TRAINING UPDATE

Lab Location:	SGMC & WOMC	**Date Distributed:**	2/15/2021
Department:	Core Lab	**Due Date:**	3/15/2021

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

Urine Buprenorphine Screen by Dimension Vista® System SGMC.C2004 v3

Description of change(s):

The DI rule to hold positive BUP results was implemented on February 12, 2021. The SOP is being revised to match that process.

Section	Reason
10.6	Added QC requirement for positive results

This revised SOP will be implemented as soon at it's approved in Media Lab

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

Technical SOP

Title	**Urine Buprenorphine Screen by Dimension Vista® System**
Prepared by	Ashkan Chini Date: 5/18/2020
Owner	Robert SanLuis Date: 5/18/2020

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

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Test Code
Urine Buprenorphine, Qualitative	Dimension Vista® System	UBUP

Synonyms/Abbreviations
Subutex®, BUP Included in Urine Drug Screen (UDRGT) and Urine Drug Screen with TCA(UDRGW)

Department
Chemistry

2. ANALYTICAL PRINCIPLE

The Emit II Plus Buprenorphine Assay is a homogeneous enzyme immunoassay technique used for the analysis of specific compounds in human urine. The assay is based on competition between drug in the specimen and drug labeled with the recombinant glucose-6-phosphate dehydrogenase (rG6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the specimen can be measured in terms of enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH in the presence of glucose-6-phosphate (G6P), resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme NAD functions only with the bacterial (Leuconostoc mesenteroides) enzyme employed in the assay.

3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Freshly voided urine specimens should be used for testing.
Special Collection Procedures	No additives or preservatives are needed. Adulteration of the urine specimen may cause erroneous results. If adulteration is suspected, obtain a fresh specimen. Urine specimens should be handled and treated as if they are potentially infected. Preferred method is the Urine Collection Kit with specimen transferred to Urine Chemistry Collection Tube (yellow top).

Component	Special Notations
Other	If Urine Collection Kit is not used, submit to Laboratory within 2 hours of collection.

3.2 Specimen Type & Handling

Criteria		
Type -Preferred	Urine	
-Other Acceptable	None	
Collection Container	Urine Collection Kit or sterile container	
Volume - Optimum	15 mL	
- Minimum	2 mL	
Transport Container and Temperature	Urine Chemistry Collection Tube (yellow top) or container at room temperature.	
Stability & Storage Requirements	Room Temperature:	5 days
	Refrigerated:	5 days
	Frozen:	If storage longer than 5 days is required.
Timing Considerations	Deliver specimens to laboratory immediately.	
Unacceptable Specimens & Actions to Take	Specimens that are unlabeled, improperly labeled, or those that do not meet the stated criteria are unacceptable. Samples in Urine Analysis Preservative Tubes are NOT acceptable. 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	Turbidity: Centrifuge turbid samples before analysis. Frozen samples must be thawed and mixed thoroughly prior to analysis. Avoid repeat freeze/thaw cycles.	
Other Considerations	Boric acid should not be used as a preservative. Plastic transfer pipettes should NOT be used for delivering patient specimen to sample cup.	

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.

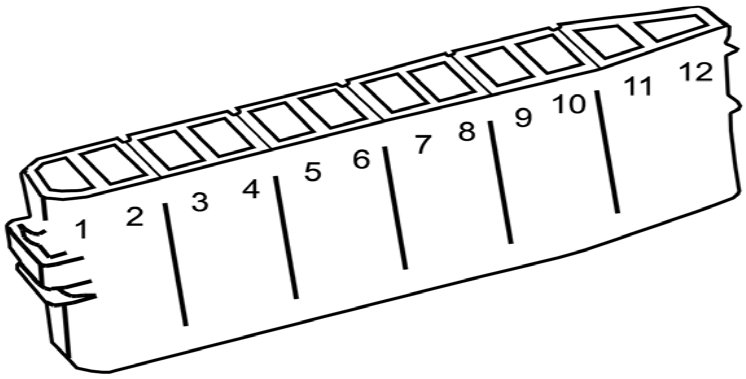
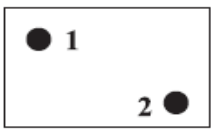
4. REAGENTS

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
Buprenorphine Assay (consists of Antibody/Substrate Reagent 1 and Enzyme Reagent 2)	Siemens, Syva® Emit II Plus, Cat. No. 10720048
Empty Flex Reagent Cartridge	Siemens, Cat. No. 10445218

4.2 Reagent Preparation and Storage

Reagents	**Antibody/Substrate Reagent 1 & Enzyme Reagent 2**
Container	Plastic vial, Flex Reagent Cartridge
Storage	Stored at 2–8ºC, upright and with screw caps tightly closed
Stability	• **Antibody/Substrate Reagent 1 & Enzyme Reagent 2:** Stable until the expiration date printed on the label • **Pre-filled Flex Reagent Cartridge:** When taped and stored at 2–8ºC, it will remain stable for 7 days. Remove the tape before loading the Flex reagent cartridge on the analyzer. • **Pre-filled Flex Reagent Cartridge:** When loaded on the Dimension Vista, it will remain stable for 24 hours.
Preparation	Both Antibody/Substrate Reagent 1 and Enzyme Reagent 2 are ready for use. No preparation is required. The wells of an empty Flex Reagent Cartridge are identified as shown below.  The Flex well must be vented before filling with reagent. To vent a Flex well, puncture the film at a corner of the well (see picture below). Care must be taken to minimize the size of the vent; do not tear the film. 

	Transfer reagent into an empty, vented Flex Reagent Cartridge according to the table below. Try to avoid bubbles as much as possible. Label the Flex Reagent Cartridge with reagent name, lot number, date prepared, expiration date, and tech code.

Reagent	Wells	Volume per Well	Tests per Well
Reagent 2	1 and 2	0.8 mL	10
Reagent 1	11 and 12	1.2 mL	10

4.3 Loading Pre-filled Flex Reagent Cartridge on Dimension Vista

Note: Load one Empty flex on board at a time. Since there is no way to differentiate between empty flexes on board, operator must load one empty flex and identify it before loading the next empty flex.

Load the flex on board. From the Home Page go to **Set Up** – **Inventory** – **Reagents** – Select "**Empty**" – Identify the method and lot number – **Finish**

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
Emit® Calibrator/Control Level 0	Siemens Syva® Emit, Cat. No. 10445406
Emit® II Plus Specialty Drug Calibrator/Control Levels 1, 2, 3, & 4	Siemens Syva® Emit, Cat. No. 10720049 - 10720052

5.2 Calibrator Preparation and Storage

Calibrator	Emit® Calibrator/Control Level 0 and Emit® II Plus Specialty Drug Calibrator/Control Levels 1, 2, 3, & 4
Preparation	Calibrator is ready for use. No preparation is required.
Storage/Stability	• Store at 2-8°C, upright • If stored as directed, calibrators are stable until the expiration date printed on the label.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	Emit® Calibrator/Control Emit® II Plus Specialty Drug Calibrator/Control

Assay Range	0 – 25 ng/mL
Suggested Calibration Level	• Level 0 = 0 ng/mL • Level 1 = 2.5 ng/mL • Level 2 = 5 ng/mL • Level 3 = 15 ng/mL • Level 4 = 25 ng/mL
Frequency	• Every new reagent cartridge lot. • Every 14 days for any one lot. • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	5 Levels

5.4 Calibration Procedure

Manual Calibration:

1. Verify that reagent is in inventory on the instrument.
2. From the Home Page select **Advanced** – **Calibration** – **Calibrations by Lot** – Select "**XBUP**" – **Order Calibration** – Designate a specimen rack and scan it - **OK**
3. Pour calibrators in Sample Cups and load them as described below:
   - Calibrator 0 on rack position 1
   - Calibrator 1 on rack position 2
   - Calibrator 2 on rack position 3
   - Calibrator 3 on rack position 4
   - Calibrator 4 on rack position 5
4. After loading the rack on the instrument, 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
Specialty Drug Controls Negative	Siemens Syva® Emit II Plus, Cat. No. 10718700
Specialty Drug Controls Positive	Siemens Syva® Emit II Plus, Cat. No. 10718701

6.2 Control Preparation and Storage

Control	Syva Emit II Plus Controls Negative and Positive
Preparation	The controls are ready for use. No preparation is required. • Aliquot 2 mL into screw top vials • Print labels from the Vista and label each vial • Immediately load onto the instrument for 2–8ºC storage
Storage/Stability	• Store at 2–8ºC • Stable opened or unopened in the original container until the expiration date printed on the vial. • On board Dimension Vista, QC vials will remain stable for 7 days.

6.3 Frequency

Analyze all levels of QC material immediately after loading a new flex cartridge*, after every calibration and each day of testing (notated on the QC frequency sheets posted on the instruments).
* Document the new flex reagent and QC assessment on the Vista Reagent QC Handoff Log.

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

Step	Action
	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
- Screw top vials, 3mL

8. PROCEDURE

XBUP Flex® reagent cartridge Cat. No. 10720048 is required to perform this test.

Buprenorphine 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

8.2	Specimen Testing
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 10.6 "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.

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

None

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

N/A

10.3 Units of Measure

N/A

10.4 Clinically Reportable Range (CRR)

N/A

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

Specimens that give an "Abnormal Reaction" message must be repeated.

If the result is Positive**, QC must be run** (Note: DI will flag and hold positive results)

- If QC is acceptable, the patient result may be released
- If QC fails, repeat QC on a fresh well. Do **not** report a positive patient result until QC passes successfully.

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

11. EXPECTED VALUES

11.1 Reference Ranges

None detected

11.2 Critical Values

None established

11.3 Standard Required Messages

The following comment is automatically added to the report by the LIS when a urine Buprenorphine test is ordered:

> This is a screening assay. Buprenorphine is detected in concentration at or above 5 ng/mL

The following comment is automatically added to the report by the LIS when a urine drug screen is ordered:

> The drug of abuse panel is a screening assay. It detects the following drugs of abuse in concentrations at or above the concentrations listed below.

Phencyclidine	25 ng/mL
Benzodiazepines	200 ng/mL
Cocaine	300 ng/mL
Amphetamines	1000 ng/mL
THC	50 ng/mL
Opiates	300 ng/mL
Barbiturates	200 ng/mL
Methadone	300 ng/mL
Buprenorphine	5 ng/mL

> The ingestion of certain herbal or plant products containing Ephedra or its metabolites may cause false positive amphetamine/metamphetamine results.
>
> This test is for medical screening purposes ONLY. For confirmation a separate order for Gas Chromatography by Mass Spectrophotometry (GCMS) is required.

12. CLINICAL SIGNIFICANCE

Buprenorphine is a semi-synthetic opioid analgesic derived from thebaine, a component of the opium poppy Papaver somniferum. Buprenorphine structurally resembles morphine, but has both antagonist and agonist properties. Buprenorphine is a schedule III drug. The Food and Drug Administration (FDA) has approved the use of Suboxone, which contains buprenorphine for treatment of opiate dependency in the US. Under the US Drug Abuse Treatment Act of 2000 (DATA) buprenorphine can be prescribed in a physician's office for treatment of opiate dependency.

It has been shown that buprenorphine has abuse potential and may itself cause dependency. It produces typical opioid effects and side effects such as euphoria and respiratory depression.

Buprenorphine is metabolized in the human liver primarily by N-dealkylation to pharmacologically active norbuprenorphine, which along with the parent compound is conjugated to form buprenorphine glucuronide and norbuprenorphine glucuronide.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/Modified
- **Validated Test Modifications:** Removed pH testing per communication from manufacturer

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.

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

Qualitative Assay: 0.7 – 25 ng/mL (for 5 ng/mL cutoff)

14.2 Precision

Urine Pool (ng/mL)	% of Cutoff	# of Results	Repeatability Results	Within-Laboratory Results
1.25	-75%	80	80 Negative	80 Negative
8.75	+75%	80	80 Positive	80 Positive

14.3 Interfering Substances

None

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.

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 Function Checks (Lab policy)
14. Specimen Acceptability Requirements (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 XBUP Flex® Reagent Cartridge 10720048
18. Vista Reagent QC Handoff Log (AG.F538)

17. REFERENCES

1. Package Insert, XBUP Flex® Reagent Cartridge 10720048, Siemens Healthcare Diagnostics Inc., 05/2019.
2. Package Insert, Emit Calibrator, Siemens Healthcare Diagnostics Inc., 05/2019.
3. Package Insert, Emit II Plus Specialty Drug Calibrator, Siemens Healthcare Diagnostics Inc., 05/2019.
4. Package Insert, Emit II Plus Specialty Drug Control, Bio-Rad Laboratories, 05/2019.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
1	9/2/20	4.2	Added tech code to flex labeling	L Barrett	R SanLuis
1	9/2/20	6.3	Added QC required after every new flex	L Barrett	R SanLuis
1	9/2/20	16	Added QC handoff log	L Barrett	R SanLuis
2	2/15/21	10.6	Added QC requirement for pos results	L Barrett	R SanLuis

19. ADDENDA

Validated Test Modification statement from manufacturer

From: Brodbeck, Beate (H USA)
Sent: Thursday, June 24, 2010 3:54 PM
To: SanLuis, Robert; Mcmillan, Wendell R
Subject: pH for urine DAU samples

Hi Robert and Wendell,

Below is the response regarding your inquiry of pH testing for drugs of abuse urines.

Beate Brodbeck

Chemistry Instrument Specialist - Western Maryland

Siemens Healthcare Diagnostics
<blocked::http://www.siemens.com/diagnostics>

C: 410-370-4382 | VM: 800-948-3234 x-2684

beate.brodbeck@siemens.com

From Kevin Mulrooney:

pH correction of urine samples prior to running the Drugs of Abuse assays on Dimension is not an absolute requirement. The Dimension IFU's all say that the acceptable pH range is 5-8. The Syva Emit IFU's for the same tests all say that the acceptable pH range is 3-11, except for THC (pH range 4.5-8). The assays all work at pH 3-11. The vast majority of urines will fall in this range. THC is an exception in that at acid pH <4.5, THC recovery is decreased, and at basic pH >8, THC recovery is increased. When the Dimension IFU's were written, I suppose the decision was made to standardize the pH acceptable range to the most narrow (THC). Dimension customers can run the DAT's without checking pH, but there is a slight chance of inaccuracy with THC. Urine pH outside the 5-8 range is not common, either.

Hope this helps. We don't have this in a formal document, but you can share this information with your customer.

Regards,

Customer Care.
With you every step of the way.

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