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

A. 510(k) Number:

k081938

B. Purpose for Submission:

New Device

C. Measurand:

Acetaminophen

D. Type of Test:

Quantitative Colorimetry

E. Applicant:

Genzyme Diagnostics P.E.I., Inc.

F. Proprietary and Established Names:

Acetaminophen L3K Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR Section 862.3030 - Acetaminophen test system

2. Classification:

   Class II

3. Product code:

   LDP – Acetaminophen, colorimetry

4. Panel:

   Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   For the quantitative measurement of acetaminophen in serum and plasma. Measurement of acetaminophen is used in the diagnosis and treatment of acetaminophen overdose toxicity. Excessive amounts of acetaminophen leads to hepatotoxicity and nephrotoxicity. In acute overdosage, acetaminophen can cause severe hepatic damage leading to hepatic failure if untreated.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Performance characteristics were established using the Hitachi 717 analyzer.

I. Device Description:

This device contains three liquid ready-to-use components; a component that contains an acetaminophen enzyme reagent, an acetaminophen color reagent, and an acetaminophen standard.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Diagnostic Chemicals, Ltd. Acetaminophen-SL Assay

2. Predicate K number(s):

   k042330

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Enzyme method	Aryl Acylamidase	Aryl Acylamidase
Sample type	Serum and Plasma	Serum and Plasma
Form	Liquid Ready to use	Liquid Ready to use
Reagent storage	2 – 8°C	2 – 8°C

Differences		
Item	Device	Predicate
Chromophore used in the oxidative coupling reaction	2,5 dimethylphenol	8 hydroxyquinoline
Measuring range	4-2500 µmol/L	20-2500 µmol/L

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

CLSI Guidance EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

L. Test Principle:

The enzyme, acyl amidohydrolase, cleaves the amide bond of the acetaminophen molecule, leaving p-aminophenol and acetate. The p-aminophenol is coupled with 2,5-dimethylphenol in the presence of manganese ions to form a colored compound, 4-(4-iminophenol)-2,5-dimethylcyclohexadiene-1-one. The increased absorbance due to the formation of 4-(4-iminophenol)-2,5-dimethylcylcohexadiene-1-one is directly proportional to the acetaminophen in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:
Total precision studies were performed on the Hitachi 717 in accordance CLSI guidance document EP5-A2. A total of 40 runs were performed on 20 different days. Each run consisted of 3 concentrations of serum controls each run in duplicate. Controls were run on the same instrument twice a day by one operator in Genzyme Diagnostics P.E.I. Inc. laboratories. Within run precision testing was performed by testing three serum controls 20 times each in one run. The results are summarized below.

Acetaminophen Concentration (µmol/L)	Total SD (µmol/L)	Total CV %	Acetaminophen Concentration (µmol/L)	Within SD (µmol/L)	Within CV %
67	1.9	2.9	67	1.0	1.5
243	3.1	1.3	240	1.9	0.8
743	9.9	1.3	729	4.6	0.6

An additional precision study consisting of a total of 40 runs on 10 different days was performed. Each run consisted of 2 concentrations of serum controls run in duplicate. Within run and total precision were calculated and are summarized below.

Acetaminophen Concentration (µmol/L)	Total SD (µmol/L)	Total CV %	Acetaminophen Concentration (µmol/L)	Within SD (µmol/L)	Within CV %
1331	17.2	1.3	67	5.3	0.4
2120	30.6	1.4	240	10.89	0.5

b. *Linearity/assay reportable range:*

Linearity was evaluated on the Hitachi 717 by testing a spiked serum set that consisted of 11 concentrations of acetaminophen across the assay range. Each sample was tested four times and linearity was calculated. All samples tested were within ±3.9% of the expected value and the linear regression calculations resulted in a slope of 0.993 and an intercept of 1.6 µmol/L. These results support the manufacture's claimed measurement range of 4-2500 umol/L.

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

The calibrator was previously cleared under k952949.

d. *Detection limit:*

The limit of quantitation (LoQ) was evaluated on the Hitachi 717 by performing serial dilutions of a commercial control, then testing each dilution n=40 over 5 days. The sponsor defined the LoQ as the lowest concentration at which the CV% did not exceed 20%. The LoQ was calculated as 4 µmol/L, supporting the claimed lower limit of the assay.

e. *Analytical specificity:*

Interferences from hemolysis, icterus, lipemia, ascorbic acid, and N-acetylcysteine were evaluated on the Hitachi 717 by testing three concentrations of acetaminophen with multiple concentrations of each interferent. Significant interference was defined by the manufacturer as > 10% or ±8 µmol/L variance from control, whichever is greater. The highest concentrations of each substance that did not show significant interference with each acetaminophen concentration tested are shown below.

Acetaminophen Concentration	Concentration without Significant Interference
µmol/L	**Hemoglobin (mg/dL)**
93	200
315	800
918	1000
µmol/L	**Conjugated Bilirubin (mg/dL)**
110	16
327	40
936	40
µmol/L	**Unconjugated Bilirubin (mg/dL)**
102	40
328	40
990	40
µmol/L	**Intralipid (mg/dL)**
101	200
341	1000
984	1000
µmol/L	**Ascorbic Acid (µg/dL)**
104	3000
313	3000
968	3000
µmol/L	**N-Acetylcysteine (mg/L)**
92	2000
322	2000
933	2000

Interferences from the following therapeutic drugs were tested as recommended in CLSI EP7-A2 Interference Testing in Clinical Chemistry at acetaminophen concentrations of 33 µmol/L and 199 µmol/L. Significant interference was defined as > 10% or ±8 µmol/L variance from control, whichever is greater. The following drugs did not show significant interference at the concentrations listed.

Substance Tested	Concentration with no Significant Interference
Theophylline	222 mmol/L
Phenylbutazone	2.89 mmol/L
Ibuprofen	2425 mmol/L
Imipramine	2.5 mmol/L
Acetysalicylic Acid	6.51 mmol/L
Levodopa	25.3 mmol/L
Ampicillin	152 mmol/L
Doxycycline	67.5 mmol/L
Amitriptyline	3.61 mmol/L
Metronidazole	701 mmol/L
Cefoxitin	1546 mmol/L
Cyclosporin	10.0 mmol/L
Methyl-I-Dopa	71 mmol/L
Rifampicin	78.1 mmol/L
Salicylate	4.34 mmol/L
Ascorbic Acid	342 mmol/L

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed on the Hitachi 717 by testing 88 patient samples in singlicate on the Acetaminophen L3K Assay and a previously cleared predicate device. The samples ranged in concentration from 38 to 2361 µmol/L. Linear regression was performed and resulted in a slope of 1.063 (95% confidence interval 1.058 to 1.068), a y-intercept of 7.0 µmol/L (95% confidence interval 3.2 to 11.2), and a correlation coefficient of 0.9998.

b. Matrix comparison:

A matrix comparison study was performed on the Hitachi 717 by testing 25 sets of matched serum and lithium heparin plasma samples with acetaminophen concentrations that spanned the full measuring range of the device. Linear regression analysis was performed and resulted in the following equation. $y = 0.999x - 2.2$. The correlation coefficient was 0.9999.

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:

The package insert contains the following reference ranges cited from literature. (Tietz Textbook of Clinical Chemistry, Second Edition, pp 1168, 2212, W.B. Saunders Company, Philadelphia (1994))

Therapeutic concentration: < 199 µmol/L (30 µg/mL)
Toxic concentration: > 1324 µmol/L (200 µg/mL)

These values are suggested guidelines. It is recommended that each laboratory establish its own expected range.

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.