TRAINING UPDATE

Lab Location:	GEC	**Date Distributed:**	8/3/2015
Department:	Core	**Due Date:**	8/31/2015
		Implementation:	**9/1/2015**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

Acetaminophen by Dimension® Xpand Chemistry Analyzer GEC.C01v2

Description of change(s):

Most changes are minor. Note the low CRR value is being changed

Section	Reason
1, 7.1	Add analyzer name
3.2	Specify anticoagulant
4.2	Add hazard statement for diluent
6.4, 6.6	Replace LIS with Unity Real Time
8.2	Remove Lynx
10.4, 10.5	Change lower value from 2.0 to 0.0
10.5	Clarified dilution process, remove use of code REP from dilutions
11.2	Reformat value to eliminate ≥ signs
14.4	Remove analytical sensitivity
16	Update titles

This revised SOP will be implemented on September 1, 2015

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

Approved draft for training (version 2)

Technical SOP

Title	**Acetaminophen by Dimension® Xpand Chemistry Analyzer**		
Prepared by	Leslie Barrett	Date:	7/7/2009
Owner	~~Jean Buss~~ Robert SanLuis	Date:	7/24/2015

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**

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TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Acetaminophen	Dimension® Xpand Chemistry Analyzer	ACTMP

Synonyms/Abbreviations
Tylenol® / ACTM

Department
Chemistry

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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.

$$\text{Acetaminophen} + H_2O \xrightarrow{\text{Amidase}} \textit{p}\text{-aminophenol} + CH_3COOH$$

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	Plasma (Lithium Heparin)	
-Other Acceptable	Serum	
Collection Container	Plasma: Mint green top tube (Lithium heparin) Serum: Red top tube, no additives	
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:	(20-25°C) 8 hours, separate sample
	Refrigerated:	(2-8°C) 2 weeks
	Frozen:	(-20°C or colder) 45 days
Timing Considerations	N/A	

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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	Specimens should be free of particulate matter.
Other Considerations	Allow to clot completely prior to centrifugation.

4. REAGENTS

Refer to the Material Safety Data Sheet (MSDS) supplied with the reagents for complete safety hazards. Refer to the section in this procedure covering "SAFETY" for additional information.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
Acetaminophen	Siemens, Flex® reagent cartridge, Cat. No. DF88

4.2 Reagent Preparation and Storage

NOTES: Date and initial all reagents upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, (6) any special storage instructions; check for visible signs of degradation.
Refer to the Material Safety Data Sheet (MSDS) for a complete description of hazards. If a specific hazard is present, it will be noted in this procedure when the hazard is first encountered in a procedural step.

Irritant.
Contains ammonium chloride, Copper sulfate, O-cresol, Sodium carbonate
Causes serious eye irritation, causes serious skin irritation. Very toxic to aquatic life.
Wear protective gloves/protective clothing/eye protection/face protection. Avoid release to the environment
IF ON EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing.

Reagent	**Acetaminophen**
Container	Reagent cartridge
Storage	Store at 2-8° C

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Stability	• Reagent is stable until expiration date stamped on the reagent cartridges. • Sealed or unhydrated cartridge wells on the instrument are stable for 30 days. • Once wells 1-6 have been entered by the instrument, they are stable for 3 days.
Preparation	Hydrating, mixing and diluting are automatically performed by the instrument.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
Drug Calibrator II	Siemens Dimension®, Cat. No. DC49D

5.2 Calibrator Preparation and Storage

NOTE: Date and initial all calibrators upon opening. Each container must be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech (6) any special storage instructions; check for visible signs of degradation.

Calibrator	Drug Calibrator II
Preparation	Allow to equilibrate at room temperature (22-28°C) before use.
Storage/Stability	• Store at 2-8° C • **Unopened product**: Stable until expiration date stamped on the box. • **Opened product**: Once opened, assigned values are stable for 30 days when vials are securely capped and stored at 2–8°C between uses.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	Drug Calibrator II
Assay Range	0.0-300.0 µg/mL
Calibration levels	See reagent package insert for lot specific assigned values in µg/mL
Frequency	• Every new reagent cartridge lot. • Every 3 months for any one lot • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay. • When required by government regulations.

Calibration Scheme	Three levels in triplicate
Assigned Coefficients	C_0 0.000 C_1 1.990

5.4 Calibration Procedure

1. From Operating Menu press F5:Process Control press F1: Calibration Enter Password press F2: SETUP and RUN
2. Select the test method to be calibrated - if lot number is incorrect Press F1: Other Lot
3. Enter all information on screen
4. Press F8: QC yes/no to change to yes
5. Press F4: Assign cups If additional methods need to be calibrated, select the method.
6. Press F7: Load/run
7. Load cups into assigned position
8. Press F4: RUN

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 & 3	Bio-Rad Laboratories Cat. No. 361, 362 & 363

6.2 Control Preparation and Storage

NOTE: Date and initial all controls upon opening. Each container should be labeled with (1) substance name, (2) lot number, (3) date of preparation, (4) expiration date, (5) initials of tech, and (6) any special storage instructions; check for visible signs of degradation.

Control	Liquichek Immunoassay Plus Control, Levels 1, 2 & 3
Preparation	Allow the frozen control to stand at room temperature (18-25°C) 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	• Unopened controls are stable until the expiration date when stored at -20 to -70°C. • **Thawed and Unopened**: When the control material is thawed and stored unopened at 2-8°C, ACTM will be stable for 30 days. Record date of thaw on vial. • **Thawed and Opened**: Once the control material is thawed and opened, it will be stable for 14 days for ACTM when stored tightly capped at 2-8°C. Record date when thawed and opened on vial. Record new expiration date on vial. • Discard the vial if there is evidence of microbial contamination or excessive turbidity. • Do not refreeze control. • Do not use after the expiration date.

6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing.

Refer to the Dimension Xpand® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension X-pand® Quick Reference Guide.

6.4 Tolerance Limits

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

Step	Action
	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 Review Patient Data

Technologist must review each result with error messages. Refer to the Dimension Xpand® system manual "Error messages" section for troubleshooting. Check for unusual patterns, trends, or distributions in patient results (such as an unusually high percentage of abnormal results). Resolve any problems noted before issuing patient reports.

6.6 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.

6.7 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 Xpand® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -20 to -70°C.
- Centrifuge

7.3 Supplies

- Calibrated pipettes and disposable tips
- Plastic serum tubes and serum cups

8. PROCEDURE

ACTM Flex® reagent cartridge Cat. No. DF88 is required to perform the Acetaminophen test.

Acetaminophen is performed on the Dimension Xpand® 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.

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.

8.1	Instrument Set-Up Protocol
1.	For instrument set up and operation: Refer to Startup and Maintenance, Siemens Dimension® Xpand procedure.
2.	Check reagent inventory
3.	Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the Dimension® Xpand system. For details of the automated parameters, see below under "Test conditions."

8.2	Specimen/Reagent Preparation
1.	Centrifuge the specimens.
2.	Specimens are placed in Dimension® Xpand segments for analysis by the instrument. Refer to the Sample Processing, Siemens Dimension® Xpand procedure. The sample container (if not a primary tube) must contain sufficient quantity to accommodate the sample volume plus 50 µL of dead volume. Precise container filling is not required.

8.3	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension® Xpand QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension® Xpand Operators 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® Xpand 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). Repeat critical values and document according to Critical Values procedure. 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 Size:	4 µL	4 µL
Enzyme Volume:	N/A	80 µL
Copper Sulfate Volume:	80 µL	80 µL
O-Cresol Volume:	80 µL	80 µL
Test Temperature:	37° C	
Wavelengths:	600 nm and 700 nm	
Type of Measurement:	Bichromatic End point	

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 to one decimal point.

10.3 Units of Measure

µg/mL

10.4 Clinically Reportable Range (CRR)

0.0 - 900.0 µg/mL

10.5 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 within the AMR or CRR may be reported without repeat. Values that fall outside these ranges must be repeated.

IF the result is …	THEN…
< 0.0 µg/mL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: <0.0 µg/mL ~~REP~~
> 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. ~~Replicates must agree within the TEa.~~ ~~Append result with code REP and document per Critical Values Policy.~~

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> 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 Minimum allowable sample for dilution: 50 microliters **Diluent**: Level 1 ~~(0 µg/mL)~~ Drug Calibrator II or drug-free serum. Enter dilution factor as a whole number on the "Enter Sample Data" screen. ~~Reassay. Resulting readout is corrected for dilution.~~ ~~If the replicates agree within the TEa, result with remark code of -REP and document per Critical Values Policy.~~
> 900.0µg/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 Priority 3 Limit(s)

None established

12. CLINICAL SIGNIFICANCE

Acetaminophen is an analgesic/antipyretic and anti-inflammatory agent. At high levels, it may cause liver damage. ACTM levels can be used in the diagnosis and treatment of acetaminophen overdose. For purposes of diagnosis and treatment, results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

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 Xpand Operator's Guide.

Concentration	**S.D.**
16.2 µg/mL	> 1.93 µg/mL
75.0 µg/mL	> 2.35 µg/mL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

0.0 – 300.0 µg/mL

14.2 Precision

Material	**Mean µg/mL [µmol/L]**	**Standard Deviation (%CV)**	
		Within-run	**Total**
Liquichek™ QC	42.9 [284]	0.91 [6.02] (2.12)	1.09 [7.22] (2.55)
Serum Pool	146.5 [790]	1.07 [7.08] (0.73)	2.13 [14.1] (1.45)
Plasma Pool	13.4 [88.7]	0.39 [2.58] (2.89)	0.59 [3.91] (4.44)

14.3 Interfering Substances

Bilirubin (unconjugated) of 20 mg/dL decreases an ACTM result of 152.5 µg/mL by 21%.
Lipemia (Intralipid®) at a concentration of 3000 mg/dL (33.9 mmol/L) and above tripped an error flag; therefore the magnitude of the interference is not available.
Albumin of 6 g/dL decreases an ACTM result of 30 µg/mL by 13%.
Immunoglobulin G (IgG) of 5 g/dL decreases an ACTM result of 30 µg/mL by 26%.
Total protein of 12 g/dL decreases an ACTM result of 30 µg/mL by 31%.

HIL Interference:
The ACTM method was evaluated for interference from hemolysis, icterus and lipemia according to CLSI/NCCLS EP7-P. 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	**Test Concentration SI Units**	**ACTM Conc µg/mL [µmol/L]**	**Bias %**
Hemoglobin (hemolysate)	1000 mg/dL [0.62 mmol/L]	150.2 [996.6]	<10
Bilirubin (unconjugated)	5 mg/dL [86 µmol/L]	152.5 [1009.1]	<10
Lipemia (Intralipid®)	1000 mg/dL [11.3 mmol/L]	149.1 [986.6]	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available.

15. SAFETY

The employee has direct responsibility to avoid injury and illness at work. Nearly all harmful exposures to infectious substances and chemicals, and other injuries, can be avoided with effective training and consistent safe work practices.

Become familiar with the Environmental Health and Safety (EHS) Manual to learn the requirements on working safely and protecting the environment from harm. Although lab work typically focuses on the hazards of working with specimens and chemicals, we must also control other important hazards.

- Slips, trips, and falls cause many serious injuries. Please ensure that spills are cleaned quickly (to avoid slippery floors) and that you can see and avoid obstacles in your path.
- Ergonomic injuries result from performing tasks with too much repetition, force, or awkward position. Ergonomic injuries include strains and back injuries. Learn about ergonomic hazards and how to prevent this type of injury.
- Scratches, lacerations, and needlesticks can result in serious health consequences. Attempt to find ways to eliminate your risk when working with sharp materials.

Report all accidents and injuries immediately to your supervisor or the business unit Environmental Health and Safety Manager or Specialist.

16. RELATED DOCUMENTS

1. Dimension Xpand® Clinical Chemistry System Operator's Manual
2. Calibration / Verification Siemens Dimension® Xpand procedure
3. Dimension Xpand® Cal Accept Guidelines
4. Dimension Xpand® Calibration summary
5. Sample Processing, Siemens Dimension® Xpand procedure
6. Start up and Maintenance, Siemens Dimension® Xpand procedure
7. Laboratory Quality Control Program
8. QC Schedule for Siemens Dimension Xpand®
9. Laboratory Safety Manual
10. Material Safety Data Sheets (MSDS)
11. Siemens Dimension Xpand® Limits Chart (AG.F143)
12. Quest Diagnostics Records Management Procedure
13. Dimension Xpand® System Error Messages Chart
14. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
15. Hemolysis, Icteria and Lipemia Interference (Lab policy)
16. Repeat Testing Requirement (Lab policy)
17. Critical Values (Lab policy)
18. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls

19. Current package insert ACTM Flex® Reagent Cartridge DF88

17. REFERENCES

1. Package Insert, ACTM Flex® Reagent Cartridge DF88, Siemens Healthcare Diagnostics Inc., 02/27/2015.
2. Package Insert, Drug Calibrator II DC49D, Dade-Behring, 4/2008.
3. Package Insert, Liquichek Immunoassay Plus Control, Bio-Rad Laboratories, 11/2014.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
			Supersedes SOP C075.001		
000	12/28/11		Update owner	L. Barrett	J. Buss
000	12/28/11	5.3	Changed Calibration Level Statement	A. Chini	J. Buss
000	12/28/11	5.5	Correct second entry of ‘and’ to ‘or’	L. Barrett	J. Buss
000	12/28/11	6.7	Add use of TEA for lot to lot runs, remove testing new calibrator lots as unknowns prior to use	L. Barrett	J. Buss
000	12/28/11	10.4	Add lower value for CRR	L. Barrett	J. Buss
000	12/28/11	10.5	Remove instruction to repeat all critical values, remove code QNSR	L. Barrett	J. Buss
000	12/28/11	11.2	Title change to local terminology	L. Barrett	J. Buss
000	12/28/11	15	Update to standard wording	L. Barrett	J. Buss
000	12/28/11	16	Update document list titles	L. Barrett	J. Buss
000	12/28/11	17	Update revision dates	A. Chini	J. Buss
000	12/28/11	19	Remove package insert	L. Barrett	J. Buss
001	7/24/15		Update owner	L. Barrett	R. SanLuis
001	7/24/15	1, 7.1	Add analyzer name	L. Barrett	R. SanLuis
001	7/24/15	3.2	Change preferred specimen to plasma	L. Barrett	R. SanLuis
001	7/24/15	4.2	Update hazard statement	L. Barrett	R. SanLuis
001	7/24/15	6.4,6.6	Replace LIS with Unity Real Time	L. Barrett	R. SanLuis
001	7/24/15	8.2	Remove Lynx	L. Barrett	R. SanLuis
001	7/24/15	16	Update titles	L. Barrett	R. SanLuis
001	7/24/15	10.4, 10.5	Change lower value from 2.0 to 0.0	L. Barrett	R. SanLuis
001	7/24/15	10.5	Clarified dilution process, remove use of code REP from dilutions	A. Chini	R. SanLuis
001	7/24/15	11.2	Reformat value to eliminate ≥ signs	L. Barrett	R. SanLuis
001	7/24/15	14.4	Remove analytical sensitivity	L. Barrett	R. SanLuis
001	7/24/15	Footer	Version # leading zero’s dropped due to new EDCS in use as of 10/7/13	L. Barrett	R. SanLuis

19. ADDENDA

None