

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k093664

B. Purpose for Submission:

New device

C. Measurand:

Urine amphetamine and urine methamphetamine

D. Type of Test:

Qualitative enzyme immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Amphetamines II

G. Regulatory Information:

1. Regulation section:

21 CFR § 862.3100 Amphetamine Test System

21 CFR § 862.3610 Methamphetamine Test System

2. Classification:

II

3. Product code:

DKZ, enzyme immunoassay, amphetamine

LAF, gas chromatography, methamphetamine

4. Panel:

Toxicology (91)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

Amphetamines II (AMP II) is an in vitro diagnostic test for the qualitative and semiquantitative detection of amphetamines and methamphetamines on COBAS INTEGRA systems at cutoff concentrations of 300 ng/mL, 500 ng/mL and 1000 ng/mL when calibrated with *d*-methamphetamine. 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).

Amphetamines 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) 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. Special conditions for use statement(s):

- a. Prescription use
- b. Amphetamines 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) is the preferred confirmatory method. Clinical consideration and professional judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are used.
- c. Recommended calibrators are Preciset DAT Plus I, Preciset DAT Plus II and CFAS DAT Qualitative Plus Calibrators (k060645, k090939).
- d. Recommended controls to be used are Control Set DAT I, Control Set DAT II, Control Set DAT III (k060645, k080183).
- e. AMP II must not be run in parallel with Roche A1C-2. Special wash programming steps are not sufficient to overcome reagent carryover issues when Amphetamines II is run in parallel with HbA1cII. The user is instructed that AMP II cannot be run in parallel with HbA1cII.

4. Special instrument requirements:

Integra 800

I. Device Description:

The Amphetamines II test is an immunoassay for use on automated clinical chemistry analyzers. The device consists of two wet reagents; an antibody working solution, and a drug-microparticle conjugate. During the assay, in the absence of sample drug in urine, free antibody binds to the drug-microparticle conjugates causing the formation of particle aggregates. 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 rate of absorbance change is proportional to the concentration of drug in the sample. Calibrators, ranging in concentration from 0-5000 ng/mL depending on cutoff and test mode, are run with the assay. Concentrations of controls and unknowns are calculated from the standard curve in semi-quantitative mode. Results for controls or calibrators are determined as preliminary positive or negative relative to the cutoff in qualitative mode.

C.f.a.s. DAT Qualitative Clinical, C.f.a.s. DAT Qualitative Plus, C.f.a.s. DAT Qualitative Plus Clinical, Preciset DAT Plus I Calibrators, and Preciset DAT Plus II Calibrators are ready to use, multianalyte calibrators prepared by the quantitative addition of drug or drug metabolite to drug-free human urine and are available separately from the reagent.

Control Set DAT I, II, and III, and Control Set DAT Clinical are ready to use multianalyte controls prepared by the quantitative addition of drug or drug metabolite to drug-free urine and are available separately from the reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ONLINE Amphetamines II Assay

2. Predicate K number(s):

k083764

3. Comparison with predicate:

Feature	Amphetamines II Assay, Integra 800	Predicate Device: Online Amphetamines II Assay, Hitachi 917 (k083764)
Methodology	Same	KIMS, Kinetic interaction of microparticles in solution

Sample Type	Same	Urine
Indications for Use/ Intended Use	Same	Qualitative and semi-quantitative detection of amphetamines and methamphetamines
Reagents	Same	<u>Conjugate Working Solution:</u> Conjugated amphetamine, and methamphetamine derivatives in buffer with bovine serum albumin (BSA) and 0.09% sodium azide. 2. <u>Antibody/Microparticle Working Solution:</u> Microparticles attached to amphetamine and methamphetamine antibodies (mouse monoclonal) in buffer with bovine serum albumin (BSA) and 0.09% sodium azide.
Cutoff	Same	300, 500, 1,000 ng/mL

K. Standard/Guidance Document Referenced (if applicable):

Draft Guidance for Industry and FDA Staff: Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests
 CLSI EP-5A: Evaluation of Precision Performance of Clinical Chemistry Devices;
 Approved Guideline -2nd ed

L. Test Principle:

The Amphetamines II assay is based on the kinetic interaction of microparticles in a solution (KIMS) as measured by changes in light transmission. In the absence of sample drug, soluble drug-polymer conjugates bind to antibody-bound microparticles, causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample, the absorbance increases. When a urine sample contains the drug in question, this drug competes with the conjugate-bound drug derivative for microparticle-bound antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample. Sample drug content is determined relative to the value obtained for a known cutoff concentration of drug.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Precision studies were performed according to CLSI EP5-A2. Two separate studies were conducted for d-methamphetamine and d-amphetamine for both the qualitative and semi-quantitative assays for each cutoff (300 ng/mL, 500 ng/mL, 1,000 ng/mL). Samples were prepared by spiking a negative human urine pool with the analyte of interest (d-methamphetamine or d-amphetamine) at the following concentrations: zero drug, -75%, -50%, and -25% below the cutoff, cutoff, and +25%, +50%, +75%, and +100% above the cutoff. Samples were tested using one reagent lot, in 2 replicates per run, 2 runs per day for 21 days, total n=84 using one reagent lot. For the d-amphetamine study, 10 calibrations were performed. For the d-methamphetamine study, 8 calibrations were performed.

d-Methamphetamine (MAMP)

300 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos
-50%	84 neg/0 pos	84 neg/0 pos
-25%	83 neg/1 pos	84 neg/0 pos
Cutoff	27 neg/57 pos	34 neg/50 pos
+25%	0 neg/84 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

500 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos
-50%	84 neg/0 pos	84 neg/0 pos
-25%	84 neg/0 pos	84 neg/0 pos
Cutoff	28 neg/56 pos	38 neg/46 pos
+25%	0 neg/84 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

1000 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos

-50%	84 neg/0 pos	84 neg/0 pos
-25%	84 neg/0 pos	84 neg/0 pos
Cutoff	13 neg/71 pos	25 neg/59 pos
+25%	0 neg/84 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

d-Amphetamines (AMP)

300 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos
-50%	84 neg/0 pos	84 neg/0 pos
-25%	84 neg/0 pos	84 neg/0 pos
Cutoff	2 neg/82 pos	4 neg/80 pos
+25%	0 neg/84 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

500 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos
-50%	84 neg/0 pos	84 neg/0 pos
-25%	82 neg/2 pos	84 neg/0 pos
Cutoff	6 neg/78 pos	0 neg/84 pos
+25%	0 neg/84 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

1000 ng/mL cutoff

Sample Concentration	Qualitative Results (#Neg/# Pos)	Semi-Quantitative Results (#Neg/# Pos)
Zero drug	84 neg/0 pos	84 neg/0 pos
-75%	84 neg/0 pos	84 neg/0 pos
-50%	84 neg/0 pos	84 neg/0 pos
-25%	82 neg/2 pos	84 neg/0 pos
Cutoff	6 neg/78 pos	6 neg/78 pos

+25%	1 neg/83 pos	0 neg/84 pos
+50%	0 neg/84 pos	0 neg/84 pos
+75%	0 neg/84 pos	0 neg/84 pos
+100%	0 neg/84 pos	0 neg/84 pos

b. *Linearity/assay reportable range:*

Recovery across the range was confirmed by serially diluting a spiked urine pool containing drug in desired levels listed in the tables below to cover their measuring ranges of 0-2,000 ng/mL and 0-5,000 ng/mL for both drugs. Each sample was assayed on Integra 800 analyzer in the semi-quantitative mode. The results were averaged and compared to the expected result and the percent recovery was calculated. Sponsor calculated the % recovery by dividing the recovered result by the target concentration and then multiplying by 100. Results are presented below:

d-Methamphetamine

300 ng/mL			500 ng/mL			1000 ng/mL		
Expected	Observed	Cutoff % Recovery	Expected	Observed	cutoff % Recovery	Expected	Observed	cutoff % Recovery
0	12	---	0	5	---	0	8	---
53.6	62	115.7	81.1	82	101.1	135.2	159	117.6
107.3	114	106.3	162	155	95.5	270.4	265	98.0
160.9	165	102.8	243.4	226	92.8	405.6	379	93.4
214.5	239	111.3	324.6	283	87.2	540.8	611	113.0
268.2	258	96.0	405.7	350	86.3	676	691	102.2
321.8	322	100.1	486.8	430	88.3	811.2	905	111.6
375.4	356	94.9	568	559	98.4	946.4	1029	108.7
429.1	411	95.7	649.1	643	99.1	1081.6	1269	117.3
482.7	441	91.3	730.2	726	99.4	1216.8	1382	113.6
536.3	536	99.9	811.4	850	104.8	1352.0	1509	111.6
590.0	557	94.4	1622.8	1767	108.9	2028	2028	100
643.6	604	93.9	2434.1	2356	96.8	2704	2703	100
858.1	809	94.2	3245.5	3256	100.3	3380	3372	99.8
1072.7	1072	99.9	4056.9	4223	104.1	4056	4045	99.7
1287.2	1253	97.4	4868.3	5290	108.7	4732	4296	90.8
1501.7	1538	102.4	5679.6	5834	102.7	5408	5103	94.4
1716.3	1730	100.8	6491	6470	99.7	6084	5482	90.1
1930.8	1946	100.8				6760	5955	88.1
2145.3	2233	104.1						

d-Amphetamine

300 ng/mL			500 ng/mL			1000 ng/mL		
Expected	Observed	Cutoff % Recovery	Expected	Observed	cutoff % Recovery	Expected	Observed	cutoff % Recovery

-14.6	0	---	0	-51.1	---	-18.5	0	---
34.2	24	70.4	69.9	111	158.5	98.2	112	114
82.9	83	99.8	190.9	210	110.1	214.8	223	103.8
131.6	132	100.1	311.9	304	97.3	331.4	306	92.4
180.3	173	96.1	432.9	412	95.1	448	442	98.7
229.1	231	100.8	553.9	504	91.0	564.6	533	94.4
277.8	263	94.8	674.9	687	101.8	681.2	665	97.7
326.5	335	102.5	795.9	776	97.5	797.8	765	95.9
375.2	369	98.3	916.9	916	99.9	914.4	891	97.5
423.9	408	96.3	1037.9	1018	98.1	1031	1056	102.4
472.7	482	102	1158.9	1095	94.5	1147.6	1142	99.5
521.4	527	101.1	1279.9	1279	99.9	1264.2	1217	96.3
570.1	563	98.7	1400.9	1403	100.2	1380.8	1389	100.6
765	792	103.6	1884.8	1975	104.8	1847.3	1852	100.3
959.9	1009	105.1	2368.8	2385	100.7	2313.7	2324	100.5
1154.8	1162	100.6	2852.8	2685	94.1	2780.1	2745	98.7
1349.7	1464	108.5	3336.7	3338	100	3246.6	3256	100.3
1544.6	1527	98.9	3820.7	3546	92.8	3713	3918	105.5
1739.5	1732	99.6	4303.7	4550	105.7	4179.4	4284	102.5
1934.4	1909	98.7	4788.7	4978	104.0	4645.8	4477	96.4

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The assay is calibrated using d-methamphetamine. Calibrators for cutoff levels (300 ng/mL, 500 ng/mL, 1000 ng/mL) included in this device have been previously cleared in k060645. Control materials for three cutoff levels have been previously cleared in k080183, k090939.

The sponsor performed both real time and accelerated stability studies for shipping, open and closed vial reagent stability, and calibration stability. The closed reagent stability at 2-8°C is one year, on-board stability is 56 days. The on-board stability for open vials is 56 days. The sponsor recommends that users should not freeze the reagents.

On board calibration stability testing was performed on the Integra 800. Calibration is stable for 28 days.

d. *Detection limit:*

Performance at low drug concentrations in the semi-quantitative assay was characterized by determination of recovery (see section b above).

e. *Analytical specificity:*

Endogenous Interfering Substances: Potential interference from substances endogenous to urine were tested in both semi-quantitative and qualitative

mode by spiking the potentially interfering compound into human urine samples containing either d-methamphetamine or d-amphetamine at concentrations roughly equivalent to the $\pm 25\%$ cutoff concentration. The stock solutions had an analytically confirmed concentration of 1 mg/mL based upon their Certificates of Analysis. The median of triplicate observed values for samples containing potentially interfering compounds were compared to the median of triplicate values for control urine not spiked with potentially interfering compounds. The percent recovery was calculated by dividing the median concentration of the sample containing the potentially interfering compound by the median concentration of the control and multiplying by 100. If interference was observed, the concentration of the interferent was lowered and retested until no interference was observed.

Interferent concentrations were determined independently for methamphetamines and amphetamines for both the semi-quantitative and qualitative modes. Interfering substances were added to urine containing *d*-methamphetamine (MAMP) or *d*-amphetamine (AMP) at - 25 % (**Neg. Level**) and + 25 % (**Pos. Level**) of the cutoff level at the concentration listed in the **Cmpd. Conc.** column. All samples were tested and the following results were obtained on a COBAS INTEGRA 800 analyzer.

For the interference study for d-methamphetamine, 1 calibration was performed during the study. For the interference study for d-amphetamine, 2 calibrations were performed during the study.

Methamphetamine Semiquantitative (ng/mL)		300 ng/mL Cutoff		500 ng/mL Cutoff		1000 ng/mL Cutoff	
Compound	Cmpd. Conc.	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff
Acetone	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ascorbic Acid	10 mg/mL	NEG	POS	NEG	POS	NEG	POS
Conjugated Bilirubin	0.1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Creatinine	5 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ethanol	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Glucose	12 mg/mL	NEG	POS	NEG	POS	NEG	POS
Hemoglobin	1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Human serum albumin	3 mg/mL	NEG	POS	NEG	POS	NEG	POS
Oxalic Acid	2 mg/mL	NEG	POS	NEG	POS	NEG	POS
Sodium Chloride	23 mg/mL	NEG	POS	NEG	POS	NEG	POS
Urea	60 mg/mL	NEG	POS	NEG	POS	NEG	POS

Methamphetamine Qualitative (ng/mL)		300 ng/mL Cutoff		500 ng/mL Cutoff		1000 ng/mL Cutoff	
Compound	Cmpd. Conc.	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff
Creatinine	5mg/mL	NEG	POS	NEG	POS	NEG	POS
Glucose	12 mg/mL	NEG	POS	NEG	POS	NEG	POS
Albumin	3 mg/mL	NEG	POS	NEG	POS	NEG	POS
NaCl	23 mg/mL	NEG	POS	NEG	POS	NEG	POS
Oxalic Acid	2 mg/mL	NEG	POS	NEG	POS	NEG	POS
Urea	60 mg/mL	NEG	POS	NEG	POS	NEG	POS
Acetone	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ascorbic acid	10 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ethanol	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Hemoglobin	1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Conjugated bilirubin	0.1 mg/mL	NEG	POS	NEG	POS	NEG	POS

Amphetamine Semiquantitative (ng/mL)		300 ng/mL Cutoff		500 ng/mL Cutoff		1000 ng/mL Cutoff	
Compound	Cmpd. Conc.	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff
Acetone	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ascorbic Acid	10 mg/mL	NEG	POS	NEG	POS	NEG	POS
Conjugated Bilirubin	0.1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Creatinine	5 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ethanol	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Glucose	12 mg/mL	NEG	POS	NEG	POS	NEG	POS
Hemoglobin	1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Human serum albumin	3 mg/mL	NEG	POS	NEG	POS	NEG	POS
Oxalic Acid	2 mg/mL	NEG	POS	NEG	POS	NEG	POS
Sodium Chloride	23 mg/mL	NEG	POS	NEG	POS	NEG	POS
Urea	60 mg/mL	NEG	POS	NEG	POS	NEG	POS

Amphetamine Qualitative (ng/mL)		300 ng/mL Cutoff		500 ng/mL Cutoff		1000 ng/mL Cutoff	
Compound	Cmpd. Conc.	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff	-25% cutoff	+25% cutoff
Creatinine	5mg/mL	NEG	POS	NEG	POS	NEG	POS
Glucose	12 mg/mL	NEG	POS	NEG	POS	NEG	POS

Albumin	3 mg/mL	NEG	POS	NEG	POS	NEG	POS
NaCl	23 mg/mL	NEG	POS	NEG	POS	NEG	POS
Oxalic Acid	2 mg/mL	NEG	POS	NEG	POS	NEG	POS
Urea	60 mg/mL	NEG	POS	NEG	POS	NEG	POS
Acetone	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ascorbic acid	10 mg/mL	NEG	POS	NEG	POS	NEG	POS
Ethanol	7.9 mg/mL	NEG	POS	NEG	POS	NEG	POS
Hemoglobin	1 mg/mL	NEG	POS	NEG	POS	NEG	POS
Conjugated bilirubin	0.1 mg/mL	NEG	POS	NEG	POS	NEG	POS

pH: To test for potential negative interference from pH, the sponsor prepared samples containing target drug at levels $\pm 25\%$ of each cutoff concentration with pH ranging from 4.5 to 8.0. Interference due to pH was $\leq 5\%$ for the semi-quantitative or qualitative modes for each cutoff for amphetamine or methamphetamine from pH 4.5 to 8.0.

Specific Gravity: Urine specific gravity samples were prepared by an outside laboratory to concentrations ranging from 1.001-1.034. Samples were analyzed in both the semiquantitative and qualitative modes for amphetamine and methamphetamine at $\pm 25\%$ of each cutoff concentration. Twenty replicates were tested in both the semi-quantitative and qualitative modes at each specific gravity level. The mean, standard deviation, and %CV were calculated as well as number of crossovers. Interference due to specific gravity was $\leq 5\%$ in the semi-quantitative or qualitative modes for each cutoff for amphetamine or methamphetamine between 1.001-1.034.

Cross Reactivity: Structurally Related: Cross-reactivity to structurally related compounds was determined by spiking related compounds into drug free human urine samples to produce assay results above and below the assay cutoff. The samples were run in triplicate in both the semi-quantitative and qualitative modes to determine the approximate quantity of each compound that is equivalent in assay reactivity to the 300, 500, and 1,000 ng/mL assay cutoff. One calibration was performed during structurally related cross reactivity testing. The table below shows the semi-quantitative and qualitative results of the study for each assay cutoff.

300 ng/mL cutoff

Compound	Concentration tested ng/mL	Semi-quantitative result	Qualitative result	ng/mL Equivalent to 300 ng/mL	Approx. Percent Cross-reactivity
d-Methamphetamine	225 375	Neg Pos	Neg Pos	327	91.82
d-Amphetamine	300	Neg	Neg	311	96.33

(±) MDEA	300	Pos	Pos	285	105.33
(±) MDA	100 325	Neg Pos	Neg Pos	249	120.5
(±) MDMA	100 150	Neg Pos	Neg Pos	114	263.61
l-Methamphetamine	1,500 3,200	Neg Pos	Neg Pos	2,754	10.89
l-Ephedrine	70,000 100,000	Neg Pos	Neg Pos	94,792	0.32
Phendimetrazine	30,000 60,000	Neg Pos	Neg Pos	156,740	0.63
Phentermine	50,000 100,000	Neg Pos	Neg Pos	294,118	0.45
(±) Phenylpropanolamine HCl	100,000	Neg	Neg	1,111,111	0.11
d-Pseudoephedrine	50,000 100,000	Neg Pos	Neg Pos	269,542	0.34
MBDB HCl	250 500	Neg Pos	Neg Pos	1,194	88.39
BDB HCl	600 1,200	Neg Pos	Neg Pos	2,262	46.30
l-Amphetamine	1,000 10,000	Neg Pos	Neg Pos	23,445	4.66
d-Ephedrine	100,000	Neg	Neg	793,651	0.09
Tyramine	70,000 100,000	Neg Pos	Neg Pos	323,625	0.35

500 ng/mL cutoff

Compound	Concentration tested ng/mL	Semi-quantitative result	Qualitative result	ng/mL Equivalent to 500 ng/mL	Approx. Percent Cross-reactivity
d-Methamphetamine	375 625	Neg Pos	Neg Pos	444	112.61
d-Amphetamine	500	Pos	Pos	460	108.80
(±) MDEA	500	Pos	Pos	494	101.20
(±) MDA	325 600	Neg Pos	Neg Pos	433	115.48
(±) MDMA	150 200	Neg Pos	Neg Pos	173	289.06
l-Methamphetamine	3,200 7,500	Neg Pos	Neg Pos	4098	12.20
l-Ephedrine	100,000	Neg	Neg	154321	0.32
Phendimetrazine	60,000 100,000	Neg Pos	Neg Pos	72500	0.9
Phentermine	100,000	Neg	Neg	118483	0.42
(±) Phenylpropanolamine HCl	100,000	Neg	Neg	390625	0.13
d-Pseudoephedrine	100,000	Neg	Neg	132275	0.38
MBDB HCl	500 750	Neg Pos	Neg Pos	713	70.08
BDB HCl	1,200	Neg	Neg	1209	41.37

	2,000	Pos	Pos		
l-Amphetamine	10,000	Neg	Neg	11174	4.47
	20,000	Pos	Pos		
d-Ephedrine	100,000	Neg	Neg	413223	0.12
Tyramine	100,000	Neg	Neg	141243	0.35

1,000 ng/mL cutoff

Compound	Concentration tested ng/mL	Semi-quantitative result	Qualitative result	ng/mL Equivalent to 1000 ng/mL	Approx. Percent Cross-reactivity
d-Methamphetamine	750	Neg	Neg	970	103.08
	1,250	Pos	Pos		
d-Amphetamine	1,000	Neg	Pos	1024	97.70
(±) MDEA	1,000	Neg	Neg	1203	83.10
(±) MDA	600	Neg	Neg	785	127.38
	1,000	Pos	Pos		
(±) MDMA	300	Neg	Neg	446	224.40
	450	Pos	Pos		
l-Methamphetamine	7,500	Neg	Neg	9008	11.10
	120,000	Pos	Pos		
l-Ephedrine	100,000	Neg	Neg	317460	0.32

Phendimetrazine	100,000	Neg	Neg	156740	0.34
Phentermine	100,000	Neg	Neg	294118	0.34
(±) Phenylpropanolamine HCl	100,000	Neg	Neg	1111111	0.09
d-Pseudoephedrine	100,000	Neg	Neg	269542	0.37
MBDB HCl	750	Neg	Neg	1194	93.75
	1,000	Pos	Pos		
BDB HCl	2,000	Neg	Neg	2262	44.22
	3,500	Pos	Pos		
l-Amphetamine	20,000	Neg	Neg	23445	4.27
	40,000	Pos	Pos		
d-Ephedrine	100,000	Neg	Neg	793651	0.13
Tyramine	100,000	Neg	Neg	323625	0.31

Cross Reactivity: Structurally Unrelated: Potential interference from structurally unrelated compounds was tested in both semi-quantitative and qualitative mode by spiking the potentially interfering compound into human urine samples containing either d- amphetamine or d-methamphetamine at concentrations roughly equivalent to ±25% cutoff concentrations for each of the three cut-offs: 300 ng/mL, 500 ng/mL and 1,000 ng/mL for the semi-quantitative and qualitative modes. For both amphetamine and methamphetamine, the interfering compounds were tested initially at 100,000 ng/mL. The d-methamphetamine and d-amphetamine stock solutions had analytically confirmed concentrations of 1 mg/mL based upon Certificates of Analysis. If cross-over of the cutoff occurred at this 100,000 ng/mL level, the concentration of the cross reactant was reduced to determine the drug level at which the compound did not cause cross-over of the cutoff. Concentrations were decreased for aspartame (40,000

ng/mL), methaqualone (75,000 ng/mL), phencyclidine (40,000 ng/mL), Δ^9 -THC (10,000 ng/mL). None of these compounds gave values in the assay that were equal to or greater than 0.19 % cross-reactivity and no results were greater than the assay cutoffs (300 ng/mL, 500 ng/mL, and 1000 ng/mL), with the following exception:

The cross-reactivity for LSD was tested at a concentration of 2500 ng/mL. The results obtained were 0.32 %, and 0.71 %, for the 300 ng/mL and 1000 ng/mL assay cutoffs respectively. One calibration was performed during the structurally unrelated cross reactivity testing.

The control level samples recovered properly for the 300, 500, and 1000 ng/mL cutoffs in both semiquantitative and qualitative modes. The results indicated that each compound listed below did not interfere with the measurements of the device. The list of compounds tested is below.

Acetaminophen	Diphenhydramine	Morphine
Acetylsalicylic acid	Diphenylhydantoin	Naloxone
Amitriptyline	Doxepin	Naltrexone
Ascorbic acid	Ecgonine	Naproxen
Aspartame	Ecgonine methyl ester	Niacinamide
Benzocaine	Erythromycin	Nicotine
Benzoyllecgonine	Furosemide	Nifedipine
Caffeine	Guaiacol glycerol ether	Nordiazepam
Cannabidiol	Hydrochlorothiazide	Omeprazole
Cocaine	Ibuprofen	Oxazepam
Codeine	Ketamine	Penicillin G
Desipramine HCL	Levothyroxine	Phencyclidine
Dextromethorphan	LSD	Phenobarbital
Dextropropoxyphene	Mepriridine	Quinine
Diazepam	Methadone	Secobarbital
Digoxin	Methaqualone	Tetracycline
		Δ^9 -THC

Special Wash Programming:

There may be interference between certain combinations of Roche assays and the AMPII assay. The sponsor maintains a master list of all special wash programming instructions for the INTEGRA 800 analyzer which is accessible to the user online. The master list recommends the specific order the AMPII assay is to be analyzed in combination with other assays and when cleaning steps are to be taken.

f. Assay cut-off:

See section M1a. above.

2. Comparison studies:

a. *Method comparison with predicate device:*

The accuracy of amphetamine and methamphetamine was determined against GC/MS results for each cutoff concentration of 300 ng/mL, 500 ng/mL and 1,000 ng/mL. The sponsor used 36 unaltered negative urine samples and 36 unaltered positive samples for each drug. Further evaluation was performed with 4 urines at concentrations from -50% of the cutoff to the cutoff, and from the cutoff to +50% of the cutoff for each of the respective drugs (N=80). An additional 4 samples were evaluated at the 500 ng/mL cutoff for methamphetamine (N=84). Near cutoff samples are categorized based on the d-amphetamine concentration only. A positive result would be expected based upon the cross reactivity of the device, Amphetamines II, towards d-amphetamine and d-methamphetamine. The positive and negative agreement between the semi-quantitative results and GC/MS and the qualitative results and GC/MS were identical for the 300 ng/mL and 500 ng/mL cutoffs for AMP and for all MAMP cutoffs. Therefore, they are represented in one table for agreement and discrepant results rather than two tables, respectively.

Amphetamine, Near Cutoff 300 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	AMP GC/MS ng/mL	MAMP GC/MS ng/mL	Total GC/MS ng/mL	
Positive	Positive	157	363	520	Near Cutoff Negatives (-50% to cutoff)
Negative	Negative	265	0	265	
Positive	Positive	181	173	354	
Positive	Positive	220	171	391	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	378	0	378	
Positive	Positive	350	879	1,229	
Positive	Positive	395	769	1,164	
Positive	Positive	356	1,394	1,750	

Amphetamine Percent Agreement, 300 ng/mL Semi-quantitative and Qualitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (-50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	3	4	36	100%
Negative	36	1	0	0	92.5%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Amphetamine Non Discriminatory Results, Semi-quantitative and Qualitative, 300 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	157	d-amphetamine
Qualitative	Positive	363	d-methamphetamine
Semi-quantitative	Positive	181	d-amphetamine
Qualitative	Positive	173	d-methamphetamine
Semi-quantitative	Positive	220	d-amphetamine
Qualitative	Positive	171	d-methamphetamine

Amphetamine, Near cutoff 500 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	AMP GC/MS ng/mL	MAMP GC/MS ng/mL	Total GC/MS ng/mL	
Negative	Negative	265	0	265	Near Cutoff Negatives (-50% to cutoff)
Positive	Positive	438	121	559	
Positive	Positive	457	1,152	1,609	
Positive	Positive	443	706	1,149	
Positive	Positive	650	472	1,122	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	734	764	1,498	
Positive	Positive	598	241	839	
Positive	Positive	693	540	1,233	

Amphetamine Percent agreement, 500 ng/mL Semi-quantitative and Qualitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	3	4	36	100%
Negative	36	1	0	0	92.5%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Amphetamine non discriminatory Results, 500 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	438	d-amphetamine
Qualitative	Positive	121	d-methamphetamine
Semi-quantitative	Positive	457	d-amphetamine
Qualitative	Positive	1152	d-methamphetamine
Semi-quantitative	Positive	443	d-amphetamine
Qualitative	Positive	706	d-methamphetamine

Amphetamine, Near cutoff 1,000 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	AMP GC/MS ng/mL	MAMP GC/MS ng/mL	Total GC/MS ng/mL	
Negative	Negative	961	0	961	Near Cutoff Negatives (-50% to cutoff)
Positive	Negative	920	0	920	
Negative	Negative	970	0	970	
Positive	Positive	837	1,163	2,000	
Positive	Positive	1,020	3,124	4,144	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	1,161	0	1,161	
Positive	Positive	1,197	3,853	5,050	
Positive	Positive	1,348	1,339	2,687	

Amphetamine Percent agreement, 1,000 ng/mL Semi-quantitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	2	4	36	100%
Negative	36	2	0	0	95.0%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Amphetamine Percent agreement, 1,000 ng/mL Qualitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	1	4	36	100%
Negative	36	3	0	0	97.5%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Amphetamine Non discriminatory Results, 1,000 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	920	d-amphetamine
Semi-quantitative	Positive	837	d-amphetamine
Qualitative	Positive	1163	d-methamphetamine

Methamphetamine, Near cutoff 300 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	MAMP GC/MS ng/mL	AMP GC/MS ng/mL	Total GC/MS ng/mL	
Positive	Positive	173	181	354	Near Cutoff Negatives (-50% to cutoff)
Positive	Positive	278	101	379	
Positive	Positive	220	171	391	
Positive	Positive	291	145	436	
Positive	Positive	313	105	418	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	356	174	530	
Positive	Positive	436	434	870	
Positive	Positive	353	252	605	

Methamphetamine Percent agreement, 300 ng/mL Semi-quantitative and Qualitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	4	4	36	100%
Negative	36	0	0	0	90.0%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Methamphetamine non discriminatory Results, 300 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	173	d-methamphetamine
Qualitative	Positive	181	d-amphetamine
Semi-quantitative	Positive	278	d-methamphetamine
Qualitative	Positive	101	d-amphetamine
Semi-quantitative	Positive	220	d-methamphetamine
Qualitative	Positive	171	d-amphetamine
Semi-quantitative	Positive	291	d-methamphetamine
Qualitative	Positive	145	d-amphetamine

Methamphetamine, Near cutoff 500 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	MAMP GC/MS ng/mL	AMP GC/MS ng/mL	Total GC/MS ng/mL
-----------------------	-----------------	------------------------	-----------------------	-------------------------

Positive	Positive	488	466	954	Near Cutoff Negatives (-50% to cutoff)
Positive	Positive	325	171	496	
Positive	Positive	291	145	436	
Positive	Positive	472	650	1,122	
Negative	Negative	85	121	206	
Negative	Negative	173	181	354	
Negative	Negative	174	0	174	
Negative	Negative	204	0	204	
Positive	Positive	506	102	608	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	514	131	645	
Positive	Positive	547	100	647	
Positive	Positive	694	688	1,382	

Methamphetamine Percent agreement, 500 ng/mL Semi-quantitative and Qualitative

	Low Neg by CG/MS (< -50%)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS (> +50%)	Percent agreement with GC/MS
Positive	0	4	4	36	100%
Negative	40	0	0	0	91%
% Samples in range	47.6%	4.8%	4.8%	42.9%	

Methamphetamine Non discriminatory Results, 500 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	325	d-methamphetamine
Qualitative	Positive	171	d-amphetamine
Semi-quantitative	Positive	291	d-methamphetamine
Qualitative	Positive	145	d-amphetamine
Semi-quantitative	Positive	472	d-methamphetamine
Qualitative	Positive	650	d-amphetamine
Semi-quantitative	Positive	488	d-methamphetamine
Qualitative	Positive	466	d-amphetamine

Methamphetamine, Near cutoff 1,000 ng/mL, Semi-quantitative and Qualitative

Semi-Quant Pos/Neg	Qual Pos/Neg	MAMP GC/MS ng/mL	AMP GC/MS ng/mL	Total GC/MS ng/mL	
Positive	Positive	706	443	1,149	Near Cutoff Negatives (-50% to cutoff)
Positive	Positive	540	693	1,233	
Positive	Positive	769	395	1,164	
Positive	Positive	572	432	1,004	

Positive	Positive	1,152	457	1,609	Near Cutoff Positives (cutoff to +50%)
Positive	Positive	1,394	356	1,750	
Positive	Positive	1,163	837	2,000	
Positive	Positive	1,244	313	1,557	

Methamphetamine Percent agreement, 1,000 ng/mL Semi-quantitative and Qualitative

	Low Neg by CG/MS ($< -50\%$)	Near Cutoff Neg by GC/MS (- 50% to cutoff)	Near Cutoff Pos by GC/MS (cutoff to +50%)	High Pos by GC/MS ($> +50\%$)	Percent agreement with GC/MS
Positive	0	4	4	36	100%
Negative	36	0	0	0	90.0%
% Samples in range	45.0%	5.0%	5.0%	45.0%	

Methamphetamine Non discriminatory Results, 1,000 ng/mL cutoff

Assay type	Result	GC/MS (ng/mL)	Metabolite
Semi-quantitative	Positive	706	d-methamphetamine
Qualitative	Positive	443	d-amphetamine
Semi-quantitative	Positive	540	d-methamphetamine
Qualitative	Positive	693	d-amphetamine
Semi-quantitative	Positive	769	d-methamphetamine
Qualitative	Positive	395	d-amphetamine
Semi-quantitative	Positive	572	d-methamphetamine
Qualitative	Positive	432	d-amphetamine

b. Matrix comparison:

Matrix comparison studies were not performed. This device is for human urine only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.