39%
225	-25	75	75/0	75/0	4.36	1.76%
300	100	75	30/45	29/46	19.24	6.11%
375	+25	75	0/75	0/75	22.23	5.40%
450	+50	75	0/75	0/75	21.06	4.41%
525	+75	75	0/75	0/75	43.78	7.87%
600	+100	75	0/75	0/75	43.77	6.54%

Urine:

Spiked Concentration (ng/mL)	% of Cutoff	Total Precision (n=75) - Urine				
		# of Determinants	Qualitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Results (Negative/ Positive)	Semi-quantitative Immunoassay Reproducibility SD Results	Semi-quantitative Immunoassay Reproducibility %CV Results
0	-100	75	75/0	75/0	N/A	N/A
75	-75	75	75/0	75/0	3.34	4.30%
150	-50	75	75/0	75/0	4.60	2.82%
225	-25	75	75/0	75/0	6.90	2.86%
300	100	75	61/14	66/9	12.05	4.01%
375	+25	75	0/75	0/75	23.21	5.85%
450	+50	75	0/75	0/75	23.96	5.28%
525	+75	75	0/75	0/75	39.74	7.73%
600	+100	75	0/75	0/75	42.36	7.86%

Accuracy

One hundred and seventeen clinical specimens were tested using DRI Tricyclics Serum Tox Assay on the Architect c4000 clinical chemistry analyzer and confirmed by LC-MS/MS. The results are presented as follows:

Qualitative Accuracy Study with LC-MS/MS as Reference Method - Serum

DRI Tricyclics Serum Tox 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	1[a]	0	31	25
Negative	1	35	24	0	0

Qualitative Accuracy Study with LC-MS/MS as Reference Method - Urine

DRI Tricyclics Serum Tox 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	0	2[d]	7	42
Negative	22	11	15	1[d]	0

Semi-quantitative Accuracy Study with LC-MS/MS as Reference Method - Serum

DRI Tricyclics Serum Tox 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[a]	0	31	25
Negative	1	34	24	0	0

Semi-quantitative Accuracy Study with LC-MS/MS as Reference Method - Urine

DRI Tricyclics Serum Tox 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	0	2[d]	7	42
Negative	22	11	15	1[d]	0

[a] Serum discordant table

Sample ID	Qualitative IA (mA/min)	Semi-Quantitative IA (ng/mL)	LC-MS/MS Value (ng/mL)
APP9489-2[b]	Negative	354 (Positive)	110
APP9474-2[c]	Positive	418 (Positive)	120

[b] 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%, 120%, and 100% by immunoassay, respectively.

[c] 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%, 120%, and 100% by immunoassay, respectively.

Note: In addition both samples APP9489-2 and APP9474-2 were confirmed by LC-MS/MS to contain Carbamazepine and Carbamazepine Epoxide with concentrations (4275 ng/mL & 5285 ng/mL) and (595 ng/mL & 955 ng/mL), respectively. Refer to the limitation section for further explanation.

[d] Urine discordant table

Sample ID	Qualitative IA (mA/min)	Semi-Quantitative IA (ng/mL)	LC-MS/MS Value (ng/mL)
APP6058-2[e]	Positive	347 (Positive)	285
APP6060-2[f]	Positive	375 (Positive)	230
APP6056-2[g]	Negative	267 (Negative)	372

[e] Sample APP6058-2 contains Amitriptyline at 146 ng/mL and Nortriptyline at 139 ng/mL by LC-MS/MS and cross-reacts at 100% and 100% by immunoassay, respectively.

[f] Sample APP6060-2 contains Amitriptyline at 114 ng/mL, Nordoxepin at 3.05 ng/mL, and Nortriptyline at 115 ng/mL by LC-MS/MS and cross-reacts at 100%, 17.1%, and 100% by immunoassay, respectively.

[g] Sample APP6056-2 contains Amitriptyline at 186 ng/mL and Nortriptyline at 186 ng/mL by LC-MS/MS and cross-reacts at 100% and 100% by immunoassay, respectively.

Analytical Recovery and Dilution Linearity

To demonstrate the dilution linearity for purposes of sample dilution and quality control of the entire assay range, drug-free serum or drug-free urine were spiked to the high calibrator level using nortriptyline and diluted with drug-free serum or drug-free urine to generate nine intermediate levels. Each sample was run in replicates of five in semi-quantitative mode and the average was used to determine percent recovery compared to the expected target value.

Expected Nortriptyline Values (ng/mL)	Serum		Urine	
	Observed Values (ng/mL)	Recovery (%)	Observed Values (ng/mL)	Recovery (%)
0	7	N/A	8	N/A
125	121	97	148	118
250	242	97	271	108
375	385	103	393	105
500	479	96	470	94
625	720	115	620	99
750	839	112	741	99
875	913	104	838	96
1000	1046	105	946	95

Specificity

Tricyclic compounds and other structurally related compounds were spiked into drug-free serum and drug-free urine at concentrations indicated and tested with DRI Tricyclics Serum Tox Assay. The following cross-reactivity results were yielded.

Structurally Related Compounds (TCA drugs and Metabolites)	Serum			Urine		
	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)
2-Hydroxy Imipramine	1,300	Positive	23.1	1,000	Positive	30
7-Hydroxy Quetiapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
7-Hydroxy Amoxapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
8-Hydroxy Amoxapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Amitriptyline	300	Positive	100	300	Positive	100
Amoxapine	125,000	Positive	0.2	100,000	Positive	0.3
10-Hydroxyamitriptyline	1,000	Positive	30	700	Positive	42.9
Clomipramine	300	Positive	100	350	Positive	85.7
Desipramine	250	Positive	120	250	Positive	120
Dosulepin	475	Positive	63.2	425	Positive	70.6
Doxepin	600	Positive	50	550	Positive	54.5
Imipramine	190	Positive	157.9	220	Positive	136.4
Lofepramine	430	Positive	69.8	460	Positive	65.2
N-Desmethyltrimipramine	350	Positive	85.7	325	Positive	92.3
Norclomipramine	375	Positive	80	450	Positive	66.7
Nordoxepin	1,750	Positive	17.1	1750	Positive	17.1
Nortriptyline	300	Positive	100	300	Positive	100
Opipramol	350	Positive	85.7	350	Positive	85.7
Protriptyline	450	Positive	66.7	400	Positive	75
Quetiapine Fumarate	50,000	Positive	0.6	45,000	Positive	0.7
Trimipramine	390	Positive	76.9	400	Positive	75

Other Structurally Related Compounds	Serum			Urine		
	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)
Alimemazine	12,000	Positive	2.5	12,000	Positive	2.5
Blonanserin	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Chlorpromazine	525	Positive	57.1	600	Positive	50
Clozapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Cyclobenzaprine	450	Positive	66.7	500	Positive	60
Desloratadine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Diphenhydramine	60,000	Positive	0.5	30,000	Positive	1
Fluoxetine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Fluphenazine	2,000	Positive	15	2,000	Positive	15
Haloperidol	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Loratadine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Loxapine	100,000	Negative	< 0.3	100,000	Positive	0.3
Maprotiline	100,000	Positive	0.3	100,000	Positive	0.3
Mianserin	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Mirtazapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
N-Desmethylclozapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Nefazodone	100,000	Negative	< 0.3	100,000	Negative	< 0.3
N-Desmethylmirtazapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Normaprotiline	100,000	Positive	0.3	100,000	Positive	0.3
Olanzapine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Paroxetine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Perphenazine	450	Positive	66.7	650	Positive	46.2
Phenoxybenzamine	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Promazine	400	Positive	75	410	Positive	73.2
Promethazine	20,000	Positive	1.5	15,000	Positive	2
Risperidone	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Sertraline	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Thioridazine	6,000	Positive	5	4,000	Positive	7.5
Thiothixene	100,000	Negative	< 0.3	100,000	Negative	< 0.3

Table continued

Other Structurally Related Compounds	Serum			Urine		
	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)	Tested Concentrations (ng/mL)	Positive/ Negative	Cross-Reactivity (%)
Tianeptine	100,000	Negative	< 0.3	90,000	Positive	0.33
Trazodone	100,000	Negative	< 0.3	100,000	Negative	< 0.3
Ziprasidone	100,000	Negative	< 0.3	100,000	Negative	< 0.3

Structurally unrelated compounds and/or concurrently used drugs were evaluated by adding each substance into nortriptyline spiked at low and high control levels (225 and 375 ng/mL) at the concentration indicated. As shown in the table below, the controls were detected accurately. Low control as negative and high control as positive indicate that all the compounds evaluated exhibited minimal cross-reactivity at the concentration tested.

Structurally Unrelated Compounds	Serum			Urine		
	Tested Concentrations (ng/mL)	Low Control (225 ng/mL)	High Control (375 ng/mL)	Tested Concentrations (ng/mL)	Low Control (225 ng/mL)	High Control (375 ng/mL)
11-nor-Δ9-THC-COOH	100,000	Negative	Positive	100,000	Negative	Positive
6-Acetyl morphine	75,000	Negative	Positive	100,000	Negative	Positive
Acetaminophen	100,000	Negative	Positive	100,000	Negative	Positive
Acetylsalicylic acid	100,000	Negative	Positive	100,000	Negative	Positive
Amisulpride	100,000	Negative	Positive	100,000	Negative	Positive
Amoxicillin	100,000	Negative	Positive	100,000	Negative	Positive
Amphetamine	100,000	Negative	Positive	100,000	Negative	Positive
Benztropine Methane Sulfonate	3,000	Negative	Positive	7,000	Negative	Positive
Benzoylecgonine	100,000	Negative	Positive	100,000	Negative	Positive
Brompheniramine	3,000	Negative	Positive	5,000	Negative	Positive
Caffeine	100,000	Negative	Positive	100,000	Negative	Positive
Carbamazepine	3,000	Negative	Positive	5,000	Negative	Positive
Carbamazepine Epoxide	10,000	Negative	Positive	30,000	Negative	Positive
Chloroquine phosphate	100,000	Negative	Positive	100,000	Negative	Positive
Cimetidine	100,000	Negative	Positive	100,000	Negative	Positive
Cocaine	75,000	Negative	Positive	100,000	Negative	Positive
Codeine	100,000	Negative	Positive	100,000	Negative	Positive
Dextromethorphan	100,000	Negative	Positive	100,000	Negative	Positive
Diacetylmorphine (Heroin)	100,000	Negative	Positive	100,000	Negative	Positive
Diazepam	100,000	Negative	Positive	100,000	Negative	Positive
Digoxin	100,000	Negative	Positive	100,000	Negative	Positive
Dihydrocodeine	100,000	Negative	Positive	100,000	Negative	Positive
EDDP Perchlorate	100,000	Negative	Positive	100,000	Negative	Positive
EMDP-HCL	100,000	Negative	Positive	100,000	Negative	Positive
Fentanyl	25,000	Negative	Positive	25,000	Negative	Positive
Glutethimide	100,000	Negative	Positive	100,000	Negative	Positive
Hydrocodone	100,000	Negative	Positive	100,000	Negative	Positive
Hydrocortisone	100,000	Negative	Positive	100,000	Negative	Positive
Hydromorphone	100,000	Negative	Positive	100,000	Negative	Positive
Hydroxyzine	3,000	Negative	Positive	5,000	Negative	Positive
Ibuprofen	100,000	Negative	Positive	100,000	Negative	Positive
Levorphanol-D3	100,000	Negative	Positive	100,000	Negative	Positive
Levothyroxine	100,000	Negative	Positive	100,000	Negative	Positive
Meperidine	25,000	Negative	Positive	25,000	Negative	Positive
Methadone	75,000	Negative	Positive	75,000	Negative	Positive
Methamphetamine	100,000	Negative	Positive	100,000	Negative	Positive
Methaqualone	500	Negative	Positive	1,000	Negative	Positive
Methsuximide	75,000	Negative	Positive	75,000	Negative	Positive
Methylphenidate	100,000	Negative	Positive	100,000	Negative	Positive
Morphine	100,000	Negative	Positive	100,000	Negative	Positive
Morphine-3β-glucuronide	100,000	Negative	Positive	100,000	Negative	Positive
Morphine-6β-glucuronide	100,000	Negative	Positive	100,000	Negative	Positive
Nalbuphine	100,000	Negative	Positive	100,000	Negative	Positive
Nalorphine	100,000	Negative	Positive	100,000	Negative	Positive
Naloxone	100,000	Negative	Positive	100,000	Negative	Positive
Naltrexone	100,000	Negative	Positive	100,000	Negative	Positive
Naproxen	100,000	Negative	Positive	100,000	Negative	Positive
Norcodeine	100,000	Negative	Positive	100,000	Negative	Positive
Nordiazepam	100,000	Negative	Positive	100,000	Negative	Positive

Table continued

Structurally Unrelated Compounds	Serum			Urine		
	Tested Concentrations (ng/mL)	Low Control (225 ng/mL)	High Control (375 ng/mL)	Tested Concentrations (ng/mL)	Low Control (225 ng/mL)	High Control (375 ng/mL)
Norethindrone	100,000	Negative	Positive	100,000	Negative	Positive
Norhydrocodone	100,000	Negative	Positive	75,000	Negative	Positive
Noroxycodone	100,000	Negative	Positive	100,000	Negative	Positive
Noroxymorphone	100,000	Negative	Positive	100,000	Negative	Positive
Norpropoxyphene	75,000	Negative	Positive	75,000	Negative	Positive
Oxaprozin	100,000	Negative	Positive	100,000	Negative	Positive
Oxazepam	100,000	Negative	Positive	100,000	Negative	Positive
Oxycodone	100,000	Negative	Positive	100,000	Negative	Positive
Oxymorphone	100,000	Negative	Positive	100,000	Negative	Positive
PCP	50,000	Negative	Positive	75,000	Negative	Positive
Phenobarbital	100,000	Negative	Positive	100,000	Negative	Positive
Phenytoin	100,000	Negative	Positive	100,000	Negative	Positive
Primidone	100,000	Negative	Positive	100,000	Negative	Positive
Procyclidine	100,000	Negative	Positive	100,000	Negative	Positive
Propoxyphene	100,000	Negative	Positive	100,000	Negative	Positive
Secobarbital	100,000	Negative	Positive	100,000	Negative	Positive
Tapentadol	100,000	Negative	Positive	100,000	Negative	Positive
Temazepam	100,000	Negative	Positive	100,000	Negative	Positive
Triprolidine	100,000	Negative	Positive	100,000	Negative	Positive
Valproic Acid	100,000	Negative	Positive	100,000	Negative	Positive
Venlafaxine	100,000	Negative	Positive	100,000	Negative	Positive
Verapamil	100,000	Negative	Positive	100,000	Negative	Positive

Interference

The potential interference of endogenous, exogenous, physiological substances, and pH on the recovery of nortriptyline using DRI Tricyclics Serum Tox Assay was assessed. Potentially interfering substances were spiked into the low and high controls (225 and 375 ng/mL) at the concentrations indicated. As shown in the tables below, the controls were detected accurately. Low control as negative and high control as positive indicate that these compounds did not show interference in the assay.

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
Albumin	7500	Negative	Positive
γ-globulin	5000	Negative	Positive
Rh Factor	1300 IU	Negative	Positive
Triglycerides	1500	Negative	Positive
Cholesterol	1400	Negative	Positive

Urine:

Compounds	Tested Concentrations (mg/dL)	Low Control (225 ng/mL)	High Control (375 ng/mL)
Acetone	500	Negative	Positive
Ascorbic Acid	150	Negative	Positive
Caffeine	5	Negative	Positive
Creatinine	400	Negative	Positive
Ethanol	1000	Negative	Positive
Galactose	5	Negative	Positive
Glucose	1000	Negative	Positive
Hemoglobin	150	Negative	Positive
Human Serum Albumin (HSA)	200	Negative	Positive
Oxalic acid	50	Negative	Positive
Riboflavin	3	Negative	Positive
Sodium Chloride	1000	Negative	Positive
Urea	1000	Negative	Positive

pH	Low Control (225 ng/mL)	High Control (375 ng/mL)
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

Specific Gravity	Low Control (225 ng/mL)	High Control (375 ng/mL)
1.004	Negative	Positive
1.006	Negative	Positive
1.008	Negative	Positive
1.010	Negative	Positive
1.011	Negative	Positive
1.012	Negative	Positive
1.013	Negative	Positive
1.016	Negative	Positive
1.022	Negative	Positive
1.030	Negative	Positive

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