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

A. 510(k) Number:

k043242

B. Purpose for Submission:

This is a new device for an Acetaminophen assay configured with other analytes which have been previously cleared (k012745) (see device description section).

C. Measurand:

Acetaminophen/paracetamol (APAP) Amphetamines (AMP), barbiturates (BAR), benzodiazepines (BZO), cocaine (COC), methamphetamines (mAMP), opiates (OPI), phencyclidine (PCP), THC and tricyclic antidepressants (TCA) in urine.

D. Type of Test:

Qualitative, Fluorescence Immunoassay

E. Applicant:

Biosite Incorporated

F. Proprietary and Established Names:

Triage® TOX Drug Screen (available in different configurations)

G. Regulatory Information:

1. Regulation section:
   862.3030 - Acetaminophen Test System
   862.3100 - Amphetamine Test System
   862.3150 - Barbiturate Test System
   862.3170 - Benzodiazepine Test System
   862.3250 - Cocaine and Cocaine Metabolite Test System,
   862.3610 - Methamphetamine Test System
   862.3650 - Opiate Test System
   862.3100 - Amphetamine test system (Phencyclidine)
   862.3870 - Cannabinoid Test System and
   862.3910 - Tricyclic Antidepressant Drug Test System

2. Classification:

   Class II

3. Product code:

   LDP, DKZ, DIS, JXM, JXO, LAF, DJG, LCM, LDJ and LFG; respectively

4. Panel:

   91, Toxicology

H. Intended Use:

1. Intended use(s):

   See indications for use.

   Indication(s) for use:

   The Triage Tox Drug Screen is a Fluoresence immunoassay intended to be used with the Triage MeterPlus for the point-of-care qualitative determination of the presence of major metabolites above the threshold concentrations of up to 8 distinct drug classes, including assays for acetaminophen/paracetamol, amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamines, opiates, phencyclidine, THC and tricyclic antidepressants in urine. The acetaminophen/paracetamol assay will yield positive results when acetaminophen/paracetamol is ingested at or above therapeutic doses.

   The threshold concentrations are provided below:

Acetaminophen/Paracetamol	**APAP**	5 µg/mL
Amphetamines	**AMP**	1000 ng/mL
Methamphetamines	**mAMP**	1000 ng/mL
Barbiturates	**BAR**	300 ng/mL
Benzodiazepines	**BZO**	300 ng/mL
Cocaine	**COC**	300 ng/mL
Opiates	**OPI**	300 ng/mL
Phencyclidine	**PCP**	25 ng/mL
THC	**THC**	50 ng/mL
Tricyclic Antidepressants	**TCA**	1000 ng/mL

2. Special conditions for use statement(s):

   This test provides only preliminary test results. Clinical consideration and professional judgment must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a confirmed analytical result, a more specific alternate chemical method is needed. Gas Chromatography/Mass Spectroscopy (GC/MS) is the preferred confirmatory method.

   A quantitative serum acetaminophen/paracetamol measurement is the common confirmatory method for preliminary positive acetaminophen/paracetamol results.

   For Prescription and Point-of-Care use. The Point-of-Care classification was address in a previously cleared submission (k012745)

4. Special instrument requirements:

   Triage® MeterPlus; k973547

I. Device Description:

The Triage TOX Drug Screen is a competitive fluorescence immunoassay used for the qualitative determination of major metabolites of acetaminophen/paracetamol (APAP), amphetamines (AMP), methamphetamines (mAMP), barbiturates (BAR), benzodiazepines (BZO), cocaine (COC), opiates (OPI), phencyclidine (PCP), THC and tricyclic antidepressants (TCA). All analytes were previously cleared (k012745) except for the acetaminophen analyte. It is a single use test device and is used in conjunction with the Triage ® MeterPlus. The device contains murine monoclonal antibodies and drug metabolites labeled with a fluorescent dye or immobilized on the solid phase and stabilizers. The testing device is inserted into and read by the Triage MeterPlus. Threshold concentrations are used to separate a negative result from a presumptive positive result.

No human source materials are used during the manufacturing of this product.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Triage® TOX Drug Screen

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

   k012745

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Qualitative determination of major metabolites in human urine.	Qualitative determination of major metabolites in human urine.
Matrix	Human Urine	HumanUrine
Test Principle	Fluorescence immunoassay	Fluorescence immunoassay

Differences		
Item	Device	Predicate
Anaylets	Acetaminophen, Amphetamines, Methamphetamines, Barbiturates, Benzodiazepines, Cocaine, Opiates, Phencyclidine, THC and Tricyclic Antidepressants	Amphetamines, Methamphetamines, Barbiturates, Benzodiazepines, Cocaine, Opiates, Phencyclidine, THC and Tricyclic Antidepressants

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

None stated.

L. Test Principle:

The Triage Tox Drug Screen is a competitive fluorescence immunoassay used for the qualitative determination of parent compound and major metabolites of drugs of abuse in urine specimens. A urine sample is added to the device which then passes through a filter. The sample moves by capillary action into a reaction chamber and is allowed to react with murine monoclonal fluorescent antibody conjugates or mix fluorescent drug conjugates. After an incubation period, the reaction mixture flows through the device detection lane. The presence of drug or drug metabolite in the urine specimen prevents binding of the fluorescent conjugates to the solid phase on the detection zone. Unbound fluorescent conjugate is washed from the detection lane by excess urine. The concentration of the drug metabolite in the urine specimen is inversely related to the fluorescence bound to the detection zone. Threshold concentrations are used to separate a negative result from a presumptive positive result.

M. Performance Characteristics (if/when applicable):

See k012745 for amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamines, opiates, phencyclidine, THC and tricyclic antidepressants. Sponsor states that performance studies have been conducted for the addition of acetaminophen through its internal Design Control process, the performance characteristics are exactly the same and data are on file at the Biosite.

1. Analytical performance:

   a. *Precision/Reproducibility:*
   The threshold for acetaminophen of 5 ng/ml was challenged by testing specimens containing the drug or drug metabolite spiked into drug-free urine at concentrations within 25% and 50% of the threshold. Each specimen was tested using the Triage® Tox Drug Screen. The data paralleled the expected agreement based on the coefficient of variation of the assay.

   b. *Linearity/assay reportable range:*

   Not applicable. The assay is intended for qualitative use.

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

   Users are instructed to run external controls with each new lot or shipment of test materials, or every 30 days, and as otherwise required by federal, state or local guidelines. Commercial control materials are required but are not specifically identified in the labeling.

   Each device has internal process controls which run with every sample. The controls monitor various procedural and functional parameters such as sufficient sample added to the test device and that the unbound fluorescent label has been washed sufficiently from the detection zone. During testing if the results are within the limits the results are reported. If the results are not within the limits the results are not reported and an error message will be displayed.

   d. *Detection limit:*
   Cutoff validation and sensitivity were evaluated. Four contrived samples were prepared by adding acetaminophen to drug-free urine at concentrations within 25% and 50% of the cutoff concentration. Samples were measured 10 times using the Triage TOX Drug Screen.

   Table IV.1: APAP Cutoff Validation

	0.5x	0.75x	1.25x	1.5x
POS	0	0	9	10
NEG	10	10	1	0
Concordance	100%	100%	90%	100%

e. Analytical specificity:

Substances that may cause interference were added to samples containing acetaminophen within 25% of the cutoff concentration. Cross-reactivity substances were added to drug-free urine. Samples were measured in duplicate. The substances did not interfere or have a cross-reaction with the acetaminophen assay at the concentrations listed below:

Table IV.2.1: Interfering Substances

Substance	Concentration	Substance	Concentration
Acetone	5 mg/mL	Hemoglobin	1.2 mg/mL
Acetylsalicylic Acid	1 mg/mL	Human Serum Albumin	5 mg/mL
Ascorbic Acid	15 mg/ml	Ibupprofen	1 mg/mL
Bilirubin	2.5µg/mL	Ketamine	25 µg/mL
Caffeine	0.125 mg/mL	Oxalic Acid	10 mg/mL
Creatinine	2.5 mg/mL	Riboflavin	75µg/mL
Dextrose	20 mg/mL	Scopalamine	62.5 µg/mL
Ethanol	5 mg mL	Sodium Chloride	30 mg/mL
Fluoxetine	0.5 mg/mL	Urea	30 mg/mL
Gamma Globulin	5 mg/mL		

Table IV.2.2: Cross-Reacting Substances

Substance	Concentration	Substance	Concentration
Acetopromazine	100 µg/mL	Methoxyphenamine	100 µg/mL
Benzphentamine	100 µg/mL	Methylphenidate	100 µg/mL
Benztropine Methane	100 µg/mL	Naloxone	80 µg/mL
Bupropin	100 µg/mL	Naproxen	100 µg/mL
Butyrophenine	100 µg/mL	Norpsuedoephedrine	100 µg/mL
Cimetidine	100 µg/mL	Phenethylamine	100 µg/mL
Clonidine	100 µg/mL	Phenmetrazine	100 µg/mL
Cotinine	100 µg/mL	Phenylephrine	100 µg/mL
Dextromethorphan	100 µg/mL	Phenylhydantoin, d/l-5-(p-hydroxyphenyl)-5-	100 µg/mL
Dextrorphan	100 µg/mL	Phenylpropanolamine	100 µg/mL
Diphenhydramine	100 µg/mL	Promrthazine	100 µg/mL
Dopamine	100 µg/mL	Propanolol, d/l	100 µg/mL
Epinephrine, 1-	100 µg/mL	Propoxyphene	100 µg/mL
Fenfluramine	20 µg/mL	Pseudoephedrine, d-	100 µg/mL
Glutethimide	100 µg/mL	Quinacrine	100 µg/mL
KetorolacTromethane	100 µg/mL	Ranitidine	100 µg/mL
Levorphanol	50 µg/mL	Thioridazine	100 µg/mL
Meperidine	100 µg/mL	Tramadol	100 µg/mL
Mesoridazine	100 µg/mL	Tyamine	60 µg/mL
Methadone d/l	100 µg/mL	Tranylcypromine	100 µg/mL
Methaqualone	100 µg/mL	Zolpidem	100 µg/mL

Acetaminophen was added at 75% and 125% of the cutoff concentration to urine samples with specific gravities ranging from 1.006 – 1.026 and to urine samples with the pH ranging from 4.5 – 7.5. Six (6) replicates of each sample were measured using the Triage TOX Drug Screen. There is no effect of specimen specific gravity or pH on the acetaminophen assay results.

f. Assay cut-off:

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

The cutoff concentration of this qualitative assay was arbitrarily chosen by the sponsor. There is no known clinical significance regarding the cutoff concentration. It indicates only that the analyte was or was not present at that level.

2. Comparison studies:

See k012745 for amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamines, opiates, phencyclidine, THC and tricyclic antidepressants.

a. Method comparison with predicate device:

Because the candidate was compared to a reference method, GC/MS. It was not compared to a predicate device.

102 specimens with known acetaminophen concentration by GC/MS were measured using the Triage TOX Drug Screen. 8 specimens were within 25% below the cutoff concentration and 12 specimens were with 25% above the cutoff concentration. The cutoff concentration for both methods was 5 μg/mL.

The overall agreement of results from both methods is 97.1% (95% confidence interval 93.8%-100%).

b. Matrix comparison:

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

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):

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.