TRAINING UPDATE

Lab Location:	SGMC & WAH	**Date Distributed:**	3/16/2018
Department:	Core Lab	**Due Date:**	4/9/2018
		Implementation:	**3/26/2018**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

Acetaminophen by Dimension Vista® System SGAH.C91 v2

Gamma Glutamyl Transferase by Dimension Vista® System SGAH.C103 v3

These have been converted to system SOPs

Description of change(s):

Note change to QC info and freezer range to both SOPs, other changes are mostly format updates

Section	Reason
Header	Add WAH
3.2	Remove specimen onboard stability
4,5,6	Remove individual section labeling instructions and add general one
6.1, 6.2	Update QC material and storage
7.2	Change freezer range to -50C
10.5	Move patient review from section 6
10.6	Remove repeat value below AMR/CRR
15	Update to new standard wording, move hazard statement from 4.2
17	Update QC product and PI dates

These revised SOPs will be implemented on March 26, 2018

Document your compliance with this training update by taking the quiz in the MTS system.

Technical SOP

Title	**Acetaminophen by Dimension Vista® System**
Prepared by	Ashkan Chini Date: 6/25/2012
Owner	Robert SanLuis Date: 6/25/2012

Laboratory Approval	**Local Effective Date:**	
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		

Review		
Print Name	**Signature**	**Date**

Form revised 2/02/2007

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Acetaminophen	Dimension Vista® System	ACTMP

Synonyms/Abbreviations
Tylenol

Department
Chemistry

Form revised 2/02/2007

2. ANALYTICAL PRINCIPLE

The methodology for ACTM is based on the enzymatic hydrolysis of acetaminophen producing acetate and *p*-aminophenol. The *p*-aminophenol is determined colorimetrically by reaction with *o*-cresol and ammoniacal copper sulfate. The amount of aminophenol produced is proportional to the acetaminophen concentration and is measured using a bichromatic endpoint technique.

Amidase
Acetaminophen + H2O ----------> *p*-aminophenol + CH3COOH

p-aminophenol + *o*-cresol/ammoniacal copper sulfate ----------> indophenol (absorbs at 600 nm

3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Normal procedures for collecting and storing serum and plasma may be used for samples to be analyzed by this method.
Special Collection Procedures	N/A
Other	N/A

3.2 Specimen Type & Handling

Criteria		
Type -Preferred **-Other Acceptable**	Plasma (Lithium Heparin) Serum	
Collection Container	Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)	
Volume - Optimum **- Minimum**	1.0 mL 0.5 mL	
Transport Container and Temperature	Collection container or Plastic vial at room temperature	
Stability & Storage Requirements	Room Temperature:	8 hours
	Refrigerated:	2 weeks
	Frozen:	45 days
Timing Considerations	Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection.	
Unacceptable Specimens & Actions to Take	Specimens that are unlabeled, improperly labeled, or those that do not meet the stated criteria are unacceptable.	

Criteria	
	Request a recollection and credit the test with the appropriate LIS English text code for "test not performed" message. Examples: Quantity not sufficient-QNS; Wrong collection-UNAC. Document the request for recollection in the LIS.
Compromising Physical Characteristics	Gross hemolysis. Reject sample and request a recollection. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed)
Other Considerations	Allow Red Top or SST to clot completely prior to centrifugation.

NOTE: Labeling requirements for all reagents, calibrators and controls include: (1) Open date, (2) Substance name, (3) Lot number, (4) Date of preparation, (5) Expiration date, (6) Initials of tech, and (7) Any special storage instructions. Check all for visible signs of degradation. When placed onboard the analyzer, the instrument captures the date / time loaded and calculates and tracks the opened expiration.

4. REAGENTS

The package insert for a new lot of kits must be reviewed for any changes before the kit is used. A current Package Insert is included as a Related Document.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
Acetaminophen	Siemens, Flex® reagent cartridge, Cat. No. K5088

4.2 Reagent Preparation and Storage

Reagent	**Acetaminophen**
Container	Reagent cartridge
Storage	Store at 2-8°C
Stability	• Stable until expiration date stamped on reagent cartridges. • Sealed wells on the instrument are stable for 30 days. • Open wells: 3 days for wells 1 - 12
Preparation	Hydration, mixing and diluting are automatically performed by the instrument.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
DRUG 2 CAL	Siemens Dimension Vista®, Cat. No. KC420

5.2 Calibrator Preparation and Storage

Calibrator	DRUG 2 CAL
Preparation	Calibrator is ready for use. No preparation is required.
Storage/Stability	• Store at 2-8°C • **Unopened Calibrator:** until expiration date on the box. • **Opened Calibrator:** once the stopper is punctured, stable for 15 days when stored on board the Dimension Vista System. • **Opened Calibrator:** once cap is removed, stable for 31 days when recapped immediately after use and stored at 2-8° C. **Do not use this vial on board the instrument.**

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	DRUG 2 CAL
Assay Range	2.0 – 300.0 µg/mL
Suggested Calibration Level	See Reagent Package Insert for lot specific assigned values in µg/mL
Frequency	• Every new reagent cartridge lot. • Every 90 days for any one lot • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	2 levels, n = 5

5.4 Calibration Procedure

Auto Calibration:

1. Place the required calibrator vials in a carrier. Make sure the barcode labels are entirely visible through the slots.
2. Place the carrier in the loading area.
3. Position the carrier with the labels facing away from the user.
4. Press the **Load** button.
5. Automatic calibration requires that calibrators be on the instrument. As the time for processing approaches, the instrument reviews onboard inventory for the appropriate calibrators.

Manual Calibration:

1. Verify that calibrators and reagents are in inventory on the instrument.
2. Press **System > Method Summary > Calibration**.
3. Select a method from the sidebar menu. Press the **Order Calibration** button on the screen.

4. Verify that the information on the screen is correct. Verify that the calibrator lot is correct using the drop-down menu.
   a. When calibrating using Vials press **OK**.
   b. When calibrating using Cups, check the Use Cups box. This displays the rack and cup position fields. For additional cups use the positions in ascending order. Be sure to use the number of calibration levels and cups as specified in the method IFU. Scan the rack barcode and place calibrator cups in an adapter in position 1 on a rack. Press **OK** and load the rack on the instrument.
5. The status field in the calibration screen changes sequentially to Awaiting Scheduling, Preparing Calibrators and Processing.

5.5 Tolerance Limits

IF……	THEN……
If result fall within assay-specific specification, and QC values are within acceptable limits,	proceed with analysis
If result falls outside assay-specific specification, or QC values are out of Acceptable limits,	troubleshoot the assay and/or instrument and repeat calibration

6. QUALITY CONTROL

6.1 Controls Used

Controls	Supplier and Catalog Number
Liquichek™ Immunoassay Plus Control Levels 1, 2 and 3	Bio-Rad Laboratories Cat. No. 267, 268 and 269

6.2 Control Preparation and Storage

Control	Liquichek Immunoassay Plus Controls, Level 1, 2 and 3
Preparation	Allow the vials to stand at room temperature (18-25°C) until it is completely thawed. Before sampling, gently swirl the vials several times to ensure homogeneity. After each use, promptly replace the stopper and return to 2-8° C storage.
Storage/Stability	**Thawed:** all analytes will be stable for 4 days at 2-8°C. **Frozen:** stable until the expiration date at -20 to -50°C.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing (notated on the QC frequency sheets posted on the instruments).

Refer to the Dimension Vista® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension Vista® Quick Reference Guide.

6.4 Tolerance Limits and Criteria for Acceptable QC

Step	Action
1	Acceptable ranges for QC are programmed into the instrument's Quality Control software system and Unity Real Time, and may be posted near the instrument for use during computer downtime.
2	**Run Rejection Criteria** • Anytime the established parameters are exceeded (if one QC result exceeds 2 SD), the run is considered out of control (failed) and patient results must not be reported. • The technologist must follow the procedure in the Laboratory QC Program to resolve the problem.
3	**Corrective Action**: • All rejected runs must be effectively addressed through corrective action. Steps taken in response to QC failures must be documented. Patient samples in failed analytical runs must be reanalyzed according to the Laboratory QC Program. Supervisors may override rejection of partial or complete runs only with detailed documentation and criteria for overrides that are approved by the Medical Director. Consult corrective action guidelines in Laboratory QC Program. Follow corrective action guidelines in the Laboratory QC Program. • Corrective action documentation must follow the Laboratory Quality Control Program.
4	**Review of QC** • QC must be reviewed weekly by the Group Lead or designee and monthly by the Supervisor/Manager or designee. • If the SD and/or CV are greater than established ranges, investigate the cause for the imprecision and document implementation of corrective actions.

6.5 Documentation

- QC tolerance limits are programmed into the instrument and Unity Real Time; it calculates cumulative mean, SD and CV and stores all information for easy retrieval.
- Quality control records are reviewed daily at the bench, weekly by the Group Lead or designee, and monthly by the Supervisor/Manager or designee.
- Refer to complete policies and procedures for QC documentation and for record retention requirements in the Laboratory QC Program.

6.6 Quality Assurance Program

- Each new lot number of reagent or new shipment of the same lot of reagent must be tested with external control materials and previously analyzed samples. Performance of the new lot must be equivalent to the previous lot; utilize published TEA for acceptability criteria.
- Training must be successfully completed and documented prior to performing this test. This procedure must be incorporated into the departmental competency assessment program.
- The laboratory participates in CAP proficiency testing. All proficiency testing materials must be treated in the same manner as patient samples.
- Monthly QC must be presented to the Medical Director or designee for review and signature.
- Monthly QC mean and SD are sent to Bio-Rad Laboratories for peer group comparison.
- Consult the Laboratory QC Program for complete details.

7. EQUIPMENT and SUPPLIES

7.1 Assay Platform

Dimension Vista® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -20 to -50°C.
- Centrifuge

7.3 Supplies

- Aliquot Plates
- System Fluids
- Assorted calibrated pipettes (MLA or equivalent) and disposable tips

8. PROCEDURE

ACTM Flex® reagent cartridge Cat. No. K5088 is required to perform this test.

Acetaminophen is performed on the Dimension Vista® System after the method is calibrated (see Reference Material in Calibration section) and Quality Controls are acceptable.

NOTE: For all procedures involving specimens, buttoned lab coats, gloves, and face protection are required minimum personal protective equipment. Report all accidents to your supervisor.

8.1	Sample Processing
1.	A sample rack holding tubes or cups is placed on the rack input lane.
2.	The sample shuttle moves the rack to the barcode reader which identifies the rack and samples to the system.
3.	The rack moves into the sample server and to the rack positioner.
4.	At the same time, aliquot plates move from the aliquot loader into position.
5.	The aliquot probe aspirates the sample from the tubes or cups and dispenses it into the wells of the aliquot plates.
6.	After each aspirate-dispense action, the probe is thoroughly rinsed inside and out to prevent sample carryover.
7.	When sample aspiration is completed, the sample server moves the rack back to the sample shuttle, where it is placed on the output lane and can be removed by the operator.

8.2	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension Vista® QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension Vista® Operator's Manual
3.	The instrument reporting system contains error messages to warn the user of specific malfunctions. Results followed by such error messages should be held for follow-up. Refer to the Dimension Vista® system manual "Error messages" section for troubleshooting.
4.	Follow protocol in Section 10.5 "Repeat criteria and resulting" for samples with results above or below the Analytical Measurement Range (AMR). Investigate any failed delta result and repeat, if necessary.
5.	Append the appropriate English text code qualifier messages to any samples requiring a comment regarding sample quality and/or any other pertinent factors.

Test Conditions		
	Blank	**Test**
Sample Volume:	1.875 µL	1.875 µL
Enzyme Volume:	0 µL	37.5 µL
Copper Sulfate Volume	30 µL	37.5 µL
O-cresol Volume:	30 µL	37.5 µL
Reaction Time:	6.4 minutes	
Test Temperature:	37°C	
Wavelength:	600 & 700 nm	
Type of measurement:	Bichromatic endpoint	

NOTE: In the event that the test system becomes inoperable, notify supervision or designee for further direction. Patient specimens must be stored in a manner that maintains the integrity of the specimen.

9. CALCULATIONS

The instrument automatically calculates the concentration of Acetaminophen in µg/mL.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

No rounding is necessary. Instrument reports results up to one decimal point.

10.3 Units of Measure

µg/mL

10.4 Clinically Reportable Range (CRR)

2.0 – 900.0 µg/mL

10.5 Review Patient Data

Each result is reviewed for error messages. Refer to the Dimension Vista system manual "Error messages" section for troubleshooting. Resolve any problems noted before issuing patient reports.

10.6 Repeat Criteria and Resulting

All repeats must replicate the original result within the total allowable error (TEa) of the assay. Refer to TEa listing for specific information.

Values that fall below or within the AMR or CRR may be reported without repeat. Values that exceed the upper ranges must be repeated.

IF the result is …	THEN…
< 2.0 µg/mL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 2.0 µg/mL
≥ 300.0 µg/mL	**On Board Automated Dilution:** Results ≥ 300.0 µg/mL will automatically have repeat testing performed into the instrument using dilution factor of 2. No multiplication is necessary.

Form revised 2/02/2007

IF the result is …	THEN…
> 600.0 µg/mL	**Manual Dilution:** Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 3 **Diluent:** Drug free serum or level 1 drug 2 cal. Enter dilution factor as a whole number. Re-assay. Readout is corrected for dilution.
> 900.0 µg/mL	If the recommended dilution does not give results within the clinically reportable range, report as: "> 900.0 µg/mL -REP" Bring to the attention of your supervisor prior to releasing result.

Message	Code
Verified by repeat analysis	Append –REP to the result.

11. EXPECTED VALUES

11.1 Reference Ranges

10.0 – 30.0 µg/mL

11.2 Critical Values

> 49.9 µg/mL

11.3 Standard Required Messages

None established

12. CLINICAL SIGNIFICANCE

Acetaminophen is an analgesic found in many "over-the-counter" pain remedies. It is rapidly and completely absorbed from the gastrointestinal tract. After oral administration, peak plasma concentrations are reached in less than an hour. Approximately 90% of a therapeutic dose is eliminated by conjugation with glucoronic acid (and to a slight extent, sulfuric acid) in the liver. Another 3-5% is catabolized by the P-450 mixed function oxidase enzyme system to the acid and cysteine conjugates. All of these metabolites are excreted in the urine. Only a slight amount of the drug is excreted unchanged. Intermediate metabolites of uncertain structure formed during the biotransformation in the liver are believed to be responsible for the hepatotoxicity. After a therapeutic dose of acetaminophen, the biologic half-life in normal adults is 2–3 hours. Metabolism is more rapid in children (except newborns). Because the hepatic conjugation is the rate-limiting step in the catabolic pathway, the half-life is prolonged in patients with liver disease, alcoholics, or in the presence of other drugs which compete for the hepatic conjugation mechanism. Acetaminophen does not have

anti-inflammatory activity and it does not affect blood clotting (hemostasis). It is preferred over aspirin when the hemostatic side effects of aspirin must be avoided. Severe liver damage in adults is generally associated with ingestion of 15 grams or more. Since the drug is catabolized in the liver, hepatoxicity will result in elevated plasma drug levels and prolonged half-life. The availability of a rapid accurate plasma acetaminophen assay is of extreme importance in cases of suspected intoxication because effective antidotes are available. Therapy with N-acetylcysteine (NAC) must be started within eight hours after ingestion to prevent hepatic injury as signified by elevations in AST and ALT.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/cleared
- **Validated Test Modifications:** None

The instrument reporting system contains error messages to warn the operator of specific malfunctions. Any report slip containing such error messages should be held for follow-up. Refer to your Dimension Vista Operator's Guide.

The expected maximum observed standard deviations for repeatability using n = 5 replicates at the following Acetaminophen concentrations are:

ACTM Concentration	Acceptable S.D. Maximum
15.3 µg/mL	3.0 µg/mL
152.5 µg/mL	9.0 µg/mL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

2.0 – 300.0 µg/mL

14.2 Precision

Material	Mean µg/mL	Standard Deviation (%CV)	
		Repeatability	Within-Lab
DRUG 2 CAL	18.2	0.7 (4)	1.1 (6)
QC Levels 2 and 3 blend	148.5	2.3 (2)	2.7 (2)

14.3 Interfering Substances

Substance	Test Concentration	Bias %
Immunoglobulin G (IgG)	5 g/dL	-18.9
Bilirubin (unconjugated)	5 mg/dL	-59.1
Bilirubin (conjugated)	10 mg/dL	-11.2
Total Protein	12 g/dL	-24.8

HIL Interference:
The ACTM method was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias, defined as the difference between the control sample (does not contain interferent) and the test sample (contains interferent), is shown in the table below. Bias exceeding 10% is considered "interference".

Substance tested	Substance Concentration	ACTM µg/mL	Bias %
Hemoglobin (hemolysate)	1000 mg/dL	32	<10
Bilirubin (unconjugated)	2 mg/dL 5 mg/dL	32	<10 -59.1
Bilirubin (conjugated)	5 mg/dL 10 mg/dL	32	<10 -11.2
Lipemia (Intralipid®)	3000 mg/dL	32	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available

15. SAFETY

Refer to your local and corporate safety manuals and Safety Data Sheet (SDS) for detailed information on safety practices and procedures and a complete description of hazards.

ACTM Flex® Reagent Cartridge causes serious eye irritation, causes skin irritation.
Contains: Ammonium chloride; Copper sulphate; o-Cresol; Sodium carbonate.
Wear protective gloves/protective clothing/eye protection/face protection.
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.

16. RELATED DOCUMENTS

1. Dimension Vista® Clinical Chemistry System Operator's Manual
2. Dimension Vista® Calibration/Verification Procedure
3. Dimension Vista® Cal Accept Guidelines
4. Dimension Vista® Calibration summary
5. Dimension Vista® Sample Processing, Startup and Maintenance procedure
6. Laboratory Quality Control Program
7. QC Schedule for Siemens Dimension Vista®
8. Laboratory Safety Manual
9. Safety Data Sheets (SDS)
10. Dimension Vista® Limits Chart (AG.F200)
11. Quest Diagnostics Records Management Procedure
12. Dimension Vista® System Error Messages Chart
13. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
14. Hemolysis, Icteria and Lipemia Interference (Lab policy)

15. Repeat Testing Requirement (Lab policy)
16. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
17. Current package insert ACTM Flex® Reagent Cartridge K5088

17. REFERENCES

1. Package Insert, ACTM Flex® Reagent Cartridge K5088, Siemens Healthcare Diagnostics Inc., 12/27/2017.
2. Package Insert, DRUG 2 CAL, Siemens Healthcare Diagnostics Inc., 05/2017.
3. Package Insert, Liquichek Immunoassay Plus Control, Bio-Rad Laboratories, 12/2015.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
000	8/21/15	3.2	Change preferred specimen to plasma	L. Barrett	R. SanLuis
000	8/21/15	4.2	Add hazard statement	L. Barrett	R. SanLuis
000	8/21/15	6.4,6.6	Replace LIS with Unity Real Time	L. Barrett	R. SanLuis
000	8/21/15	11.2	Reformat value to eliminate ≥ sign	L. Barrett	R. SanLuis
000	8/21/15	16	Update titles	L. Barrett	R. SanLuis
000	8/21/15	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13	L. Barrett	R. SanLuis
1	3/13/18	Header	Add WAH	L Barrett	R SanLuis
1	3/13/18	3.2	Remove specimen onboard stability	L Barrett	R SanLuis
1	3/13/18	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
1	3/13/18	6.1, 6.2	Update QC material and storage	L Barrett	R SanLuis
1	3/13/18	7.2	Change freezer upper limit to -50C	L Barrett	R SanLuis
1	3/13/18	10.5	Move patient review from section 6	L Barrett	R SanLuis
1	3/13/18	10.6	Remove repeat value below AMR/CRR	L Barrett	R SanLuis
1	3/13/18	15	Update to new standard wording, move hazard statement from 4.2	L Barrett	R SanLuis
1	3/13/18	17	Update QC product and PI dates	L Barrett	R SanLuis

19. ADDENDA

None

Technical SOP

Title	**Gamma Glutamyl Transferase by Dimension Vista® System**
Prepared by	Ashkan Chini Date: 6/25/2012
Owner	Robert SanLuis Date: 10/21/2013

Laboratory Approval	**Local Effective Date:**	
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		

Review		
Print Name	**Signature**	**Date**

Form revised 2/02/2007

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Gamma Glutamyl Transferase	Dimension Vista® System	GGT

Synonyms/Abbreviations
GGT

Department
Chemistry

Form revised 2/02/2007

2. ANALYTICAL PRINCIPLE

The γ-glutamyl transferase method is an adaptation of the methodology recommended by the International Federation of Clinical Chemistry (IFCC). The method uses the substrate L-gamma-glutamyl-3-carboxy-4-nitranilide with glycylglycine.
γ-glutamyl transferase catalyzes the transfer of the glutamyl moiety from γ-glutamyl-3-carboxy-4-nitranilide (GCNA) to glycylglycine thereby releasing 5-amino-2-nitrobenzoate which absorbs at 405 nm. This change is proportional to the γ-glutamyl transferase activity and is measured using a bichromatic (405, 600 nm) rate technique.

$$\text{GCNA} + \text{glycylglycine} \xrightarrow{\text{GGT}} \text{L-}\gamma\text{-glutamyl-glycylglycine} + \text{5-amino-2-nitrobenzoate}$$

3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Normal procedures for collecting and storing serum and plasma may be used for samples to be analyzed by this method.
Special Collection Procedures	N/A
Other	N/A

3.2 Specimen Type & Handling

Criteria		
Type	**-Preferred**	Plasma (Lithium Heparin)
	-Other Acceptable	Serum
Collection Container		Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)
Volume	**- Optimum**	1.0 mL
	- Minimum	0.5 mL
Transport Container and Temperature		Collection container or Plastic vial at room temperature
Stability & Storage Requirements	Room Temperature:	7 days
	Refrigerated:	7 days
	Frozen:	6 months
Timing Considerations		Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of two hours from the time of collection.

Criteria	
Unacceptable Specimens & Actions to Take	Specimens that are unlabeled, improperly labeled, or those that do not meet the stated criteria are unacceptable. Request a recollection and credit the test with the appropriate LIS English text code for "test not performed" message. Examples: Quantity not sufficient-QNS; Wrong collection-UNAC. Document the request for recollection in the LIS.
Compromising Physical Characteristics	Gross hemolysis. Reject sample and request a recollection. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed)
Other Considerations	Allow Red Top or SST to clot completely prior to centrifugation.

NOTE: Labeling requirements for all reagents, calibrators and controls include: (1) Open date, (2) Substance name, (3) Lot number, (4) Date of preparation, (5) Expiration date, (6) Initials of tech, and (7) Any special storage instructions. Check all for visible signs of degradation. When placed onboard the analyzer, the instrument captures the date / time loaded and calculates and tracks the opened expiration.

4. REAGENTS

The package insert for a new lot of kits must be reviewed for any changes before the kit is used. A current Package Insert is included as a Related Document.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
GGT	Siemens, Flex® reagent cartridge, Cat. No. K2045
Enzyme Diluent	Dimension® Clinical Chemistry System, REF 790035901

4.2 Reagent Preparation and Storage

Reagent	**Gamma Glutamyl Transferase**
Container	Reagent cartridge
Storage	Store at 2-8°C
Stability	• Stable until expiration date stamped on reagent cartridges. • Sealed wells on the instrument are stable for 30 days. • Open wells: 7 days for wells 1 - 12
Preparation	Hydration, mixing and diluting are automatically performed by the instrument.

Reagent	**Enzyme Diluent**
Container	Manufacturer supplied vial
Storage	Store at 2-8°C before and after reconstitution

Stability	• Un-reconstituted product is stable until expiration date on vial. • Reconstituted product is stable for 7 days following reconstitution or immediately if visible turbidity appears.
Preparation	• Remove vial from refrigerator, proceed directly to next step. • Remove stopper and volumetrically add 10.0 mL of reagent grade water. • Replace stopper and invert gently 10 times. • Let vials sit for 15 minutes, then invert gently 10 times. • Let vials sit for an additional 15 minutes, then invert 10 times and swirl gently. • Use immediately or store at 2-8°C. • Before use, allow to come to room temperature, then invert 10 times and swirl gently

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
ENZ 1 CAL	Siemens Dimension Vista®, Cat. No. KC310

5.2 Calibrator Preparation and Storage

Calibrator	ENZ 1 CAL
Preparation	Calibrator is ready for use. No preparation is required.
Storage/Stability	• Store at 2-8°C • **Unopened Calibrator:** until expiration date on the box. • **Opened Calibrator:** once the stopper is punctured, stable for 7 days when stored on board the Dimension Vista System.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	ENZ 1 CAL
Assay Range	3 – 800 U/L
Suggested Calibration Level	See Reagent Package Insert for lot specific assigned values in U/L
Frequency	• Every new reagent cartridge lot. • Every 90 days for any one lot • When major maintenance is performed on the analyzer.

	• When control data indicates a significant shift in assay.
Calibration Scheme	2 levels, n = 5

5.4 Calibration Procedure

Auto Calibration:

1. Place the required calibrator vials in a carrier. Make sure the barcode labels are entirely visible through the slots.
2. Place the carrier in the loading area.
3. Position the carrier with the labels facing away from the user.
4. Press the **Load** button.
5. Automatic calibration requires that calibrators be on the instrument. As the time for processing approaches, the instrument reviews onboard inventory for the appropriate calibrators.

Manual Calibration:

1. Verify that calibrators and reagents are in inventory on the instrument.
2. Press **System > Method Summary > Calibration**.
3. Select a method from the sidebar menu. Press the **Order Calibration** button on the screen.
4. Verify that the information on the screen is correct. Verify that the calibrator lot is correct using the drop-down menu.
   a. When calibrating using Vials press **OK**.
   b. When calibrating using Cups, check the Use Cups box. This displays the rack and cup position fields. For additional cups use the positions in ascending order. Be sure to use the number of calibration levels and cups as specified in the method IFU. Scan the rack barcode and place calibrator cups in an adapter in position 1 on a rack. Press **OK** and load the rack on the instrument.
5. The status field in the calibration screen changes sequentially to Awaiting Scheduling, Preparing Calibrators and Processing.

5.5 Tolerance Limits

IF……	THEN……
If result fall within assay-specific specification, and QC values are within acceptable limits,	proceed with analysis
If result falls outside assay-specific specification, or QC values are out of Acceptable limits,	troubleshoot the assay and/or instrument and repeat calibration

6. QUALITY CONTROL

6.1 Controls Used

Controls	Supplier and Catalog Number
Liquid Assayed Multiqual® Levels 1 and 3	Bio-Rad Laboratories Cat. No. 337 and 339

6.2 Control Preparation and Storage

Control	Liquid Assayed Multiqual® Levels 1 and 3
Preparation	Allow the frozen control to stand at room temperature (18-25°C) for 30 minutes or until completely thawed. Swirl the contents gently to ensure homogeneity. (Do not use a mechanical mixer) Use immediately. After each use, promptly replace the stopper and return to 2-8°C storage.
Storage/Stability	**Frozen**: stable until the expiration date at -20 to -50°C. **Thawed and Unopened**: When stored at 2-8°C and the stopper is not punctured, it will be stable for 30 days for GGT This product can be used for 7 days when stored on-board the Siemens Dimension Vista at 2-8°C. **Thawed and Opened**: Once the stopper is punctured, all analytes will be stable for 5 days when stored at 2-8°C. Store away from light.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing (notated on the QC frequency sheets posted on the instruments).

Refer to the Dimension Vista® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension Vista® Quick Reference Guide.

6.4 Tolerance Limits and Criteria for Acceptable QC

Step	Action
1	Acceptable ranges for QC are programmed into the instrument's Quality Control software system and Unity Real Time, and may be posted near the instrument for use during computer downtime.
2	**Run Rejection Criteria** • Anytime the established parameters are exceeded (if one QC result exceeds 2 SD), the run is considered out of control (failed) and patient results must not be reported. • The technologist must follow the procedure in the Laboratory QC Program to resolve the problem.
3	**Corrective Action**: • All rejected runs must be effectively addressed through corrective action. Steps taken in response to QC failures must be documented. Patient samples in failed analytical runs must be reanalyzed according to the Laboratory QC Program. Supervisors may override rejection of partial or complete runs only with detailed

Step	Action
	documentation and criteria for overrides that are approved by the Medical Director. Consult corrective action guidelines in Laboratory QC Program. Follow corrective action guidelines in the Laboratory QC Program. • Corrective action documentation must follow the Laboratory Quality Control Program.
4	**Review of QC** • QC must be reviewed weekly by the Group Lead or designee and monthly by the Supervisor/Manager or designee. • If the SD and/or CV are greater than established ranges, investigate the cause for the imprecision and document implementation of corrective actions.

6.5 Documentation

- QC tolerance limits are programmed into the instrument and Unity Real Time; it calculates cumulative mean, SD and CV and stores all information for easy retrieval.
- Quality control records are reviewed daily at the bench, weekly by the Group Lead or designee, and monthly by the Supervisor/Manager or designee.
- Refer to complete policies and procedures for QC documentation and for record retention requirements in the Laboratory QC Program.

6.6 Quality Assurance Program

- Each new lot number of reagent or new shipment of the same lot of reagent must be tested with external control materials and previously analyzed samples. Performance of the new lot must be equivalent to the previous lot; utilize published TEA for acceptability criteria.
- Training must be successfully completed and documented prior to performing this test. This procedure must be incorporated into the departmental competency assessment program.
- The laboratory participates in CAP proficiency testing. All proficiency testing materials must be treated in the same manner as patient samples.
- Monthly QC must be presented to the Medical Director or designee for review and signature.
- Monthly QC mean and SD are sent to Bio-Rad Laboratories for peer group comparison.
- Consult the Laboratory QC Program for complete details.

7. EQUIPMENT and SUPPLIES

7.1 Assay Platform

Dimension Vista® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -20 to -50°C.
- Centrifuge

7.3 Supplies

- Aliquot Plates
- System Fluids
- Assorted calibrated pipettes (MLA or equivalent) and disposable tips

8. PROCEDURE

GGT Flex® reagent cartridge Cat. No. K2045 is required to perform this test.

Gamma Glutamyl Transferase is performed on the Dimension Vista® System after the method is calibrated (see Reference Material in Calibration section) and Quality Controls are acceptable.

NOTE: For all procedures involving specimens, buttoned lab coats, gloves, and face protection are required minimum personal protective equipment. Report all accidents to your supervisor.

8.1	Sample Processing
1.	A sample rack holding tubes or cups is placed on the rack input lane.
2.	The sample shuttle moves the rack to the barcode reader which identifies the rack and samples to the system.
3.	The rack moves into the sample server and to the rack positioner.
4.	At the same time, aliquot plates move from the aliquot loader into position.
5.	The aliquot probe aspirates the sample from the tubes or cups and dispenses it into the wells of the aliquot plates.
6.	After each aspirate-dispense action, the probe is thoroughly rinsed inside and out to prevent sample carryover.
7.	When sample aspiration is completed, the sample server moves the rack back to the sample shuttle, where it is placed on the output lane and can be removed by the operator.

8.2	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension Vista® QC Schedule in the Laboratory QC Program.

8.2	Specimen Testing
2.	Follow the instructions, outlined in the Dimension Vista® Operator's Manual
3.	The instrument reporting system contains error messages to warn the user of specific malfunctions. Results followed by such error messages should be held for follow-up. Refer to the Dimension Vista® system manual "Error messages" section for troubleshooting.
4.	Follow protocol in Section 10.5 "Repeat criteria and resulting" for samples with results above or below the Analytical Measurement Range (AMR). Investigate any failed delta result and repeat, if necessary.
5.	Append the appropriate English text code qualifier messages to any samples requiring a comment regarding sample quality and/or any other pertinent factors.

Test Conditions	
Sample Volume:	11.43 µL
Reagent 1 Volume:	26.79 µL
Reaction Time:	1.9 minutes
Test Temperature:	37°C
Wavelength:	405 & 600 nm
Type of measurement:	Bichromatic rate

NOTE: In the event that the test system becomes inoperable, notify supervision or designee for further direction. Patient specimens must be stored in a manner that maintains the integrity of the specimen.

9. CALCULATIONS

The instrument automatically calculates the concentration of Gamma Glutamyl Transferase in U/L.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

No rounding is necessary. Instrument reports results as a whole number.

10.3 Units of Measure

U/L

10.4 Clinically Reportable Range (CRR)

3 – 16,000 U/L

10.5 Review Patient Data

Each result is reviewed for error messages. Refer to the Dimension Vista system manual "Error messages" section for troubleshooting. Resolve any problems noted before issuing patient reports.

10.6 Repeat Criteria and Resulting

All repeats must replicate the original result within the total allowable error (TEa) of the assay. Refer to TEa listing for specific information.

Values that fall below or within the AMR or CRR may be reported without repeat. Values that exceed the upper ranges must be repeated.

IF the result is …	THEN…
< 3 U/L	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 3 U/L
≥ 800 U/L	**On Board Automated Dilution:** Results ≥ 800 U/L will automatically have repeat testing performed into the instrument using dilution factor of 2. No multiplication is necessary.
> 1600 U/L	Manual Dilution: Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 20 **DILUENT**: Enzyme Diluent Enter dilution factor as a whole number. Re-assay. Readout is corrected for dilution.
> 16,000 U/L	If the recommended dilution does not give results within the clinically reportable range, report as: "> 16,000 U/L-REP" Bring to the attention of your supervisor prior to releasing result.

Message	Code
Verified by repeat analysis	Append –REP to the result.

11. EXPECTED VALUES

11.1 Reference Ranges

Age	Female	Male
Adult (>19 years):	5 - 55 U/L	5 - 85 U/L
Pediatric:		
16 – 19 years	6 - 23	6 - 30
14 – 15 years	10 - 22	8 - 29
12 – 13 years	10 - 20	12 - 39
10 – 11 years	12 - 23	12 - 25
7 – 9 years	9 - 20	9 - 20
4 – 6 years	5 - 17	5 - 17
1 – 3 years	2 - 15	2 - 15
7 – 11 months	8 - 59	8 - 38
4 – 6 months	13 - 123	5 - 93
1 – 3 months	16 - 140	16 - 147
8 days – 30 days	16 - 140	23 - 174
0 – 7 days	18 - 148	25 - 168

11.2 Critical Values

None established

11.3 Standard Required Messages

None established

12. CLINICAL SIGNIFICANCE

Gamma-glutamyl transferase is markedly **increased** in lesions that cause intrahepatic or extrahepatic obstruction of bile ducts, including parenchymatous liver diseases with a major cholestatic component (e.g., cholestatic hepatitis). Lesser elevations of gamma-GT are seen in other liver diseases, and in infectious mononucleosis, hyperthyroidism, myotonic dystrophy, and after renal allograft. Drugs causing hepatocellular damage and cholestasis may also cause gamma-GT elevation. Gamma-GT is a very sensitive test for liver damage, and unexpected, unexplained mild elevations are common. Alcohol consumption is a common culprit. Decreased gamma-GT is not clinically significant.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/cleared
- **Validated Test Modifications:** None

The instrument reporting system contains error messages to warn the operator of specific malfunctions. Any report slip containing such error messages should be held for follow-up. Refer to your Dimension Vista Operator's Guide.

The expected maximum observed standard deviations for repeatability using n = 5 replicates at the following Gamma Glutamyl Transferase concentrations are:

GGT Concentration	Acceptable S.D. Maximum
49 U/L	6.3 U/L
119 U/L	5.1 U/L

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

3 – 800 U/L

14.2 Precision

Material	Mean U/L	Standard Deviation (%CV)	
		Repeatability	Within-Lab
Multiqual Unassayed Control			
Level 1	49	2 (3)	3 (6)
Level 2	119	1 (1)	3 (2)

14.3 Interfering Substances

HIL Interference:
The GGT method was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias, defined as the difference between the control sample (does not contain interferent) and the test sample (contains interferent), is shown in the table below. Bias exceeding 10% is considered "interference".

Substance tested	Substance Concentration	GGT U/L	Bias %
Hemoglobin (hemolysate)	500 mg/dL 1000 mg/dL	88	<10 -19
Bilirubin (unconjugated)	60 mg/dL	89	<10
Bilirubin (conjugated)	60 mg/dL	89	<10
Lipemia Intralipid®	1000 mg/dL 3000 mg/dL	78	<10 33

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available

15. SAFETY

Refer to your local and corporate safety manuals and Safety Data Sheet (SDS) for detailed information on safety practices and procedures and a complete description of hazards.

GGT Flex® Reagent Cartridge may cause an allergic skin reaction.
Contains: 2-Chloracetamide. Wear protective gloves/protective clothing/eye protection/face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention.

16. RELATED DOCUMENTS

1. Dimension Vista® Clinical Chemistry System Operator's Manual
2. Dimension Vista® Calibration/Verification Procedure
3. Dimension Vista® Cal Accept Guidelines
4. Dimension Vista® Calibration summary
5. Dimension Vista® Sample Processing, Startup and Maintenance procedure
6. Laboratory Quality Control Program
7. QC Schedule for Siemens Dimension Vista®
8. Laboratory Safety Manual
9. Safety Data Sheets (SDS)
10. Dimension Vista® Limits Chart (AG.F200)
11. Quest Diagnostics Records Management Procedure
12. Dimension Vista® System Error Messages Chart
13. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
14. Hemolysis, Icteria and Lipemia Interference (Lab policy)
15. Repeat Testing Requirement (Lab policy)
16. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
17. Current package insert GGT Flex® Reagent Cartridge K2045

17. REFERENCES

1. Ghoshal, Amit K. and Soldin, Steven J., Evaluation of the Dade Behring Dimension® RxL: Integrated chemistry system-pediatric reference ranges. Clinica Chimica Acta 2003; 331:144.
2. Package Insert, GGT Flex® Reagent Cartridge K2045, Siemens Healthcare Diagnostics Inc., 02/24/2015.
3. Package Insert, ENZ 1 CAL, Siemens Healthcare Diagnostics Inc., 03/2014.
4. Package Insert, Liquid Assayed Multiqual® Chemistry Controls, Bio-Rad Laboratories, 09/2015.
5. Package Insert, Enzyme Diluent, Siemens Healthcare Diagnostics Inc., 10/2012.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
000	10/21/13		Update owner	L Barrett	R SanLuis
000	10/21/13	11.1	Change adult female range	L Barrett	R SanLuis
000	10/21/13	16	Update titles	L Barrett	R SanLuis

Version	Date	Section	Reason	Reviser	Approval
000	10/21/13	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13.	L Barrett	R SanLuis
1	10/30/15	3.2	Specify anticoagulant	L Barrett	R SanLuis
1	10/30/15	4.2	Add hazard information	A Chini	R SanLuis
1	10/30/15	5.2	Delete opened off board stability	A Chini	R SanLuis
1	10/30/15	6.4, 6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
2	3/13/18	Header	Add WAH	L Barrett	R SanLuis
2	3/13/18	3.2	Remove specimen onboard stability	L Barrett	R SanLuis
2	3/13/18	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
2	3/13/18	6.1, 6.2	Update QC material and storage	L Barrett	R SanLuis
2	3/13/18	7.2	Change freezer range to -50C	L Barrett	R SanLuis
2	3/13/18	10.5	Move patient review from section 6	L Barrett	R SanLuis
2	3/13/18	10.6	Remove repeat value below AMR/CRR	L Barrett	R SanLuis
2	3/13/18	15	Update to new standard wording; move hazard statement from 4.2	L Barrett	R SanLuis
2	3/13/18	17	Update QC insert	L Barrett	R SanLuis

19. ADDENDA

None