

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

A. 510(k) Number: K032334

B. Analyte: lidocaine

C. Type of Test: homogeneous microparticle immunoassay

D. Applicant: Roche Diagnostics Corporation

E. Proprietary and Established Names: Roche Online TDM Lidocaine Assay

F. Regulatory Information:

1. Regulation section:
21CFR862.3555, Lidocaine Test System
2. Classification:
Class II
3. Product Code:
91 KLR
4. Panel:
Toxicology

G. Intended Use:

1. Indication(s) for use:
The Roche Online TDM Lidocaine assay is intended for the quantitative determination of lidocaine in human serum or plasma on automated clinical chemistry analyzers. Lidocaine is an antiarrhythmic agent administered intravenously by either injection or continuous infusion. It is indicated in the acute management of ventricular arrhythmias such as those occurring in relation to acute myocardial infarction, or during cardiac manipulation, such as cardiac surgery. The proposed labeling indicates the Roche Hitachi 911, 912, 917 and Modular P analyzers can be used with the Roche ONLINE Lidocaine assay reagent kit.
2. Special condition for use statement(s):
For prescription use.
3. Special instrument Requirements:
The test is for use on automated clinical chemistry analyzers.

H. Device Description:

The test consists of ready-to-use reagents containing anti-lidocaine antibody and conjugated lidocaine-derivative microparticles.

I. Substantial Equivalence Information:

1. Predicate device name(s):
Roche Cobas Integra Lidocaine
2. Predicate K number(s):
K954992
3. Comparison with predicate:
The devices are similar in terms of intended use and indications for use. They each use different technologies. Detection of the analyte in the predicate assay is based on fluorescence polarization. Detection in this assay is based on changes in scattered light resulting from microparticle aggregation.

J. Standard/Guidance Document Referenced (if applicable):**K. Test Principle:**

The test is a homogenous assay based on measuring changes in scattered light resulting from aggregation of microparticles. Microparticles coated with lidocaine aggregate in the presence of the lidocaine antibody. Samples containing lidocaine inhibit the aggregation to varying degrees depending on the lidocaine concentration.

L. Performance Characteristics (if/when applicable):1. Analytical performance:*a. Precision/Reproducibility:*

Precision was evaluated on the Hitachi 917 at the manufacturer's site using control material and spiked human serum pools. The evaluation included 3 runs/day over 21 days. Calculations were similar to those described in NCCLS EP-5A. Recalibrations were performed several times during the evaluation as necessary for changes in reagent. Results are tabulated below:

Specimen	Low spike	High spike	Control 1	Control 2	Control 3
Total mean (ug/ml)	2.34	8.31	1.34	4.47	7.03
Within-run SD (ug/ml)	0.05	0.15	0.04	0.07	0.14
Within-run %cv	2.1	1.8	2.7	1.5	1.9
Total SD (ug/ml)	0.16	0.23	0.08	0.15	0.24
Total %CV	6.6	2.7	5.9	3.3	3.4
Between-day SD (ug/ml)	0.15	0.17	0.07	0.13	0.20
Between-day %CV	6.3	2.1	5.2	2.9	2.8

b. Linearity/assay reportable range:

The reportable range, based on the upper limit of the linear range and the limit of the blank (sensitivity), is 0.3-10.0 ug/ml. To evaluate linearity, spiked human serum pools were diluted with a lidocaine negative human serum pool in a dilution series. Percent recoveries within the reportable range ranged from 98-102%. (Lidocaine values above this range have decreased recovery.)

c. *Traceability (controls, calibrators, or method):*

Controls and calibrators were previously cleared (K954992 and K981532) and are sold separately.

d. *Detection limit:*

The detection limit of 0.3 ug/ml is based on the mean and two standard deviations of 21 determinations of zero calibrator material. A linear interpolation model, based on these determinations of the zero calibrator material, as well as five replicate determinations of the 0.5 calibrator material, was used to calculate the concentration equivalent to the mean plus two standard deviations.

e. *Analytical specificity:*

To evaluate potential interference from drugs and metabolites, serum pools were spiked with potential interferents and approximately 2.5 ug/ml lidocaine. Drugs found to cross-react at high concentrations were run in a series of dilutions. Percent cross reactivity for drugs and metabolites were defined as: $[(Da-Dt)/C] \times 100$, where Dt = the measured concentration of the control analyte, Da = measured concentration of the control analyte + cross-reactant and C= known concentration of cross-reactant. Calculated cross-reactivities are based on the median of triplicate determinations. Observed cross-reactivities with the compounds tested are tabulated below:

Compound	Concentration (ug/ml)	% cross-reactivity
Mepivacaine	1	95
Bupivacaine	10	24
PPX (L-Pipecolic acid-2,6-xylidide)	10	3.4
MEGX (Monoethylglycinexylidide)	100	1.7

No cross-reactivity was detected for the following drugs (concentrations in ug/ml): tocanide (100), digoxin (1), disopyramide (100), ephedrine (10), Flecainide (10), Furosemide (100), GX (glycinexylidie) (10), hydrochlorothiazide (10), isoproterenol (10), lidocaine-N-ethyl bromide (100), d-methamphetamine (10),

mexiletine (100), phenytoin (1000), procainamide (100), propranolol (1), quinidine (100).

Sixteen common drugs were tested for interference. Recoveries of lidocaine in this sample ranged from 98-102%. No significant interference was observed for the following drugs at the concentrations tested (concentrations in ug/ml):

acetylcysteine (150) , ampicillin (1000) , ascorbic acid (300) , K-Dobesilate (200), methyldopa (20), Doxycycline (50), cyclosporine (5), levodopa (20), metronidazole (200), phenylbutazone (400) , acetylsalicylic acid (1000) , rifampicin (60), acetaminophen (200), ibuprofen (500), cefoxitin (2500), theophylline (100).

To evaluate interference from endogenous compounds, a series of dilutions containing varying levels of the endogenous compounds was prepared from spiked and negative serum pools. Testing was in the presence of approximately 2 ug/ml lidocaine (except for HAMA testing, in which samples contained 5 ug/ml lidocaine.) Percent recovery was calculated relative to control samples containing lidocaine without spiked endogenous compounds. The median of triplicate determinations was used in calculations of recovery. Concentrations ranges of endogenous compound in which assay recovery $\geq 90\%$ is observed are tabulated below:

Compound/sample condition tested	Concentration range within recovery criteria (+/- 10% bias)	Recoveries/ trends
Bilirubin (conjugated and unconjugated)	I index up to 66 (approximately equivalent to 66 mg/dL)	Near 100% at low bilirubin concentrations, decreasing to 95% at values between 65 and 70 mg/dL
Hemoglobin	I index up to 1000 (approximately equivalent to 1000 mg/dL)	Near 100% at lower levels increasing to 109% at I index values near 1000
Lipemia	L index up to 2000 (approximately equivalent to 2000 mg/dL intralipid)	Near 100% at lower levels, decreasing to 91% at levels near 2000.
Rheumatoid factor	Up to 300 IU/ml	Near 100% at low levels, decreasing to 92% at levels near 300 IU/ml
Samples containing HAMA 1 and HAMA 2		97-106% recovery
Total protein	Range: 0-11.8 g/dL	91-108% recovery.

Clinical samples (n=7) containing triglycerides in the range 100-1700 mg/dL were tested. Recoveries ranged from 100- 109% (with highest recoveries observed at higher triglyceride concentrations).

- f. Assay cut-off:*
NA. This is a quantitative assay.

2. Comparison studies:

a. Method comparison with predicate device

Clinical serum samples were obtained from a third party vendor and selected to contain samples below, within and above the medical decision points. Ninety nine samples were analyzed in singlicate using the new device and the predicate device. Sample values ranged from 0.4-9.5 ug/ml. Results of the sponsor's analysis based on Passing-Bablok model are shown below:

$$Y = 1.024X - 0.050, \text{md}(95) = 0.279, r = 0.995$$

b. Matrix comparison:

To evaluate the effect of plasma anticoagulants, comparisons of serum samples versus samples containing EDTA, sodium heparin, and lithium heparin were conducted. Fifteen samples were included for each anticoagulant. No significant bias due to these anticoagulants was observed.

3. Clinical studies:

- a. Clinical sensitivity:* N/A. (Not typically reviewed for this type of test.)

- b. Clinical specificity:* N/A. (Not typically reviewed for this type of test.)

4. Clinical cut-off: See expected values.

5. Expected values/Reference range: The therapeutic range for this specific assay was not determined. However, therapeutic ranges of serum lidocaine are discussed in the literature and cited and discussed in the package insert. Test findings should always be assessed in conjunction with patient's medical history, clinical examination and other medical findings.

M. Conclusion:

I recommend that the Roche Online TDM Lidocaine is substantially equivalent to the predicate device.