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

A. 510(k) Number:

k110446

B. Purpose for Submission:

New Device

C. Measurand:

Amphetamine

D. Type of Test:

Qualitative and semi-quantitative immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

DAT Oral Fluid Amphetamine (OFAMP)
Oral Fluid DAT Qual Cal B
Oral Fluid DAT SQ Cal B
Oral Fluid DAT Control Set B

G. Regulatory Information:

1. Regulation section:

   862.3100, amphetamine test system
   862.3200, clinical toxicology calibrator
   862.3280, clinical toxicology control material

2. Classification:

   Class II
   Class II
   Class I, reserved

3. Product Code:

   DKZ, enzyme immunoassay, amphetamine
   DKB, calibrator, drug mixture
   DIF, drug mixture control materials

4. Panel:

   All are Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See Indications for use below.

2. Indication(s) for use:

   DAT Oral Fluid Amphetamine (OFAMP) is an in vitro diagnostic test for the qualitative and semiquantitative detection of amphetamine in human oral fluid at a cutoff concentration of 120 ng/mL in neat oral fluid. The specimen must be collected exclusively with the Intercept® Oral Specimen Collection Device. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program and to estimate a dilution of the specimen for confirmation by a confirmatory method such as LC/MS/MS.

   DAT Oral Fluid Amphetamine provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Chromatography/mass spectrometry is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

   The Oral Fluid DAT Control Set B is for use as assayed controls with the DAT Oral Fluid assays on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

   The Oral Fluid DAT Qual Cal B calibrators are designed for the calibration of oral fluid assays for drugs of abuse on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

   The Oral Fluid DAT SQ Cal B calibrators are designed for the calibration of oral fluid assays for drugs of abuse on automated clinical chemistry analyzers for human oral fluid samples collected with the Intercept Oral Specimen Collection Device.

3. Special conditions for use statement(s):

For prescription use only.

The assay is not designated for use in point-of-care settings.

Tests for amphetamine cannot distinguish between abused drugs and certain prescribed medications.

Certain foods or medications may interfere with tests for amphetamine and cause false positive results.

4. Special instrument Requirements:

Roche Modular P analyzer

I. Device Description:

The Oral Fluid Amphetamine assay consists of two ready for use reagent solutions, calibrators, and controls. Calibrators and controls are required but not supplied with the reagents.

Reagent 1 (R1) contains antibody/microparticle working solution with microparticles attached to amphetamine antibody (mouse monoclonal) in buffer with bovine serum albumin (BSA) and 0.09% sodium azide.

Reagent 2 (R2) contains conjugate working solution with conjugated amphetamine derivative in buffer with bovine serum albumin (BSA) and 0.09% sodium azide.

Calibrators: *Qualitative* assay required calibrator: CAL 2 (40 ng/mL)

Semiquantitative assay required calibrators: CAL 0 (0 ng/mL), CAL 1 (20 ng/mL), CAL 2 (40 ng/mL), CAL 3 (80 ng/mL), CAL 4 (160 ng/mL), CAL 5 (320 ng/mL)

Controls: Zero, Negative (0.5X), and Positive (1.5X)

J. Substantial Equivalence Information:

1. Predicate device name(s):

STC Amphetamine-Specific Intercept Micro-Plate EIA

2. Predicate 510(k) number(s):

k992918

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Indications for Use	Same	For use in the determination of amphetamine in oral fluid collected with the Intercept Drugs of Abuse (DOA) Oral Specimen Collection Device. For In Vitro Diagnostic Use.
Methodology	Same	Immunoassay
Differences		
Item	**Device**	**Predicate**
Cutoff	120 ng/mL in neat oral fluid	40 ng/mL when oral fluid collected with the Oral Specimen Collection Device
Platform	Roche Modular P analyzer	Microplate
Control concentrations	Synthetic oral fluid matrix: Zero, Negative (.5X), and Positive (1.5X)	Negative (.5X) and Positive (2X)
Calibrator concentrations	Zero, .5X, Cutoff, 2X, 4X, and 8X	Zero, Cutoff
Measurement Mode	Qualitative and semi-quantitative measurements	Qualitative measurements only

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

The sponsor referenced the following standard in their submission:

- CLSI EP5-A2 Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline - 2nd edition

The sponsor referenced the following guidance document in their submission:

- Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests - Draft Guidance for Industry and FDA Staff

L. Test Principle:

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

The Intercept® Oral Specimen Collection Device contains a preservative buffer that dilutes the neat oral fluid sample. The calibrator and control levels are set at diluted levels so that sample absorbance values can be compared directly to the absorbance values of the calibration curve. The assay result is reported as a positive or negative result relative to the neat oral fluid cutoff of 120 ng/mL.

NOTE: To correlate a semi-quantitative Intercept® result from the assay or the associated LC/MS/MS confirmation result to a neat oral fluid value, the result from the Intercept sample should be multiplied by a factor of 3.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All analytical performance data was collected on human oral fluid samples collected with the Intercept Oral Specimen Collection Device and analyzed on the Roche MODULAR P analyzer. The Intercept collection device includes a diluent that results in a dilution of approximately 1/3. The assay cannot be used to measure undiluted (neat) samples. Analyte concentrations refer to the neat oral fluid concentration, unless otherwise noted.

a. Precision/Reproducibility:

Two studies were performed with the assay to evaluate precision.

In the first study, a d-amphetamine solution was added to each of 9 samples which were obtained from a human oral fluid pool of samples collected with the Intercept® Oral Specimen Collection Device to achieve concentrations at approximately -100 %, -75 %, -50 %, -25 %, 0 %, +25 %, +50 %, +75 %, and +100 % of the cutoff calibrator value. The samples were tested for precision in qualitative and semiquantitative modes. Following a CLSI (EP5-A2) precision protocol, samples were tested in 2 replicates per run, 2 runs per day for 21 days, total n = 84. One lot each of reagent, calibrator, and control were used during the study and nine calibrations were performed during the study.

Qualitative Mode

Note: this study was performed on samples already collected with the Intercept collection device. Therefore the data in the table below do not reflect any imprecision inherent in the collection process itself. Results were as follows:

	Drug	Concentration of Sample, ng/mL	Number of Determinations	Results #Neg / #Pos
Semiquant Se	AMP	zero drug	84	84 Neg / 0 Pos
	AMP	-75%	84	84 Neg / 0 Pos
	AMP	-50%	84	84 Neg / 0 Pos
	AMP	-25%	84	84 Neg / 0 Pos
	AMP	cutoff	84	75 Neg / 9 Pos
	AMP	+25%	84	0 Neg / 84 Pos
	AMP	+50%	84	0 Neg / 84 Pos
	AMP	+75%	84	0 Neg / 84 Pos
	AMP	+100%	84	0 Neg / 84 Pos

Semiquantitative Mode

Note: this study was performed on samples already collected with the Intercept collection device. Therefore the data in the table below do not reflect any imprecision inherent in the collection process itself. Results were as follows:

Drug	**Conc. of Sample, ng/mL**	**Results #Neg / #Pos**	**Within-run Precision**		**Total Precision**	
			SD ng/mL	CV %	SD ng/mL	CV %
Amphetamine	zero drug	84 Neg / 0 Pos	0.4	284	0.4	296
Amphetamine	-75%	84 Neg / 0 Pos	1.0	10.8	1.3	13.9
Amphetamine	-50%	84 Neg / 0 Pos	1.3	6.4	1.6	8.3
Amphetamine	-25%	84 Neg / 0 Pos	1.2	4.1	1.5	4.9
Amphetamine	cutoff	72 Neg / 12 Pos	1.5	3.9	1.7	4.5
Amphetamine	+25%	0 Neg / 84 Pos	1.7	3.3	1.8	3.5
Amphetamine	+50%	0 Neg / 84 Pos	2.1	3.5	2.3	3.7
Amphetamine	+75%	0 Neg / 84 Pos	2.1	2.9	2.6	3.6
Amphetamine	+100%	0 Neg / 84 Pos	2.4	3.0	2.7	3.3

In the second study, a d-amphetamine solution was added to neat human oral fluid sample pools at concentrations of 60, 90, 150, and 180 ng/mL. Each spiked sample pool was then processed through each of 21 Intercept® Devices to achieve final concentrations at approximately -50%, -25%, +25 %, and +50 % of the cutoff calibrator value. The intra-assay precision of the samples, including the processing of the samples through the collection device was then tested in qualitative and semiquantitative modes with the Oral Fluid Amphetamine assay.

Qualitative Mode

Note: The values obtained in this study were collected from samples spiked with amphetamine prior to the collection step. Therefore the data in the table below reflects the performance of the entire system including the collection step.

Drug	Concentration of Sample	Number of Determinations	Results #Neg / #Pos
AMP	-50%	21	21 Neg / 0 Pos
AMP	-25%	21	21 Neg / 0 Pos
AMP	+25%	21	0 Neg / 21 Pos
AMP	+50%	21	0 Neg / 21 Pos

Semiquantitative Mode

Note: The values obtained in this study were collected from samples spiked with amphetamine prior to the collection step. Therefore the data in the table below reflects the performance of the entire system including the collection step.

Drug	Conc. of Sample	Results #Neg / #Pos	Precision	
			SD ng/mL	CV %
AMP	-50%	21 Neg / 0 Pos	2.1	8.7
AMP	-25%	21 Neg / 0 Pos	1.8	5.2
AMP	+25%	0 Neg / 21 Pos	2.0	3.5
AMP	+50%	0 Neg / 21 Pos	3.1	4.4

b. *Linearity/assay reportable range*:

To assess recovery, aliquots of a neat OF pool were spiked with d-amphetamine at concentrations of: 0, 60, 90, 120, 150, 180, 240, 480, and

960 ng/mL. Each level was processed through 2 separate Intercept collection devices. The diluted sample from both Intercept devices was then analyzed once in semi-quantitative mode. The data below was analyzed with one calibration using one lot of reagent.

Results were as follows:

Spiked Neat Concentration (ng/mL)	Recovery (%)
0	n/a
60	126.0
90	121.0
120 (cutoff)	123.3
150	123.4
180	134.3
240	130.0
480	103.7
960	100.5

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

The assay is calibrated against d-amphetamine.

Calibrators and control materials are specified in the labeling but are supplied separately from the reagents. For the qualitative assay, only CAL 2 (40 ng/mL) is required. For the semi-quantitative assay, six levels of calibrator material, ranging in concentration from 0 to 320 ng/mL are required. Calibrators and controls consist of a synthetic oral fluid matrix spiked with known concentrations of d-amphetamine.

The concentration of amphetamine in the calibrators and controls is verified by LC/MS/MS.

The open vial stability claim for calibrators and controls is 20 days after opening when stored at 2–8° C. The closed vial stability claim for calibrators and controls is one year from the time of manufacture when stored at 2–8° C.

The sponsor's stability protocols were reviewed and found to be acceptable.

d. Detection limit:

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

e. Analytical specificity:

The sponsor performed analytical specificity studies on four categories of potential interferents: structurally related substances, structurally unrelated substances, substances endogenous to oral fluid, and food and dental substances.

Cross Reactivity to Structurally Related Compounds

Cross-reactivity was evaluated by spiking various concentrations of similarly structured drug compounds into a drug-free oral fluid pool collected with the Intercept Oral Fluid Specimen Collection Device. By analyzing various concentration of each compound the sponsor determined the concentration of the drug that produced a response approximately equivalent to the cutoff concentration of the assay. Results of those studies appear in the table below:

Drug compound	Approximate Percent Cross-reactivity
para-Methoxyamphetamine (PMA)	113
Methylenedioxyamphetamine (MDA)	61
Benzodioxolylbutanamine (BDB)	22.86
l-amphetamine	2.35
Paramethoxymethamphetamine (PMMA)	0.91
Methylenedioxymethamphetamine (MDMA)	0.28
Methylenedioxyethylamphetamine (MDEA)	0.25
d-Methamphetamine	0.20
Phentermine	0.20
Phenylpropanolamine	0.14
Tyramine	0.10
l-Methamphetamine	0.08
Methylbenzodioxolylbutanamine (MBDB)	0.05
d-Pseudoephedrine	0.02

No cross-reactivity was detected for d-Ephedrine, l-Ephedrine, or Phendimetrazine when tested at a concentration of 10,000 ng/mL.

Interference from Structurally Unrelated Compounds

Potential interference from structurally unrelated compounds was tested in both semi-quantitative and qualitative mode by spiking the potentially interfering compound into pools of human oral fluid collected with the Intercept Oral Fluid Specimen Collection Device. Both a positive concentration (+50% of the cutoff) and a negative concentration (-50% of the cutoff) of amphetamine were evaluated. All potential interferents were tested at a concentration of 10,000 ng/mL.

Generic Name	Tested Concentration (ng/mL)	Approximate Neat Concentration (ng/mL)
4-Aminophenyl sulfone	10000	30000
Acetaminophen	10000	30000
Acetylsalicylic acid	10000	30000
Alprazolam	10000	30000
Amitryptyline	10000	30000
Amobarbital	10000	30000
Ampicillin	10000	30000
Aspartame	10000	30000
Atropine	10000	30000
Benzococaine	10000	30000
Benzoylecgonine	10000	30000
Buprenorphine	10000	30000
Butabarbital	10000	30000
Caffeine	10000	30000
Chlordiazepoxide	10000	30000
Cocaine	10000	30000
Cotinine	10000	30000
Cyclizine	10000	30000

Generic Name	Tested Concentration (ng/mL)	Approximate Neat Concentration (ng/mL)
Desipramine	10000	30000
Dextromethorphan	10000	30000
Diazepam	10000	30000
Diphenhydramine	10000	30000
Doxepin	10000	30000
Fenoprofen	10000	30000
Fluoxetine	10000	30000
Gentisic acid	10000	30000
Glipizide	10000	30000
Ibuprofen	10000	30000
Imipramine	10000	30000
Ketamine	10000	30000
Loperamide	10000	30000
LSD	10000	30000
Meperidine	10000	30000
Methadone	10000	30000
Methaqualone	10000	30000
Morphine	10000	30000
Naloxone	10000	30000
Naltrexone	10000	30000
Naproxen	10000	30000
Niacinamide	10000	30000
Nicotine	10000	30000
Nordiazepam	10000	30000
Oxazepam	10000	30000
Oxycodone	10000	30000

Generic Name	Tested Concentration (ng/mL)	Approximate Neat Concentration (ng/mL)
Pantoprazole	10000	30000
Penicillin G	10000	30000
Pentazocine	10000	30000
Pentobarbital	10000	30000
Phencyclidine	10000	30000
Phenobarbital	10000	30000
Phenylephrine	10000	30000
Procainamide	10000	30000
Procaine	10000	30000
Promethazine	10000	30000
Quetiapine	10000	30000
Quinidine	10000	30000
Ranitidine	10000	30000
Rifampin	10000	30000
Secobarbital	10000	30000
Δ9-THC	10000	30000
Tramadol	10000	30000
Trifluoroperazine	10000	30000
Trimipramine	10000	30000
Venlafaxine	10000	30000
Zomepirac	10000	30000

No negative or positive interference was seen in this study.

Interference from Endogenous Interferents and pH

Potential interference from substances endogenous to oral fluid were tested in both semi-quantitative and qualitative mode by spiking the potentially interfering substance into pools of human oral fluid collected with the Intercept Oral Fluid Specimen Collection Device. Both a positive concentration (+50% of the cutoff) and a negative concentration (-50% of the cutoff) of amphetamine were evaluated.

The following potential endogenous interferents were spiked into the negative and positive oral fluid samples at the noted concentrations. No negative or positive interference was seen in this study.

Compound	Concentration Tested	Approximate Neat Concentration
Albumin	5 mg/mL	15 mg/mL
Salivary α-Amylase	833 U/mL	2499 U/mL
Ascorbic Acid	10 mg/mL	30 mg/mL
Bilirubin	50 µg/mL	150 µg/mL
Hemoglobin	1 mg/mL	3 mg/mL
IgA	0.33 mg/mL	0.99 mg/mL
IgG	0.17 mg/mL	0.51 mg/mL
IgM	0.033 mg/mL	0.099 mg/mL

An additional study was performed in which samples containing amphetamine at +50% and -50% of the cutoff with pH ranging from 2.0 to 8.5 were tested. All of the samples above the cutoff read positive and all of the samples below the cutoff read negative.

Interference from Food and Dental Products

The following potential interferents were evaluated by spiking into oral fluid samples collected with the intercept device: Alcohol (ethanol), Antiseptic Mouthwash, Baking soda, Whole blood, Cough Syrup, Cranberry juice, Hemoglobin, Hydrogen peroxide, Orange juice, Sodium chloride, Sugar, Toothpaste, and Water. None of these substances caused positive or negative interference.

The following potential interferents, which are either consumed or placed in the mouth, were evaluated by asking participants to consume or use the specific substance, after which oral fluid samples were collected and

spiked with amphetamine at concentrations of cutoff – 50% and cutoff + 50%: Antacid, Chewing tobacco, Cigarettes, Chewing gum, Cola, Hard candy, and Tooth whitening strips. None of these substances caused positive or negative interference when oral fluid samples were collected at least 10 minutes after consumption or use, as specified in the labeling for the collection device.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision above.

2. Comparison studies:

a. Method comparison with predicate device:

Two method comparison studies were performed. In the first study, 19 positive and 21 negative samples were analyzed. In order to evaluate the performance of the entire system, three measurements were taken on each specimen: the LC/MS/MS concentration of the neat sample, the LC/MS/MS concentration of the diluted Intercept sample, and the immunoassay concentration of the diluted Intercept sample.

Sample description: clinical oral fluid samples
Number of study sites: one
Description of the site: manufacturer's facility
Type of study site: manufacturer's staff
Operator description: manufacturer's staff
Number of instruments used: one

The LC/MS/MS values of the neat and diluted samples confirmed the dilution ratio of approximately 1/3. When the LC/MS/MS values of the neat oral fluid samples were compared to the immunoassay values, the following results were obtained. Note: The values obtained in this study were collected from samples containing amphetamine prior to the collection step. Therefore the results reflect the performance of the entire system including the collection step.

Semi-Quantitative Mode				
Candidate Device	**Less** than half the cutoff	**Near Cutoff Negative**	**Near Cutoff Positive**	**High Positive** (greater than

Results	concentration by LC/MS/MS analysis	(Between 50% below the cutoff and the cutoff concentration)	(Between the cutoff and 50% above the cutoff concentration)	50% above the cutoff concentration)
Positive	0	1*	7	12
Negative	18	2	0	0

* The concentration of amphetamine in this sample was 114 ng/mL as measured by LC/MS/MS.

LC/MS/MS values used to categorize samples in this table are based on the concentration of amphetamine in the sample.

% Agreement among positives is 100%
% Agreement among negatives is 95%

Qualitative Mode				
Candidate Device Results	**Less** than half the cutoff concentration by LC/MS/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	0	3*	7	12
Negative	18	0	0	0

* The concentrations of amphetamine in these samples were 92, 95, and 114 ng/mL, respectively, as measured by LC/MS/MS.

LC/MS/MS values used to categorize samples in this table are based on the concentration of amphetamine in the sample.

% Agreement among positives is 100%
% Agreement among negatives is 86%

In the second study, 40 negative and 40 positive samples were analyzed. These included four negative near cutoff samples and four positive near cutoff samples.

Note: this study was performed on samples already collected with the Intercept collection device. Therefore the results below do not reflect any inaccuracy inherent in the collection process itself. When the LC/MS/MS values of the diluted samples were compared to the immunoassay values, the following results were obtained.

Semi-Quantitative Mode				
Candidate Device	**Less** than half the cutoff	**Near Cutoff Negative**	**Near Cutoff Positive**	**High Positive** (greater than

Results	concentration by LC/MS/MS analysis	(Between 50% below the cutoff and the cutoff concentration)	(Between the cutoff and 50% above the cutoff concentration)	50% above the cutoff concentration)
Positive	0	0	3	36
Negative	36	4	1*	0

* The concentration of amphetamine in this neat oral fluid sample was approximately 126 ng/mL as measured by LC/MS/MS.

LC/MS/MS values used to categorize samples in this table are based on the concentration of amphetamine in the sample.

% Agreement among positives is 98%
% Agreement among negatives is 100%

Qualitative Mode				
Candidate Device Results	**Less** than half the cutoff concentration by LC/MS/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	0	0	3	36
Negative	36	4	1*	0

* The concentration of amphetamine in this neat oral fluid sample was approximately 126 ng/mL as measured by LC/MS/MS.

LC/MS/MS values used to categorize samples in this table are based on the concentration of amphetamine in the sample.

% Agreement among positives is 98%
% Agreement among negatives is 100%

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a. and b. are 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.