SYNCHRON® System(s)          LIP
Chemistry Information Sheet   Lipase

REF (30 tests/cartridge) 465126
REF (60 tests/cartridge) 476851

For In Vitro Diagnostic Use

ANNUAL REVIEW

Reviewed by:          Reviewed by:          Date

Refer to coversheet in front of method

PRINCIPLE

INTENDED USE

LIP reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 600/800 System(s) and SYNCHRON® Systems Enzyme Validator Set, is intended for the quantitative determination of Lipase activity in human serum or plasma in random access mode.

CLINICAL SIGNIFICANCE

Lipase measurements are used primarily in the diagnosis and treatment of pancreatic disorders.

METHODOLOGY

The Random Access Lipase reagent utilizes the methodology of Panteghini to determine pancreatic lipase activity in serum and plasma. The SYNCHRON® System(s) monitors the rate of formation of methylresorufin which forms spontaneously from two coupled reactions which utilize a 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6'-methylresorufin)-ester as a substrate. The measured rate of color formation at 560 nm is directly proportional to the pancreatic lipase activity.

The SYNCHRON® System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 54 parts reagent. The system monitors the change in absorbance at 560 nanometers. The rate of formation of the methylresorufin is directly proportional to the activity of LIP in the sample and is used by the System to calculate and express the LIP activity.

One unit (U) is defined as the amount of enzyme activity which liberates 1 µmol of methylresorufin from 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6'-methylresorufin)-ester per minute at +37°C.

\[
\begin{align*}
1,2-O\text{-DILAURYL-RAC-GLYCERO-3-GLUTARIC ACID-(6'-METHYLRESORUFIN)-ESTER} & \xrightarrow{\text{PANCREATIC LIPASE + OH}^-} \\
1,2-O\text{-DILAURYL-RAC-GLYCEROL + GLUTARIC ACID-6'-METHYLRESORUFIN-ESTER} & \xrightarrow{\text{OH}^-} \\
\text{GLUTARIC ACID + METHYLRESORUFIN}
\end{align*}
\]
SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test. Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood, urine, ascitic, and pleural fluids are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells as soon as possible. A maximum limit of eight hours from the time of collection is recommended.

2. Separated serum or plasma should not remain at room temperature longer than 4 hours. If assays are not completed within 4 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.

ADDITIONAL SPECIMEN STORAGE AND STABILITY CONDITIONS AS DESIGNATED BY THIS LABORATORY:

Refer to "Sample Integrity in Chemistry" write up in "Policies and Procedures" manual

SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.
CRITERIA FOR SAMPLE REJECTION AS DESIGNATED BY THIS LABORATORY:

Refer to “Sample Integrity in Chemistry” write up in “Policies and Procedures” manual

PATIENT PREPARATION

SPECIAL INSTRUCTIONS FOR PATIENT PREPARATION AS DESIGNATED BY THIS LABORATORY:

Refer to “Sample Integrity in Chemistry” write up in “Policies and Procedures” manual

SPECIMEN HANDLING

SPECIAL INSTRUCTIONS FOR SPECIMEN HANDLING AS DESIGNATED BY THIS LABORATORY:

Refer to “Sample Integrity in Chemistry” write up in “Policies and Procedures” manual

REAGENTS

CONTENTS

Each kit contains the following items:
Two Lipase Reagent Cartridges (2 x 30 tests) or (2 x 60 tests)

VOLUMES PER TEST

<table>
<thead>
<tr>
<th>Component</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Volume</td>
<td>4 µL</td>
</tr>
<tr>
<td>ORDAC Sample Volume</td>
<td>2 µL</td>
</tr>
<tr>
<td>Total Reagent Volume</td>
<td>217 µL</td>
</tr>
<tr>
<td>Cartridge Volumes</td>
<td></td>
</tr>
<tr>
<td>A (for cuvette and probe washing)</td>
<td>660 µL</td>
</tr>
<tr>
<td>B (buffer)</td>
<td>167 µL</td>
</tr>
<tr>
<td>C (substrate)</td>
<td>50 µL</td>
</tr>
</tbody>
</table>

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

<table>
<thead>
<tr>
<th>Component</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tris buffer</td>
<td>31 mmol/L</td>
</tr>
<tr>
<td>Colipase (porcine pancreas)</td>
<td>1.2 mg/L</td>
</tr>
<tr>
<td>Taurodeoxycholic Acid, Sodium Salt</td>
<td>5.4 mmol/L</td>
</tr>
<tr>
<td>Deoxycholic acid, Sodium salt</td>
<td>1.4 mmol/L</td>
</tr>
<tr>
<td>1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6'- methy/ resinorfin)-ester</td>
<td>0.3 mmol/L</td>
</tr>
<tr>
<td>Sodium tartrate</td>
<td>3.4 mmol/L</td>
</tr>
</tbody>
</table>
REAGENT CONSTITUENTS
Calcium Chloride 0.2 mmol/L
Avoid skin contact with reagent. Use water to wash reagent from skin.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT
At least two levels of control material
SYNCHRON® Systems Enzyme Validator Set

REAGENT PREPARATION
No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE
The acceptability of a reagent is determined by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY
LIP 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 21 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

REAGENT STORAGE LOCATION:
Chemistry section, room L568. Refer to reagent "map" on Chemistry refrigerator #6.

CALIBRATION

CALIBRATOR REQUIRED
SYNCHRON® Systems Enzyme Validator Set

CALIBRATOR PREPARATION
No preparation is required.

CALIBRATOR STORAGE AND STABILITY
SYNCHRON® Systems Enzyme Validator Set when stored unopened at -15°C to -20°C will remain stable until the expiration date printed on the label. Once opened, resealed calibrators are stable for 60 days at -15°C to -20°C unless the expiration date is exceeded.
CAUTION

Because this product 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 to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.4

CALIBRATOR STORAGE LOCATION:

Refer to “DXC800 Calibration Quick Reference” chart in DXC800 procedure manual. Unopened Enzyme Validator kept frozen (-15°C to -20°C) in Chemistry freezer #8.

CALIBRATION INFORMATION

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

2. Under typical operating conditions the LIP reagent cartridge must be calibrated every 5 days and also with certain parts replacements or maintenance procedures, as defined in the SYNCHRON LX Maintenance Manual and Instrument Log, or the UniCel DxC 600/800 Systems Instructions For Use (IFU) manual. This assay has within-lot calibration available. Refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 Systems Instructions For Use (IFU) manual for information on this feature.

3. For detailed calibration instructions, refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) 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 be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the SYNCHRON LX Diagnostics and Troubleshooting Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

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 appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.
The SYNCHRON® System(s) Random Access lipase (LIP) reagent is designed for human pancreatic lipase. Control materials consisting of porcine lipase do not perfectly mimic the performance of the reagent with patient samples.

Due to human pancreatic lipase specificity, excessive lot-to-lot shifts with animal based control materials may occur. To aid you in ensuring consistent reagent quality for human samples, you may run several known patient samples on both the new and old lots. Alternatively, you may contact the Clinical Support Center at 1-800-854-3633 from the United States and Canada, or your local Beckman Coulter Representative for the results of human patient samples performed during manufacture.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

The lipase reagent is intended for use with human pancreatic lipase. Animal-based control materials may not accurately demonstrate reagent performance.

### TABLE 1 QUALITY CONTROL MATERIAL

<table>
<thead>
<tr>
<th>CONTROL NAME</th>
<th>SAMPLE TYPE</th>
<th>STORAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitrol levels 1 and 2 vials in use kept refrigerated after thawing. Unopened Monitrol kept frozen until just before use. Refer to “DXC 800 Control Analysis” in DXC 800 procedure manual for other control material used and storage. Control preparations and acceptance of QC results are in “Policies and Procedures” manual.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual.

### CALCULATIONS

The SYNCHRON® System(s) performs all calculations internally to produce the final reported result. The system 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

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

### REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference interval listed below was taken from a study performed on SYNCHRON Systems.
TABLE 2 REFERENCE INTERVALS

<table>
<thead>
<tr>
<th>INTERVALS</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S. I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNCHRON</td>
<td>Serum or Plasma</td>
<td>22 – 51 U/L</td>
<td>0.36 – 0.85 µkat/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERVALS</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory</td>
<td>Serum or Plasma</td>
<td>19-56 U/L</td>
</tr>
</tbody>
</table>

1. Normal range was determined by testing 271 male and female healthy adult blood donors at UCSF. Separate pediatric ranges not defined.

Refer to References (5,6,7) for guidelines on establishing laboratory-specific reference intervals.

ADDITIONAL REPORTING INFORMATION AS DESIGNATED BY THIS LABORATORY:

Refer to “DXC800 Linearity and Reportable Range” chart in Technical notes section of DXC800 Procedure manual

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

The following anticoagulants were assessed by Deming regression analysis with a minimum of 50 paired serum and plasma samples. Values of serum (X) ranging from 24 U/L to 219 U/L were compared with the values for plasma (Y) yielding the following results.

TABLE 3 ANTICOAGULANT TEST RESULTS

<table>
<thead>
<tr>
<th>ANTICOAGULANT</th>
<th>LEVEL OF ANTICOAGULANT TESTED</th>
<th>DEMING REGRESSION ANALYSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium Heparin</td>
<td>14 Units/mL</td>
<td>[Y = 0.999X + 0.9; r = 0.999]</td>
</tr>
<tr>
<td>Sodium Heparin</td>
<td>14 Units/mL</td>
<td>[Y = 1.006X + 0.0; r = 0.999]</td>
</tr>
</tbody>
</table>

LIMITATIONS

EDTA was found to report results 15% lower than serum.

INTERFERENCES

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

TABLE 4 INTERFERENCES

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>SOURCE</th>
<th>LEVEL TESTED</th>
<th>OBSERVED EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>Porcine</td>
<td>30 mg/dL</td>
<td>NSI</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>RBC hemolysate</td>
<td>200 mg/dL</td>
<td>NSI</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Human</td>
<td>3 +</td>
<td>NSI</td>
</tr>
</tbody>
</table>

2. Lipemic samples greater than 3+ (visual turbidity) should be ultracentrifuged and the analysis performed on the infranate.

3. Refer to References (8,9,10) for other interferences caused by drugs, disease and preanalytical variables.
PERFORMANCE CHARACTERISTICS

Analytic Range

The SYNCHRON® System(s) method for the determination of this analyte provides the following analytical ranges:

**TABLE 5 ANALYTICAL RANGE**

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S.I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum or Plasma</td>
<td>10 – 200 U/L</td>
<td>0.17 – 3.40 µkat/L</td>
</tr>
<tr>
<td>Serum or Plasma (ORDAC)</td>
<td>180 – 400 U/L</td>
<td>3.06 – 6.80 µkat/L</td>
</tr>
</tbody>
</table>

Samples with activities exceeding the high end of the analytical range should be rerun with ORDAC enabled or diluted with a patient sample of low Lipase value, and reanalyzed.

**REPORTABLE RANGE (as determined on site):**

**TABLE 6 REPORTABLE RANGE**

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S.I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum or Plasma (ORDAC)</td>
<td>10 – 400 U/L</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**SENSITIVITY**

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for LIP determination is 10 U/L (0.17 µkat/L).

**EQUIVALENCY**

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

**Serum or Plasma (in the range of 2 to 375 U/L):**

\[
Y (\text{SYNCHRON LX Systems}) = 0.447X + 19.77
\]

\[
N = 52
\]

\[
\text{MEAN (SYNCHRON LX Systems LIP Reagent)} = 48
\]

\[
\text{MEAN (SYNCHRON LX Systems LIPA Reagent)} = 62
\]

\[
\text{CORRELATION COEFFICIENT (r)} = 0.9625
\]

**Serum or Plasma (in the range of 18 to 151 U/L):**

\[
Y (\text{SYNCHRON LX Systems}) = 1.33X - 7.8
\]

\[
N = 51
\]

\[
\text{MEAN (SYNCHRON LX Systems)} = 73
\]

\[
\text{MEAN (SENTINEL Lipase Liquid on spectrophotometric analyzer) }^a = 60
\]

\[
\text{CORRELATION COEFFICIENT (r)} = 0.9891
\]

Refer to References (11) for guidelines on performing equivalency testing.


**PRECISION**

A properly operating SYNCHRON® System(s) should exhibit precision values less than or equal to the following:

**TABLE 7 PRECISION VALUES**

<table>
<thead>
<tr>
<th>TYPE OF PRECISION</th>
<th>SAMPLE TYPE</th>
<th>1 SD</th>
<th>CHANGEOVER VALUE&lt;sup&gt;c&lt;/sup&gt;</th>
<th>% CV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>U/L</td>
<td>µkat/L</td>
<td>U/L</td>
</tr>
<tr>
<td>Within-run</td>
<td>Serum or Plasma</td>
<td>7.0</td>
<td>0.12</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Serum or Plasma</td>
<td>NA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>(ORDAC)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Serum or Plasma</td>
<td>10.5</td>
<td>0.18</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Serum or Plasma</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>(ORDAC)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Comparative performance data for a SYNCHRON LX® System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below. Each laboratory should characterize their own instrument performance for comparison purposes.

**TABLE 8 NCCLS EP5-T2 PRECISION ESTIMATE METHOD**

<table>
<thead>
<tr>
<th>TYPE OF IMPRECISION</th>
<th>SAMPLE TYPE</th>
<th>No. Systems</th>
<th>No. Data Points&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Test Mean Value (U/L)</th>
<th>EP5-T2 Calculated Point Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>30.8</td>
<td>SD 1.54</td>
</tr>
<tr>
<td>Within-run</td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>64.4</td>
<td>SD 1.27</td>
</tr>
<tr>
<td></td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>106.1</td>
<td>SD 3.09</td>
</tr>
<tr>
<td>Total</td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>30.8</td>
<td>SD 4.50</td>
</tr>
<tr>
<td></td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>64.4</td>
<td>SD 4.84</td>
</tr>
<tr>
<td></td>
<td>Serum</td>
<td>1</td>
<td>80</td>
<td>106.1</td>
<td>SD 6.68</td>
</tr>
</tbody>
</table>

**NOTICE**

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

**ADDITIONAL INFORMATION**

For more detailed information on SYNCHRON LX Systems or UniCel DxC Systems, refer to the appropriate system manual.

**SHIPPING DAMAGE**

If damaged product is received, notify your Beckman Coulter Clinical Support Center.
REFERENCES


ENDNOTES

a  NSI = No Significant Interference (within ±14 U/L or 14%).

b  SENTINEL Lipase Liquid is manufactured by SENTINEL DIAGNOSTICS.

c  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 guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

d  NA = Not applicable.

e  The point estimate is based on the data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer’s instructions.