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

A. 510(k) Number:

k060738

B. Purpose for Submission:

New device

C. Measurand:

N-acetylprocainamide

D. Type of Test:

Homogeneous enzyme immunoassay

E. Applicant:

ROCHE DIAGNOSTICS CORP.

F. Proprietary and Established Names:

ONLINE TDM N-ACETYLPROCAINAMIDE

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Enzyme Immunoassay, N-acetylprocainamide (LAN)	Class II	21 CFR 862.3320, Digoxin test system.	91 CLINICAL TOXICOLOGY (TX)

H. Intended Use:

1. Intended use(s):

See Indications for Use.

2. Indication(s) for use:

The ONLINE TDM N-acetylprocainamide assay is for the quantitative determination of N-acetylprocainamide in human serum or plasma on Roche automated clinical chemistry analyzers. Measurements obtained from this device are used in the diagnosis and treatment of N-acetylprocainamide overdose and in monitoring the levels of N-acetylprocainamide to help ensure appropriate therapy.

3. Special conditions for use statement(s):

The device is for prescription use.

4. Special instrument requirements:

Evaluations represented in the 510(k) were performed on the Hitachi 917. See manufacturer's application sheets for other instruments validated with this assay.

I. Device Description:

The assay uses a homogeneous enzyme immunoassay technique based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity.

J. Substantial Equivalence Information:

Predicate	**k951595, COBAS Integra N-acetylprocainamide**
Describe the item being compared	
The Roche ONLINE TDM N-acetylprocainamide assay is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Roche COBAS INTEGRA N-acetylprocainamide (k951595).	
Similarites	
The ONLINE TDM N-acetylprocainamide and the COBAS INTEGRA N-acetylprocainamide assays are both indicated for the quantitative determination of N-acetylprocainamide in human serum or plasma on automated clinical analyzers.	

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

Other Standards
CLSI EP5-A

GUIDANCE			
Document Title	**Office**	**Division**	**Web Page**
Guidance for Industry and FDA Staff; Replacement Reagent and Instrument Family Policy	**OIVD**		**http://www.fda.gov/cdrh/oivd/guidance/950.html**

L. Test Principle:

The assay is based on a homogeneous enzyme immunoassay technique used for the quantitative analysis of N-acetylprocainamide in human serum or plasma. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme functions only with the bacterial (Leuconostoc mesenteroids) enzyme employed in the assay.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-lab precision was evaluated at the manufacturer's site on the Hitachi 911 and 917. One run consisting of triplicates of each sample was performed over 21 days. The evaluation was performed by one operator using one lot of reagents and controls. Control material and spiked human serum pools were evaluated. Two to three calibrations were performed throughout the study. Calculations were performed according to CLSI EP-5A, appendix C. Results are shown below.

Sample	control I	control II	control III	Low HSP	High HSP
Total mean (ug/mL)	1.69	4.00	8.18	4.91	21.05
Within-run SD (ug/mL)	0.07	0.08	0.17	0.093	0.74
Within-run CV (%)	3.9	2.0	2.1	1.9	3.5
Total SD (ug/mL)	0.08	0.16	0.26	0.17	1.29
Total CV (%)	5.0	4.0	3.2	3.4	6.1

b. Linearity/assay reportable range:

The measuring range of the device is 0.8 - 30 µg/mL. To determine the linearity of the assay, an evenly distributed dilution series with positive samples ranging in expected concentration from approximately 3-30 ug/mL (dilutions varying by 10% increments) was prepared using a NAPA spiked human serum pool diluted with a nonspiked serum pool. Recoveries, representing the observed result (median value, n=3) divided by the

expected result, ranged from 97% to 104%. An additional series, evaluated to include values below 3 ug/mL, supports linearity to the low end of the assay range of 0.8 ug/mL.

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

Calibrators were cleared under k031856.

Controls were cleared under k060429.

d. Detection limit:

The manufacturer defines the detection limit as the mean plus 2 standard deviations of the 0 calibrator. For this evaluation, the assay was calibrated as in the normal procedure. The 0 Calibrator was measured in 21 replicates and Calibrator B in 5 replicates in a single run and absorbance values were recorded. Results support the detection limit of 0.8 ug/mL.

e. Analytical specificity:

The assay was evaluated on the Hitachi 917 for interference from drugs, and endogenous compounds.

Cross-reactivity:

The following compounds were tested for cross-reactivity in serum samples containing approximately 5 ug/mL N-acetylprocainamide. Results were compared to those of control samples without cross-reactant. Desethyl-N-acetylprocainamide had a cross-reactivity of 16%. The other compounds tested had undetectable cross-reactivity (ND), defined by the manufacturer as a difference in values less than the sensitivity of the assay.

Compound	**Maximum concentration tested (ug/mL)**
Acetaminophen	100
Desethyl_N-acetylprocainamide	100
Digoxin	0.1
Disopyramide	100
Ephedrine	100
Furosemide	100
Hydrochlorothiazide	100
Isoproterenol	100
Lidocaine	100
p-Acetamidobenzoic acid	100
p-Aminobenzoic acid	100

Compound	Maximum concentration tested (ug/mL)
Phenytoin	100
Quinidine	100
Glycinexilidide	100
N-(2-Diethylaminoethyl)isonicotinamide	100
MonoethylglycinexylidideProcainamide	100
Procaine	100
Propranolol	100
Tocainide	100

Other drugs:
The drugs listed below were spiked into normal human serum pools containing 8 ug/mL N-acetylprocainamide, to the drug levels shown below. The manufacturer indicated that the drug levels evaluated were at a concentration greater than what would be expected for a maximum daily dose. Control samples consisted of serum spiked with N-acetylprocainamide, without any additional added drug. The drugs and concentrations tested are shown below. Less than 10% interference was observed at the concentrations shown.

Drug (maximum concentration tested)
Acetaminophen (200 ug/mL)
Acetyl cysteine (150 ug/mL)
Ampicillin-Na (1000 ug/mL)
Acetylsalycilic acid (1 mg/mL)
Ascorbic acid (300 ug/mL)
Ca-Dobesilate (200 ug/mL)
Cyclosporine (5000 ng/mL)
Cefoxitin-Na (2500 ug/mL)
Doxycycline HCl (50 ug/mL)
Heparin (5 ug/mL)
Ibuprofen (500 ug/mL)
Levodopa (20 ug/mL)
Methyldopa + 1,5 (20 ug/mL)
Metronidazole (200 ug/mL)
Phenylbutazone (400 ug/mL)
Rifampicin (60 ug/mL)
Theophylline (100 ug/mL)

Endogenous substances:
The effect of endogenous substances on assay recovery was evaluated using spiked serum pools containing 3 and 5 µg/mL N-acetylprocainamide. Dilution series of the endogenous compounds listed were prepared and each level was evaluated in triplicate. Less than 10% interference was observed for the following concentrations.

I index of 1-30 (approximate conjugated and unconjugated bilirubin concentration: 30 mg/dL)

H index of 0-800 (approximate hemoglobin concentration: 800 mg/dL)

Lipemic index of 0-500 (0-500 mg/dL intralipid).

HAMA 1 and HAMA 2 samples

Rheumatoid factors up to 100 IU/mL.

Total protein 2-12 g/dL.

Triglycerides up to 1000 mg/dL

f. Assay cut-off:

Not applicable. This is a quantitative test.

2. Comparison studies:

a. Method comparison with predicate device:

For one of the evaluations, a comparison of the ONLINE TDM N-acetylprocainamide assay on the Roche/Hitachi 917 analyzer (y) with the COBAS FP N-acetylprocainamide on a COBAS INTEGRA 700 analyzer was performed at the manufacturer's site. Fifty non-pooled human samples were assayed in singlicate in 1 run. Sample concentrations ranged between 0.5 and 16.3 µg/mL. Results of the analysis are shown:

Passing/Bablok:
$y = 1.033 x + 0.09$
$r=0.995$
SD (md 95) = 0.39

Another evaluation compared samples measured with the ONLINE TDM N-acetylprocainamide assay on a Roche/Hitachi 917 analyzer (y) with an N-acetylprocainamide assay on the Roche COBAS Integra. Forty eight samples ranging from near the low end of the assay range to approximately 25 ug/mL were evaluated. Results of the analysis are shown:

Passing/Bablok:
$Y= 0.99 x + 0.11$
$r=0.99$

SD (md 95) = 0.75

b. Matrix comparison:

A series of serum samples were tested and compared to concentration equivalent plasma samples. No significant matrix effects were observed. Results are shown below*:*

Sample type	N	Min x	Max x	Slope	Intercept	r
X: Serum, Y: Li Heparin	15	4.48	20.49	1.04	0.00	0.99
X: Serum Y: K2-EDTA	15	4.48	20.49	1.06	-0.39	0.99
X: Serum Y: K3 EDTA	15	4.61	19.35	1.08	-0.29	0.99
X: Serum Y: Citrate	30	4.48	20.49	1.02	-0.22	0.99
X: Serum Y: Oxalate	30	4.48	20.49	1.05	0.05	0.99
X: Serum Y: Na Heparin	15	4.61	19.35	1.08	-0.36	0.99

3. Clinical studies:

a. Clinical Sensitivity:

Not typically submitted for this device type

*b. Clinical specificity**:***

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:

Ranges based on the literature are presented in the package insert.

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.