For In Vitro Diagnostic Use

ANNUAL REVIEW

Reviewed by:  Date  Reviewed by:  Date

Refer to “Review and Revision Coversheet” in front of each method

PRINCIPLE

INTENDED USE

Glucose (GLU) Reagent, in conjunction with the SYNCHRON CX SYSTEMS CX MULTI™ Calibrator, is intended for the quantitative determination of glucose concentration in serum, plasma, urine or cerebrospinal fluid on SYNCHRON CX Systems.

CLINICAL SIGNIFICANCE

Glucose measurements are used in the diagnosis and treatment of carbohydrate metabolism disorders including diabetes mellitus, neonatal hypoglycemia, and idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

METHODOLOGY

Glucose Reagent is used to measure the glucose concentration by a timed endpoint method.\(^1\) In the reaction, hexokinase (HK) catalyses the transfer of a phosphate group from adenosine triphosphate (ATP) to glucose to form adenosine diphosphate (ADP) and glucose-6-phosphate. The glucose-6-phosphate is then oxidized to 6-phosphogluconate with the concomitant reduction of \(\beta\)-nicotinamide adenine dinucleotide (NAD) to reduced \(\beta\)-nicotinamide adenine dinucleotide (NADH) by the catalytic action of glucose-6-phosphate dehydrogenase (G6PDH).

The SYNCHRON CX System automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 100 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is directly proportional to the concentration of glucose in the sample and is used by the SYNCHRON CX System to calculate and express glucose concentration.

CHEMICAL REACTION SCHEME

\[
\text{Glucose} + \text{ATP} \xrightarrow{\text{HK}} \text{glucose-6-phosphate} + \text{ADP}
\]
\[
\text{Glucose-6-phosphate} + \text{NAD}^+ \xrightarrow{\text{G6PDH}} \text{6-phosphogluconate} + \text{NADH} + \text{H}^+
\]
SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test. Freshly drawn serum, plasma, or cerebrospinal fluid or freshly collected urine are the specimens of choice. Acceptable anticoagulants are listed in PROCEDURAL NOTES section of this chemistry information sheet. Whole blood is not recommended for use as a sample. The use of fluoride as a glycolysis inhibition is recommended.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood should be kept closed at all times in a vertical, stopper-up position. Serum or plasma should be physically separated from contact with cells as soon as possible. A maximum limit of two hours from the time of collection is recommended.\(^2\)

2. Separated serum or plasma should not remain at +15°C to +30°C longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.\(^3\)

3. It is recommended that urine assays be performed within 2 hours of collection. For timed specimens, the collection container is to be kept in the refrigerator or on ice during the timed period. If a special preservative is required, it should be added to the container before urine collection begins.\(^4\)

4. CSF specimens should be centrifuged and analyzed without delay. Specimens may be refrigerated or frozen for 7 to 10 days for repeat determinations.\(^5\)

Additional specimen storage and stability conditions as designated by this laboratory:

Refer to “Sample Integrity in Chemistry” write up in “Chemistry Technical Policies & Procedures Manual”

SAMPLE VOLUME

A filled 0.5 mL sample cup is the optimum volume. For optimum volume in primary tube samples, refer to Primary Sample Tube Chart Template (P/N 015-248511).

Refer to the Quick Reference Guide at the beginning of this manual for minimum volumes.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet or the SPECIMEN REQUIREMENTS section of this manual for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:
Refer to “Sample Integrity in Chemistry” write up in Chemistry Technical Policies & Procedures Manual

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

Refer to “Sample Integrity in Chemistry” write up in “Chemistry Technical Policies & Procedures Manual”

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

Refer to “Sample Integrity in Chemistry” write up in “Chemistry Technical Policies & Procedures Manual”

REAGENTS

CONTENTS

Each kit as supplied from Beckman Instruments, Inc. contains the following items:

Two Glucose Reagent Cartridges (2 x 300 tests).

VOLUMES PER TEST

<table>
<thead>
<tr>
<th>Sample Volume</th>
<th>3 µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Reagent Volume</td>
<td>300 µL</td>
</tr>
<tr>
<td>Cartridge Volumes</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>273 µL</td>
</tr>
<tr>
<td>B</td>
<td>27 µL</td>
</tr>
<tr>
<td>C</td>
<td>--</td>
</tr>
</tbody>
</table>
REACTIVE INGREDIENTS

<table>
<thead>
<tr>
<th>REAGENT CONSTITUENTS</th>
<th>REACTION CONCENTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosine triphosphate</td>
<td>3.8 mmol/L</td>
</tr>
<tr>
<td>NAD⁺</td>
<td>2.7 mmol/L</td>
</tr>
<tr>
<td>Hexokinase</td>
<td>2.0 KIU/L</td>
</tr>
<tr>
<td>Glucose-6-phosphate dehydrogenase</td>
<td>3.0 KIU/L</td>
</tr>
</tbody>
</table>

Also non-reactive chemicals necessary for optimal system performance.

CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See National Institute for Occupational Safety and Health Bulletin: Explosive Azide Hazards (8/18/76).
Avoid skin contact with reagent. Use water to wash reagent from skin.
Incineration of used reagent cartridges may produce toxic fumes.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

CX MULTI Calibrator.
At least two levels of control material.
Saline.

REAGENT PREPARATION

No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria, as defined in the CONTROL PROCEDURES section of this manual.

REAGENT STORAGE AND STABILITY

Glucose Reagent when stored unopened at +2°C to +8°C will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 30 days unless the expiration date is exceeded. DO NOT FREEZE.

Glucose Reagent storage location:

Chemistry Refrigerator P18 or “Walk In” cold room M567A.
CALIBRATION

CALIBRATOR REQUIRED

CX MULTI Calibrator.

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

If unopened, the CX MULTI Calibrator may be stored at -15°C to -20°C until the expiration date printed on the calibrator bottle. Opened calibrators that are resealed and stored at +2°C to +8°C are stable for 20 days unless the expiration date is exceeded.

Calibrator storage location:

Refer to “LX20 Calibration Procedures” in “LX20 Procedure Manual”

CALIBRATION INFORMATION

1. The system must have a valid calibration factor in memory before controls or patient samples can be run.

2. Under typical operating conditions the Glucose Reagent cartridge must be calibrated every 14 days and also with certain parts replacements or maintenance procedures, as defined in the Operating Instructions manual. This assay has within lot calibration available. Refer to Section 6 of the Operating Instructions manual for information on this feature.

3. For calibration instructions, refer to the Quick Reference Guide at the beginning of this manual. For detailed calibration instructions, refer to Section 6 of the Operating Instructions manual.

4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will print out with error codes and the system will alert the operator of the failure. The explanation of these error codes can be found in Appendix G of Section 10 in the Operating Instructions manual.

CAUTION

Because this calibrator is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HBsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples be handled at the Centers for Disease Control's Biosafety Level 2.
QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge and after specific maintenance or troubleshooting procedures as detailed in the Operating Instructions manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on work load and work flow.

The following controls should be prepared and used in accordance with the package inserts. Copies of these inserts can be found in the CONTROL PROCEDURES section of this manual. Out of range quality control results should be evaluated and handled as described in the CONTROL PROCEDURES section of this manual.

Table 1. Quality Control Material

<table>
<thead>
<tr>
<th>CONTROL NAME</th>
<th>SAMPLE TYPE</th>
<th>STORAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer to “LX20 Control and Patient Analysis” in “LX20 Procedure Manual” for control Material used and storage conditions.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional procedures for acceptance of QC are in “QC Failure Policy” in “LX20 Procedure Manual”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TESTING PROCEDURE

1. If necessary, load the reagent onto the system as directed in the Quick Reference Guide at the beginning of this manual or refer to Section 6 of the Operating Instructions manual.

2. After reagent load is completed, calibration may be required. Refer to the Quick Reference Guide or Section 6 of the Operating Instructions manual for details of the calibration procedure.

3. Program samples and controls for analysis as directed in the Quick Reference Guide or refer to Section 6 of the Operating Instructions manual.

4. After loading samples and controls onto the system, follow the protocols for system operation as directed in the Quick Reference Guide or refer to Section 6 of the Operating Instructions manual.

CALCULATIONS

The system performs all calculations internally to produce the final reported result. SYNCHRON CX4/5 Systems do not calculate the final result for sample dilutions made by the operator. In these cases, the result produced by the instrument must be multiplied by the dilution factor before reporting the final result. SYNCHRON CX4CE/5CE/7 Systems (including the CX DELTA Systems) will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.
REPORTING RESULTS

REFERENCE INTERVAL

Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed below were taken from literature.⁵

Table 2. Reference Interval

<table>
<thead>
<tr>
<th>INTERVAL</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S. I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature</td>
<td>Serum or Plasma</td>
<td>70 to 105 mg/dL</td>
<td>3.9 to 5.8 mmol/L</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>1 to 15 mg/dL</td>
<td>0.06 to 0.83 mmol/L</td>
</tr>
<tr>
<td></td>
<td>CSF</td>
<td>40 to 70 mg/dL</td>
<td>2.2 to 3.9 mmol/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERVAL</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S. I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory</td>
<td>Serum or Plasma</td>
<td>Fasting for &gt;10 hrs</td>
<td>Normal: 70-99mg/dl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suggest impaired glucose homestasis: 100-125 mg/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diabetis mellitus: &gt; 125mg/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-fasting (random)</td>
<td>Normal 70-199 mg/dl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impaired glucose tolerance 140-199 mg/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diabetes mellitus , &gt;199 mg/dl</td>
<td>and symptoms of diabetes such as polyuria, polydipsia or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>unexplained loss of weight</td>
</tr>
</tbody>
</table>

Refer to References (5, 7, 8) for guidelines on establishing laboratory reference intervals.

Procedures for reporting results to the appropriate personnel can be found in the HOW TO REPORT RESULTS section of this manual.

Additional reporting information as designated by this laboratory:

Refer to “LX20 Linearity and Reportable Ranges” chart appended to “LX20 Technical Information and Procedures” in “LX20 Procedure Manual”

PROCEDURAL NOTES

LIMITATIONS

1. If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method, based on a study of 20 healthy volunteers:

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Table 3. Compatible Anticoagulants

<table>
<thead>
<tr>
<th>ANTICOAGULANT</th>
<th>LEVEL TESTED FOR IN VITRO INTERFERENCE</th>
<th>AVERAGE PLASMA-SERUM BIAS* (mg/dL) 37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium Heparin</td>
<td>29 units/mL</td>
<td>NSI</td>
</tr>
<tr>
<td>Lithium Heparin</td>
<td>29 units/mL</td>
<td>NSI</td>
</tr>
<tr>
<td>Sodium Heparin</td>
<td>29 units/mL</td>
<td>NSI</td>
</tr>
<tr>
<td>Potassium Oxalate/ Sodium Fluoride</td>
<td>4.0 mg/mL / 5.0 mg/mL</td>
<td>NSI</td>
</tr>
</tbody>
</table>

* NSI = No significant Interference (within ±4.0 mg/dL or 4%)

2. The following anticoagulants were found incompatible based on the same study.

Table 4. Incompatible Anticoagulants

<table>
<thead>
<tr>
<th>ANTICOAGULANT</th>
<th>LEVEL TESTED FOR IN VITRO INTERFERENCE</th>
<th>PLASMA-SERUM BIAS* (mg/dL) 37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDTA</td>
<td>3.0 mg/mL</td>
<td>≤±9.0</td>
</tr>
<tr>
<td>Sodium Citrate</td>
<td>1.7 mg/mL</td>
<td>≤27</td>
</tr>
</tbody>
</table>

* Bias is based on worst case instead of average.  
Plus (+) or minus (−) signs signify negative or positive interference.

INTERFENCES

1. The following substances were tested for interference with this methodology:

Table 5. Interferences

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>SOURCE</th>
<th>MAXIMUM LEVEL TESTED</th>
<th>OBSERVED EFFECT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>RBC Hemolysate</td>
<td>400 mg/dL (4+)</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Bovine</td>
<td>24 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Intralipid†</td>
<td>400 mg/dL (4+)</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Ascorbic Acid</td>
<td>NA</td>
<td>3.0 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Urea</td>
<td>NA</td>
<td>500 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Uric acid</td>
<td>NA</td>
<td>20 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>EDTA</td>
<td>NA</td>
<td>8 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>NA</td>
<td>30 mg/dL</td>
<td>≤±3.2 mg/dL or ±3.2%</td>
</tr>
</tbody>
</table>

* Plus (+) or minus (−) signs in this column signify positive or negative interference.

2. Refer to References (9, 10, 11) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTICAL RANGE

The SYNCHRON CX Systems method for the determination of glucose provides the following analytical range:

Table 6. Analytical Range

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S.I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum, Plasma, Urine or CSF</td>
<td>5 to 700 mg/dL</td>
<td>0.3 to 38.8 mmol/L</td>
</tr>
<tr>
<td>UCSF Validated Linearity</td>
<td>5 to 600 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>
Samples with concentrations exceeding the high end of the analytical range should be diluted with saline and reanalyzed.

† Intralipid is a registered trademark of KabiVitrum, Inc.

REPORTABLE RANGE (as determined on site):

Table 7. Reportable Range

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S.I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/dL</td>
<td>mmol/L</td>
</tr>
</tbody>
</table>

Refer to “LX20 Linearity and Reportable Range” chart appended to “LX20 Technical Information and Procedures” in “LX20 Procedure Manual”

EQUIVALENCY

Equivalency was assessed by correlation analysis of patient samples to accepted clinical methods.

Serum or plasma:

\[
Y (\text{SYNCHRON CX Systems}^*) = 1.050X - 3.38 \\
N = 84 \\
\text{MEAN (SYNCHRON CX Systems}^*) = 181.8 \\
\text{MEAN (SYNCHRON AS}^\text{®}) = 176.4 \\
\text{CORRELATION COEFFICIENT (r)} = 0.9997
\]

Urine:

\[
Y (\text{SYNCHRON CX Systems}^*) = 1.017X + 3.19 \\
N = 54 \\
\text{MEAN (SYNCHRON CX Systems}^*) = 205.2 \\
\text{MEAN (SYNCHRON CX}^\text{® 3}) = 198.7 \\
\text{CORRELATION COEFFICIENT (r)} = 0.998
\]

* Data shown was collected using the SYNCHRON CX4/CX5 Systems. Equivalency between SYNCHRON CX Systems has been established by correlation analysis to SYNCHRON CX4/CX5 Systems.

Refer to References (12) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON CX System should exhibit precision values less than or equal to the following:

Table 8. Precision Values

<table>
<thead>
<tr>
<th>TYPE OF PRECISION</th>
<th>SAMPLE TYPE</th>
<th>1 SD</th>
<th>CHANGEOVER VALUE *</th>
<th>%CV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/dL</td>
<td>mmol/L</td>
<td>mg/dL</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Within-Run</td>
<td>Serum/Plasma, Urine or CSF</td>
<td>2.0</td>
<td>0.11</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>Serum/Plasma, Urine or CSF</td>
<td>3.0</td>
<td>0.17</td>
<td>100.0</td>
</tr>
</tbody>
</table>
When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test %CV to the %CV guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

Refer to References (13) for guidelines on performing on-site precision testing.

NOTE

These degrees of precision and equivalency were obtained in typical testing procedures on the SYNCHRON CX Systems and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on the operation of SYNCHRON CX Systems, refer to the appropriate Beckman SYNCHRON CX Clinical Systems Operating Instructions manual. Copies of this manual are available from Beckman Instruments, Inc., Brea, CA 92622-8000.

REFERENCES


