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

A. 510(k) Number:
k042407

B. Purpose for Submission:
Indications for Use was modified. Change from:

"*The Emit® Caffeine Assay is a homogenous enzyme Immunoassay intended for use in determining* ***caffeine as a metabolite***"

Note: The use of caffeine for the treatment of apnea in premature infants is not an approved drug use in the United States. Values obtained from the Emit® Caffeine Assay should be interpreted in light of the serum theophylline levels and other clinical signs and symptoms.

to

"*The Emit® Caffeine Assay is a homogeneous enzyme immunoassay intended for use in the quantitative analysis of* ***caffeine levels*** *in human serum in subjects undergoing* ***therapy with caffeine, especially in cases of neonatal apnea***."

Additional study located in the Matrix Comparison Section.

C. Measurand:
Caffeine

D. Type of Test:
Quantitative

E. Applicant:
Dade Behring, Inc.

F. Proprietary and Established Names:
Emit Caffeine Assay

G. Regulatory Information:
1. Regulation section:
   21 CFR 862.3880 Theophylline Test System

2. Classification:
   Class II.

3. Product code:
   KLS

4. Panel:
   91 Toxicology

H. Intended Use:

1. Intended use(s):
   See Indication(s) for Use Statement below.

2. Indication(s) for use:
   The Emit® Caffeine Assay is a homogeneous enzyme immunoassay intended for use in the quantitative analysis of caffeine levels in human serum in subjects undergoing therapy with caffeine, especially in cases of neonatal apnea.

3. Special conditions for use statement(s):
   For Prescription Use Only

4. Special instrument requirements:
   Dade Behring Inc. provides instructions for using this assay on a number of chemistry analyzers. Analyzers must be capable of maintaining a constant reaction temperature, pipetting specimens/reagents and measuring enzyme rates precisely, timing the reaction accurately and mixing reagents thoroughly.

I. Device Description:

The Emit® Caffeine assay consists of Reagents A and B(3 mL each) , 6 levels of Calibrators (1 mL each) and a buffer (13.3 mL). Reagent A is sheep antibodies reactive to caffeine, glucose-6-phosphate and nicotinamide adenine dinucleotide. Reagent B is caffeine labeled with bacterial glucose-6-phosphate dehydrogenase.

The Emit® Caffeine assay includes 6 levels of dry calibrators: 0, 1, 3, 7, 15 and 30 mg/mL prepared from human serum and caffeine.

The Emit® Caffeine assay contains human blood source material that has been tested and found nonreactive for human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), hepatitis B surface antigen (HBsAg) and antibodies to hepatitis C virus (anti-HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Emit® Caffeine Assay

2. Predicate 510(k) number(s):
   k853872

3. Comparison with predicate:

Differences		
Item	Device	Predicate
Indications for Use	The Emit® Caffeine Assay is a homogeneous enzyme immunoassay intended for use in the quantitative analysis of caffeine levels in human serum in subjects undergoing therapy with caffeine, especially in cases of neonatal apnea. Note: The use of caffeine for the treatment of apnea in premature infants is not an approved drug use in the United States. Values obtained from the Emit® Caffeine Assay should be interpreted in light of the serum theophylline levels and other clinical signs and symptoms.	The Emit® Caffeine Assay is a homogeneous enzyme immunoassay intended for use in determining caffeine as a metabolite.

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

Not Applicable

L. Test Principle:

The Emit® Caffeine Assay is a homogeneous immunoassay that utilizes competition between caffeine in samples and caffeine labeled with glucose-6-phosphate dehydrogenase for antibody binding sites. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. *Precision/Reproducibility:*
   Performance Characteristics have been addressed in k853872.

   b. *Linearity/assay reportable range:*
   Performance Characteristics have been addressed in k853872.

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
   Performance Characteristics have been addressed in k853872.

   d. *Detection limit:*
   Performance Characteristics have been addressed in k853872.

e. *Analytical specificity:*
Performance Characteristics have been addressed in k853872.

f. *Assay cut-off:*
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

To determine that the device is equally effective for both uses as caffeine therapy and neonatal apnea, the sponsor performed a comparison study to include both populations. 110 neonate samples that spanned the range of the Emit® Caffeine Assay were compared to HPLC results. 31/110 samples were from patients who received Theophylline and 79/110 were from patients who received Caffeine. The statistical data revealed a slope of 1.04 μg/mL and an intercept of 0.44 μg/mL. The correlation coefficient was 0.99. Note: In a visual examination of the regression plot, no difference between the two populations was observed.

b. *Matrix comparison:*
Not Applicable

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:
Caffeine therapy is observes as a >50% reduction of episodes of apnea. Observed therapeutic ranges for caffeine in neonates is 8-20 μg/mL. Literature indicates that toxicity occurs when the serum level of caffeine exceeds 50 μg/mL (Pesce A.J., Rashkin M., Kotagal U. Standards of laboratory practice: Theophylline and caffeine monitoring. Clinical Chemistry 1990; 44(5); 1124-1128).

N. Proposed Labeling:

The changes in the labeling were reviewed however; previous performance information that was address in k853872 was not re-reviewed.

O. Conclusion:

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