Quinidine Assay

Serum quinidine concentrations correlate better with pharmacologic activity than does for the following reasons:

- Specifically for use on a variety of AU® Clinical Chemistry Systems.
- Assay, chromatographic assay, and immunoassay.

The Emit® 2000 Quinidine Calibrators* are provided ready to use in liquid form.

Note: Reagents 1 and 2 are provided as a matched set. They should not be interchanged with components of kits with different lot numbers.

Required for calibrating the Emit® 2000 Quinidine Assay. Sold separately.

Additional negative calibrator is provided.


** Additional negative calibrator is provided.

### Intended Use

The Emit® 2000 Quinidine Assay is a homogeneous enzyme immunoassay intended for use in the quantitative analysis of quinidine in human serum or plasma. These reagents are packaged specifically for use on a variety of AU® Clinical Chemistry Systems.

### Summary

Monitoring serum quinidine concentrations, along with careful clinical assessment, is the most effective means of achieving an optimum antiarrhythmic effect and reducing the risk of toxicity for the following reasons:

- Serum quinidine concentrations correlate better with pharmacologic activity than does dosage.
- The quinidine dosage required to control cardiac arrhythmias varies substantially in different patients and in the same patient at different times. These variations are due to differences in absorption and metabolism and to the influences of disease states and coadministered drugs.
- Quinidine is safe and effective only in a narrow range of serum concentrations.
- The symptoms of serious quinidine toxicity can mimic those of an ineffectively controlled cardiac disorder.

Methods historically used to monitor serum quinidine concentrations include spectrophotometric assay, chromatographic assay, and immunoassay.

### Methodology

The Emit® 2000 Quinidine Assay is a homogeneous enzyme immunoassay technique used for the analysis of specific compounds in biological fluids. The assay is based on competition between the drug in the sample and the 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 mesenteroides) enzyme employed in the assay.

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### Quality Control

**Validate the calibration by assaying multi-level (eg, low, medium, and high) controls in every run.** Commercial controls are available for this purpose. Ensure that control results fall within acceptable limits as defined by your own laboratory. Once the calibration is validated, run samples.

**Refer to the instrument User’s Guide for appropriate instrument checks and maintenance instructions.**
Diluting High Concentration Samples
To estimate quinidine concentrations above the assay range, patient samples containing more
than 8.0 µg/mL (25 µmol/L) quinidine may be diluted with one or two parts distilled or deionized
water or Emit® 2000 Quinidine Calibrator 0. After diluting the sample, repeat the entire assay
sequence and multiply the results by the dilution factor. Some analyzers dilute and retest high
concentration samples automatically. See the analyzer User’s Guide or appropriate Application
Sheet for instructions.

Evaluation and Interpretation of Results
• This assay uses Math Model No. 1.
• The factors that can influence the relationship between quinidine serum or plasma
concentrations and clinical response include the type and severity of arrhythmia, liver
function, kidney function, general state of health, and use of other drugs.1–3
• The concentration of quinidine 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 of absorption, distribution, biotransformation, and
excretion. These parameters must be considered when interpreting results.1–3

7 LIMITATIONS OF THE PROCEDURE
o-Desmethylquinidine (DMQ), a minor metabolite of quinidine, cross-reacts with this assay (see
Section 9, Specific Performance Characteristics, Specificity).

8 EXPECTED VALUES
The Emit® 2000 Quinidine Assay accurately quantitates quinidine concentrations in human
serum or plasma containing 0.5–8.0 µg/mL (1.5–25 µmol/L) quinidine. Dihydroquinidine (DHQ), a constituent of pharmaceutical quinidine preparations, has antiarrhythmic activity and pharmacokinetic properties similar to those of quinidine. DHQ makes a small, but measurable, contribution to the assayed value. Levels of DHQ in serum are reported to be approximately 5% to 10% of the total quinidine level.6

Note: To convert from µg/mL to µmol/L quinidine, multiply by 3.08.
Clinicians should be aware of the differences among the various analytical methods used to
measure quinidine and how these differences may affect the range of quinidine concentrations
that are defined as therapeutic. Regardless of the method used to measure quinidine
concentrations, the therapeutic range is variable between patients. Plasma quinidine levels
between approximately 2 and 5 µg/mL have commonly been considered effective.1–4,8 In all
cases, the clinician should carefully consider patient response and evidence of toxicity along with
blood levels in determining optimal quinidine therapy.

9 SPECIFIC PERFORMANCE CHARACTERISTICS
The information presented in this section is based on Emit® 2000 Quinidine Assay studies on the AU400®/AU600® Clinical Chemistry System. Refer to the Application Sheets for other AU Clinical Chemistry Systems and for additional information. Results may vary due to analyzer-to-analyzer differences. The following performance characteristics represent total system performance and should not be interpreted to pertain only to reagents.

Endogenous Substances
No clinically significant interference has been found in samples to which 800 mg/dL hemoglobin, 1000 mg/dL triglycerides, or 30 mg/dL bilirubin were added to simulate hemolytic, lipemic, or icteric samples.

Precision
Within-run precision was determined by assaying 20 replicates of each level of a tri-level control. Table 1 summarizes the data.

Table 1 — Within-Run Precision

<table>
<thead>
<tr>
<th>Level</th>
<th>Level 1 Mean (µg/mL)</th>
<th>Level 2 Mean (µg/mL)</th>
<th>Level 3 Mean (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.45</td>
<td>3.28</td>
<td>4.67</td>
</tr>
<tr>
<td>%CV</td>
<td>2.9</td>
<td>3.4</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Total precision was calculated according to NCCLS guideline EPS-T2 using data collected from
controls run in duplicate twice daily over twenty (20) days. Table 2 summarizes the data.

Table 2 — Total Precision

<table>
<thead>
<tr>
<th>Level</th>
<th>Level 1 Mean (µg/mL)</th>
<th>Level 2 Mean (µg/mL)</th>
<th>Level 3 Mean (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.39</td>
<td>3.34</td>
<td>4.68</td>
</tr>
<tr>
<td>%CV</td>
<td>8.5</td>
<td>6.7</td>
<td>9.3</td>
</tr>
</tbody>
</table>

Comparative Analysis
In this study, samples from patients were analyzed on the TDx analyzer and on the AU600 Clinical
Chemistry System. A summary of the results is as follows:

Table 3 — Comparative Analysis Results

<table>
<thead>
<tr>
<th>Slope</th>
<th>1.02</th>
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<tbody>
<tr>
<td>Intercept</td>
<td>-0.06</td>
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<tr>
<td>Mean</td>
<td>TDx</td>
</tr>
<tr>
<td></td>
<td>AU600</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.98</td>
</tr>
<tr>
<td>Number</td>
<td>53</td>
</tr>
</tbody>
</table>

Specificity
The Emit® 2000 Quinidine Assay measures the total (protein-bound plus unbound) quinidine
concentration in serum or plasma. In addition, dihydroquinidine (DHQ) makes a small, but
measurable, contribution to the assayed value (see Section 8, Expected Values).

Compounds whose chemical structure or concurrent therapeutic use would suggest possible
cross-reactivity have been tested. o-Desmethylquinidine (DMQ), a minor metabolite of quinidine,
cross-reacts with this assay.

The compounds listed in Table 4 do not interfere with the Emit® 2000 Quinidine Assay when
tested in the presence of 2.0 µg/mL quinidine. Levels tested were at or above maximum
physiological or pharmacological concentrations.

Table 4 — Compounds That Do Not Interfere

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration Tested (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Structurally Related Compounds</td>
</tr>
<tr>
<td>3-Hydroxyquinidine</td>
<td>5</td>
</tr>
<tr>
<td>2'-Oxoquinidinone</td>
<td>2</td>
</tr>
<tr>
<td>Quinidine</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
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Sensitivity
The sensitivity level of the Emit® 2000 Quinidine Assay is 0.25 µg/mL. This level represents the
lowest measurable concentration of quinidine that can be distinguished from 0 µg/mL with a
confidence level of 95%.

Calibration Stability
Studies have shown calibration stability of more than two weeks. When proper reagent handling,
instrument maintenance, and operating procedures are followed, the calibration should remain
stable for at least two weeks.
REFERENCES


For technical assistance:
Beckman Coulter customers contact their technical assistance center.
1-800-223-0130

Siemens Healthcare Diagnostics customers contact their technical assistance center.
1-800-227-8994 in the USA
1-800-284-0083 in Canada

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