Acetaminophen using Abbott Architect ci4100

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Department:	STAT Lab	**Effective Date:**	8/24/18
Policy, Procedure, or Both:	Procedure	**Revision Date(s):**	
Author:	Kim Clark, MT (ASCP)	**Version:**	1

Applicable Standards	
Standard	Organization
COM.10000	CAP
Related Documents	

Version History		
Version	Effective Date	Retired Date
1	08/24/2018	

Review History (Up to the Last 15 Occurrences)			
Date	Version	Revision Type	Review By
8/22/18	1	**New Policy/Procedure**	System Laboratory Medical Director, Joe A. Lewis. M.D.. F.C.A.P.

Distribution
Christus Spohn Shoreline STAT Lab

TECHNICAL PROCEDURE MANUAL
CHRISTUS Spohn Hospital Corpus Christi Shoreline STAT Lab
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Proc.#: HSL0330.01

Intended Use
The MULTIGENT Acetaminophen assay is intended for the quantitative determination of acetaminophen in human serum or plasma on the ARCHITECT *c* Systems.

Clinical Significance
Acetaminophen (paracetamol) is used as an analgesic in many different formulations.1 While therapeutic doses rarely cause adverse side effects, the effect of long term treatment with acetaminophen is unclear. Cases have been reported where chronic excessive use of acetaminophen led to hepatotoxicity and nephrotoxicity. In cases of acute overdosage, acetaminophen can cause severe hepatic damage leading to hepatic failure if untreated.
The management of acetaminophen overdose requires early recognition of the drug in the bloodstream. Toxicity is generally reported at concentrations over 200 µg/mL (1,324 µmol/L). *N*-acetylcysteine has been used as an antidote in conjunction with intensive support care. Early diagnosis of acetaminophen-induced hepatotoxicity is important since initiation of therapy within 8 hours of ingestion lessens the potential for hepatic injury, and decreases the mortality rate.

Principle

The enzyme, aryl acylamidase, cleaves the amide bond of the acetaminophen molecule, leaving *p*-aminophenol and acetate. The *p*-aminophenol is reacted with 8-hydroxyquinoline-5-sulfonic acid in the presence of manganese ions to form a colored compound, 5-(4-iminophenol)-8-quinolone. The increased absorbance at 615 nm due to the formation of 5-(4-iminophenol)-8-quinolone is directly proportional to the concentration of acetaminophen in the sample.

Methodology: Enzymatic/Colorimetric

Specimen Collection and Handling

Suitable Specimens
• **Serum:** Use serum collected by standard venipuncture techniques into glass or plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation.
Centrifuge according to tube manufacturer's instructions to ensure proper separation of serum from blood cells.
• **Plasma:** Use plasma collected by standard venipuncture techniques into glass or plastic tubes. Acceptable anticoagulants are lithium heparin (with or without gel barrier) and sodium heparin. EDTA is not suitable for use. Ensure centrifugation is adequate to remove platelets. Centrifuge according to tube manufacturer's instructions to ensure proper separation of plasma from blood cells.
Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.

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It is the responsibility of the operator to verify that the correct sample type(s) is (are) used in the MULTIGENT Acetaminophen assay.
Specimens containing particulate matter or red blood cells may give inconsistent results and should be centrifuged before testing (recommended 8,000 to 10,000 RCF* x 10 minutes).
*Relative Centrifugal Force
Separated samples may be stored for up to 14 days at 4 to 8°C prior to being tested. If testing will be delayed more than 14 days, separated samples may be stored frozen at ≤ -20°C for up to 45 days.
NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Materials and Equipment Required

TEST INSTRUMENT: Abbott ARCHITECT System

MATERIALS PROVIDED

3R11-30 Acetaminophen Reagent Kit (506-30)

MATERIALS REQUIRED BUT NOT PROVIDED

- 506-30E-6 MULTIGENT Acetaminophen Calibrator
- Biorad Immunoassay Plus Controls (361-362-363)
- Saline (0.85% to 0.90% NaCl) for specimens that require dilution

Reagent Handling and Storage:

***CAUTION*:**

1. For in vitro diagnostic use.
2. Do not use components beyond the expiration date.
3. Do not mix materials from different kit lot numbers.

CAUTION: This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.

For a detailed discussion of safety precautions during system operation, refer to *Section 8* of the **ARCHITECT System Operations Manual.**

The following warnings and precautions apply to R2:

DANGER:	Contains polyethylene glycol octylphenyl ether and sodium hydroxide.
H318	Causes serious eye damage.
H315	Causes skin irritation.
Prevention	
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves/protective clothing/eye protection.
Response	
P305+P351 +P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310	Immediately call a POISON CENTER or doctor/ physician.
P302+P352	IF ON SKIN: Wash with plenty of water.
P332+P313	If skin irritation occurs: Get medical advice/ attention.
P362+P364	Take off contaminated clothing and wash it before reuse.

Reagent Handling

- R1 Ready for use. Before use, invert several times, avoiding the formation of bubbles.
- R2 Ready for use. Before use, invert several times, avoiding the formation of bubbles.
- Remove air bubbles, if present in the reagent cartridge, with a new applicator stick.

Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate.

To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration that could impact results.

- When either the R1 or the R2 reagent cartridge becomes empty, replace both cartridges.

Reagent Storage

- Reagent stability is 12 days if the reagent is uncapped and onboard.
- Unopened reagents are stable until the expiration date when stored at 2 to 8°C.

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Reagent Preparation:

2K99 Acetaminophen is supplied as a liquid, ready-to-use, two- reagent kit which contains: **R1 & R2**

Reactive Ingredients		Concentration
R1	Manganese (II) chloride	0.2 mmol/L
	Aryl acylamidase	≥ 0.9 KU/L
R2	8-hydroxyquinoline-5-sulfonic acid	30 mmol/L

Inactive Ingredients: R1 contains bovine serum albumin, sodium azide, and preservatives. R1 and R2 contain surfactant and buffer. R2 contains NaOH 0.09 mol/L.

Calibrator: ARCHITECT Acetaminophen Calibrator 2K99-01

Calibration

Frequency:
Calibration is stable for 12 days (288 hours) for any one lot.

A new calibration is required:

1. If quality control results do not meet acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.
2. Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Calibrator Required: ARCHITECT Acetaminophen Calibrator 2K99-01

Reagents:

506-30E-6 MULTIGENT Acetaminophen Calibrator, 2 x 5 mL MULTIGENT Acetaminophen Calibrator consists of:

- Acetaminophen 151 µg/mL (1,000 µmol/L)
- Buffer (pH 5.0 at 25°C)
- 0.10% sodium azide as a preservative

Calibrator Preparation:
The calibrator is supplied in liquid form and is ready to use. Invert bottle several times before use, avoiding the formation of foam.

Calibration Procedure:
Before performing the assay, refer to the ASSAY PARAMETERS, which are included in the MULTIGENT Acetaminophen reagent package insert. For further instructions, refer to the CALIBRATION and QUALITY CONTROL sections of the MULTIGENT Acetaminophen reagent package insert.

1. Verify that the calibrator values are correct in the instrument parameter files.
2. Mix bottles several times by gentle inversion.
3. Open the bottle, place an appropriate amount of the calibrator in a separate sample cup, and place in the assigned position.
4. Calibrate as outlined in *Section 6* of the **ARCHITECT System Operations Manual.**
5. Follow the established quality control procedures for your laboratory and the instructions found in *Section 5* of the **ARCHITECT System Operations Manual**.
6. Cap bottle tightly and return to refrigerated storage after use.
7. Verify control results are within acceptable limits before reporting patient results.

Troubleshooting and Overall Acceptance Criteria Failure

See ARCHITECT Operations Manual for further calibration troubleshooting.

Quality Control:

Controls are tested according to each location/site Quality Control Procedure.

- If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory.
Recalibration may be necessary.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Procedure
For a detailed description of how to run an assay, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

Calculations
Refer to *Appendix C* of the **ARCHITECT System Operations Manual** for information on results calculations.

Reporting Results
The result unit for the MULTIGENT Acetaminophen assay will be reported in µg/mL

Specific Performance Characteristics
Reference Ranges
It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Serum/Plasma (Abbott Package Insert)
Treatment of acetaminophen poisoning is primarily based on serum levels and patient information about ingestion. Nomograms have been devised to determine patient's status with one serum level; the time after ingestion is plotted on the abscissa vs. drug level on the ordinate. Patient ingestion information is not always reliable and a more accurate method to estimate toxicity is to determine drug half-life. Acetaminophen half-life is normally 2 to 3 hours and hepatic damage is likely if it exceeds 4 hours. Significant liver damage is also considered likely if drug levels are greater than 300 µg/mL at 4 hours after ingestion or 50 µg/mL after 12 hours. To determine acetaminophen half-life, the first of two samples should be drawn at least 4 hours after poisoning to ensure peak levels have been achieved.

Reference Interval

	Conventional Units (µg/mL)	SI Units (µmol/L)
Therapeutic	10 to 30	66 to 199
Toxic Levels	> 200	> 1,324

Serum/Plasma (this facility)

Critical Values *(Refer to Critical Lab Policy)*

Performance Characteristics

Analytical Measurement Range (AMR): Abbott Package Insert
Serum/Plasma: 3 to 377 µg/mL (20 to 2,500 µmol/L).

This is the range of analyte values that can be measured directly from the specimen without any dilution or pretreatment that is not part of the usual analytical process and is equivalent to the assay range.

Dilution:
Specimens with acetaminophen values exceeding 377 µg/mL (2,500 µmol/L) are flagged and may be diluted by following the Automated Dilution protocol.

Automated Dilution Protocol

If using the Automated Dilution Protocol, the system performs a **1:10 dilution** of the specimen and automatically corrects the concentration by multiplying the result by the appropriate dilution factor.

Limit of Quantitation (LOQ): The LOQ for the MULTIGENT Acetaminophen assay was calculated to be 3 µg/mL (20 µmol/L). LOQ is defined as the concentration at which the CV is ≤ 20% and the recovery is within +/- 6.7% or +/- 1.25 µg/mL.

Precision:

Acceptance criteria:
≤ 5.0% total CV at ≥ 18 µg/mL or ≤ 1.25 SD from ≥ 3 µg/mL to < 18 µg/mL

Sample		Level 1	Level 2	Level 3
N		80	80	80
Mean (µg/mL)		11	36	219
Within Run	SD	0.073	0.158	0.671
	%CV	0.6	0.4	0.3
Between Run	SD	0.031	0.096	0.627
	%CV	0.3	0.3	0.3
Between Day	SD	0.204	0.210	2.213
	%CV	1.8	0.6	1.0
Total	SD	0.219	0.280	2.396
	%CV	1.9	0.8	1.1

Limitations of Procedure

Reagent cross contamination testing for the MULTIGENT Acetaminophen assay was performed on an ARCHITECT *c* System.
Configure Acetaminophen SmartWash parameters in the following assay files on an ARCHITECT *c* System.

Interfering Substances:

The following compounds, when tested with the MULTIGENT Acetaminophen assay at the concentrations indicated, resulted in less than 7.5% error in detecting acetaminophen. Interference effects were assessed by Dose Response method. Representative results are shown below.

Interfering Substance	Interferent Concentration	Acetaminophen (µg/mL)	Recovery %
Bilirubin*	24 mg/dL	33	106.5
Hemoglobin	200 mg/dL	33	106.5
Intralipid	600 mg/dL	28	93.3

*Hyperbilirubinemic serum has been demonstrated to show positive interference with enzymatic assays for acetaminophen.
NOTE: Significantly reduced acetaminophen recovery has been demonstrated in situations where testing has been performed immediately after the introduction of NAC. It is recommended that laboratories review NAC treatment and monitoring protocols to determine the extent of the potential interference.

Specificity
This method does not measure the common metabolites of acetaminophen (glucuronide, cysteine, and mercapturate).

References:

1. ABBOTT ARCHITECT Acetaminophen package insert
   Abbott Laboratories
   Diagnostics Division
   Abbott Park, IL 60064
   May 2015 306711/R08
2. ABBOTT ARCHITECT Acetaminophen Calibrator package insert
   Abbott Laboratories
   Diagnostics Division
   Abbott Park, IL 60064
3. Abbott ARCHITECT Operator's Guide

Alternative Method

Send to sister facility if unable to perform at this site.

Effective date of this Procedure : 07/25/2018

Revised by : Kimberlee J. Clark, MT(ASCP)