

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

A. 510(k) Number:

k060773

B. Purpose for Submission:

New device

C. Measurand:

Procainamide

D. Type of Test:

Enzyme immunoassay

E. Applicant:

ROCHE DIAGNOSTICS CORP.

F. Proprietary and Established Names:

ONLINE TDM PROCAINAMIDE

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
<u>Enzyme</u> <u>Immunoassay,</u> <u>Procainamide</u> <u>(LAR)</u>	<u>Class II</u>	<u>21 CFR 862.3320,</u> <u>Digoxin test system.</u>	<u>91 CLINICAL</u> <u>TOXICOLOGY</u> <u>(TX)</u>

H. Intended Use:

1. Intended use(s):

See Indications for Use below.

2. Indication(s) for use:

The ONLINE TDM Procainamide assay is for the quantitative determination of procainamide in human serum or plasma on Roche automated clinical chemistry analyzers. Measurements are used in the diagnosis and treatment of procainamide overdose and in monitoring levels of procainamide to ensure proper therapy.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Evaluations represented in the 510(k) were performed on the Hitachi 917.

I. Device Description:

The device consists of two ready-to-use reagents ('working solutions'). R1 contains a mouse anti-procainamide monoclonal antibody, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) in buffer while R2 contains procainamide labeled with glucose-6-phosphate dehydrogenase (G6PDH) in buffer.

J. Substantial Equivalence Information:

Predicate	k951595, COBAS Integra Procainamide
Describe the item being compared	
The Roche ONLINE TDM Procainamide assay is substantially equivalent to the currently marketed Roche COAS INTEGRA Procainamide (k951595).	
Similarities	
The ONLINE TDM Procainamide and the COBAS INTEGRA Procainamide assays are both indicated for the quantitative determination of Procainamide in human serum or plasma on Roche automated clinical analyzers.	

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

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 a homogeneous enzyme immunoassay technique used for the quantitative analysis of procainamide 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:

Reproducibility was determined using three levels of controls and two levels

of a human sera pool (HSP) with a modified version of CLSI EP5-T2 where 3 replicates were tested once a day for 21 days (n = 63). Results are shown in the table below:

Precision: Roche ONLINE TDM Procainamide Assay

Sample	Mean	Within-Run		Total Precision	
		Std Dev	CV	Std Dev	CV
	ng/mL	ng/mL	%	ng/mL	%
Control 1	1.7	0.03	1.5	0.04	2.6
Control 2	7.1	0.07	1.0	0.27	3.8
Control 3	11.6	0.28	2.4	1.08	9.3
Low HSP	3.6	0.04	1.1	0.06	1.5
High HSP	8.8	0.14	1.6	0.45	5.1

b. Linearity/assay reportable range:

The reportable range of the assay is 0.33 – 14 µg/mL.

Assay linearity was evaluated by measuring percent recovery of expected values in a dilution series using a procainamide-spiked serum pool diluted with a non-spiked serum pool. Results are summarized below:

Linearity of the ONLINE TDM Procainamide Assay

Dilution of Sample	Theoretical Value (ug/mL)	Measured Value (ug/mL)	% Recovery
neat	19.20	31.59	165
0.9	17.28	17.57	102
0.8	15.36	15.26	99
0.7	13.44	12.50	93
0.6	11.52	10.44	91
0.5	9.60	8.88	93
0.4	7.68	7.24	94
0.3	5.76	5.57	97
0.2	3.84	3.94	103
0.1	1.92	1.81	94

The sponsor also performed post-dilution studies that supported their recommendation for dilution of samples above the measuring range of the device.

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

Stability: The shelf life of the Roche ONLINE TDM Procainamide Assay is claimed as 18 months based on accelerated and real time stability testing of

three lots of product. Onboard (opened and refrigerated) stability is claimed as 60 days.

Calibrators: The Preciset TDM II Calibrators are prepared to contain known quantities of procainamide in normal human serum and are traceable to USP reference standards. These calibrators are used to establish a standard curve from which the quantity of drug in unknown specimens can be determined. Please see 510(k) k031856 for more information.

Controls: The TDM Control Set contains liquid controls based on human serum and are traceable to USP reference standards. Please see 510(k) k060429 for more information.

d. Detection limit:

The manufacturer's claimed a lower assay limit of 0.33 ug/mL. This claim was determined by measuring the absorbance values of 21 replicates of the zero calibrator and adding two standard deviations to the mean of measured values.

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 4.5 ug/mL procainamide. Results were compared to those of control samples without cross-reactant. All compounds tested had undetectable cross-reactivity (ND) at the listed concentration, defined by the manufacturer as a difference in values less than the sensitivity of the assay.

Cross Reactant	Concentration (ug/ml)
Acetaminophen	100
Desethyl-N-acetylprocainamide	100
Digoxin	0.1
Diphenylhydantoin	100
Disopyramide	100
Ephedrine	100
Furosemide	100
Glycinexylidide	100
Hydrochlorothiazide	100
Isoproterenol hydrochloride	100
Lidocaine	100
Monoethylglycinexylidide	100
N-Acetylprocainamide	40

N-(2-Diethylaminoethyl)isonicotinamide	100
p-Acetamidobenzoic acid	100
p-Aminobenzoic Acid	100
Procaine	100
Propanolol	100
Quinidine	100
Tocainide	100

Other drugs:

The drugs listed below were spiked into normal human serum pools containing 2.5 ug/mL procainamide, and 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 procainamide, without any additional added drug. Less than 10% interference was observed at the concentrations shown.

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

Endogenous substances:

Interference by endogenous substances was assessed by determining the recovery of procainamide from samples spiked with procainamide (about 4 ug/mL) and different concentrations of interferents. There was no significant (< ±10%) interference from:

- 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 0-1500 (0-1500 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.

2. Comparison studies:

a. *Method comparison with predicate device:*

A comparison of the ONLINE TDM Procainamide assay on a Roche/Hitachi 917 analyzer (y) with a commercially available method (COBAS FP Procainamide on a COBAS INTEGRA 700 analyzer) (x) gave the following correlation ($\mu\text{g/mL}$) using 51 human serum samples:

Passing/Bablok:

$$y = 1.007 x + 0.247$$

$$r = 0.9975$$

$$\text{SD (md 95)} = 0.311$$

The sample concentrations were between 0.3 and 10.6 $\mu\text{g/mL}$.

A comparison of the ONLINE TDM Procainamide assay on a Roche/Hitachi 917 analyzer (y) with a commercially available method (EMIT 2000 Procainamide on a Roche/Hitachi 911 analyzer) (x) gave the following correlation ($\mu\text{g/mL}$) using 48 human serum samples:

Passing/Bablok:

$$y = 0.981 x + 0.02$$

$$r = 0.997$$

$$\text{SD (md 95)} = 0.241$$

The sample concentrations were between 1.06 and 11.18 $\mu\text{g/mL}$.

b. *Matrix comparison:*

The sponsor found serum and plasma equivalent with the following anticoagulants: heparin (sodium or lithium), potassium (K2 or K3) EDTA, citrate, and oxalate.

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:

The sponsor states that the commonly accepted therapeutic range for procainamide is 4 - 10 $\mu\text{g/mL}$ (16.9 - 42.3 $\mu\text{mol/L}$) and the sum of procainamide

and its primary active metabolite, N-acetylprocainamide (NAPA) is 5 - 30 µg/mL (21.2 - 126.9 µmol/L). Procainamide is thought to be toxic at levels greater than 16 µg/mL (>67.7 µmol/L).

The factors that can influence the relationship between procainamide serum or plasma concentrations and clinical response include: renal and circulatory function, rate of acetylation, the severity and type of cardiac arrhythmia, general state of health, and use of other drugs. The concentration of procainamide in serum or plasma depends on the time of the last drug dose; mode of administration; concomitant drug therapy; sample condition; time of sample collection; and individual variations in absorption, biotransformation, distribution, and excretion. These parameters must be considered when interpreting results. Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference 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.