Laboratories at Adventist Healthcare Washington Adventist Hospital, Shady Grove Medical Center and Germantown Emergency Center

Date: January 2, 2018

INTERNAL LABORATORY ALERT

Subject: Specimen Stability for Urine Drug Testing

The Laboratory is informing you of the following change:

Effective date:	**February 1, 2018**
Test Names:	Urine Drug Screen Urine Amphetamine/Methamphetamine Urine Barbiturates Urine Benzodiazepines Urine Cannabinoids (THC) Urine Cocaine Metabolite Urine Opiates Urine Phencyclidine (PCP)
Specimen Stability:	Room temperature stability increased to 4 hours **No change to other temperatures**: Refrigerated: 24 hours Frozen: If storage longer than 24 hours is required.
Contacts:	Robert SanLuis, Zanetta Morrow & Julie Negado
LBarrett/12.15.17	

G:\AHC_Lab\Clinical Folders\Communication_General Lab\Lab Alerts

Technical SOP

Title	**Urine Amphetamine/Methamphetamine Screen by Dimension Vista® System**
Prepared by	Ashkan Chini Date: 6/25/2012
Owner	Robert SanLuis Date: 7/6/2016

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....2
2. Analytical Principle....3
3. Specimen Requirements....3
4. Reagents....4
5. Calibrators/Standards....5
6. Quality Control....6
7. Equipment And Supplies....8
8. Procedure....9
9. Calculations....10
10. Reporting Results And Repeat Criteria....10
11. Expected Values....11
12. Clinical Significance....12
13. Procedure Notes....12
14. Limitations Of Method....12
15. Safety....13
16. Related Documents....13
17. References....14
18. Revision History....14
19. Addenda....15

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
Urine Amphetamine, Qualitative	Dimension Vista® System	UAMPT

Synonyms/Abbreviations
"Speed"/AMP Included in Batteries/Packages: Urine Drug Screen: UDRGS (SGAH) & UDRGW (WAH)

Department
Chemistry

Form revised 2/02/2007

2. ANALYTICAL PRINCIPLE

The principle of this test is based on the competition for antibody binding sites between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH). Matched lots of monoclonal antibody reactive to d-amphetamine and d-methamphetamine and d-amphetamine and d-methamphetamine labeled with glucose-6-phosphate dehydrogenase are used in this Syva® Emit® II Plus methodology.

Ab+AMPH + AMPH-G6PDH ----------> Ab-AMPH + Ab-AMPH-G6PDH + AMPH-G6PDH
(Inhibited) (active)

AMPH-G6PDH

Glucose-6-phosphate + NAD+ ----------> 6-phosphogluconolactone + NADH + H+
(active) (absorbs at 340 nm)

Where: Ab =antibody reactive to d-amphetamine and d-methamphetamine
AMPH =amphetamines and methamphetamines
AMPH-G6PDH = d-amphetamine and d-methamphetamine glucose-6-phosphate dehydrogenase conjugates

The concentration of drug in the sample determines the amount of AMPH-glucose-6-phosphate dehydrogenase (AMPH-G6PDH) conjugate that is bound to the antibody. The unbound conjugate catalyzes the oxidation of glucose-6-phosphate, with the simultaneous reduction of NAD+ to NADH, more rapidly than does the bound conjugate. The rate of increasing absorbance at 340 nm due to the increase in NADH is related to the concentration of drug in the sample.

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

3.2 Specimen Type & Handling

Criteria		
Type -Preferred **-Other Acceptable**	Urine None	
Collection Container	Urine Collection Kit or sterile container	
Volume - Optimum **- Minimum**	15 mL 2 mL	
Transport Container and Temperature	Urine Chemistry Collection Tube (yellow top) or container at room temperature.	
Stability & Storage Requirements	Room Temperature:	4 hours ~~Processing/Testing should take place immediately~~.
	Refrigerated:	24 hours
	Frozen:	If storage longer than 24 hours is required.
	~~Instrument on board aliquot stability~~	~~2 hours~~
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. Temperature: Specimens should be at a temperature of 20 – 25ºC before testing.	
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
AMPH	Siemens, Flex® reagent cartridge, Cat. No. K5091

4.2 Reagent Preparation and Storage

Reagent	**AMPH**
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. • Once wells 1 - 12 have been entered by the instrument, they are stable for 2 days.
Preparation	All reagents are liquid and ready for use.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
UDAT CAL	Siemens Dimension Vista®, Cat. No. KC510

5.2 Calibrator Preparation and Storage

Calibrator	UDAT CAL
Preparation	Calibrator is ready for use. No preparation is required.
Storage/Stability	• Store at 2-8°C • **Unopened calibrator:** Stable until expiration date stamped on the box. • **Opened Calibrator:** once the stopper is punctured, assigned values are stable for 15 days when stored on board the Dimension Vista System.

5.3 Calibration Parameter

Criteria	**Special Notations**
Reference Material	UDAT CAL
Assay Range	0 – 1000 ng/mL
Suggested Calibration Level	1000 ng/mL cutoff. Validate the calibration by assaying a positive and negative control.

Frequency	• Every new reagent cartridge lot. • Every 30 days for any one lot • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	4 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™ Urine Toxicology Control Levels S1E and S2E Low Opiate	Bio-Rad Laboratories Cat. No. 423 and 424

6.2 Control Preparation and Storage

Control	Liquichek Urine Toxicology Controls, Levels S1E and S2E
Preparation	Before sampling allow the control to reach room temperature (18-25°C) and swirl gently to ensure homogeneity. Use immediately. After each use, promptly replace the stopper and return to 2-8°C storage.
Storage/Stability	**Opened**: all analytes will be stable for 30 days at 2-8°C **Unopened**: stable until the expiration date at 2-8°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, 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

Step	Action
	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 ~~70~~°C.
- Centrifuge

7.3 Supplies

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

8. PROCEDURE

AMPH Flex® reagent cartridge Cat. No. K5091 is required to perform this test.

Urine Amphetamine/Methamphetamine Screen 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:	1.2 µL
Reagent 1 Volume:	98 µL
Reagent 2 Volume:	42 µL
Reaction Time:	5.3 minutes
Test Temperature:	37°C
Wavelength:	340 & 600 nm
Type of measurement:	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

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.

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 amphetamine test is ordered:

> This is a screening assay. Amphetamines are detected in concentrations at or above 1000 ng/mL. The ingestion of certain herbal or plant products containing Ephdra or its metabolites may cause false positive amphetamine/methamphetamine results. A more specific testing method GCMS is available from the lab.

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

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

Amphetamines are central nervous system stimulants that produce wakefulness, alertness, increased energy, reduced hunger, and an overall feeling of well-being. Amphetamines can be taken orally, intravenously, by smoking, or by snorting.

Amphetamines are readily absorbed from the gastrointestinal tract and are then either deactivated by the liver or excreted unchanged in the urine. The relative importance of these elimination modes depends on urinary pH. Amphetamine is metabolized to deaminated (hippuric and benzoic acids) and hydroxylated metabolites. Methamphetamine is partially metabolized to amphetamine, its major active metabolite.

Amphetamines appear in the urine within three hours after any type of administration1, and can be detected by this Emit® assay for as long as 24–48 hours after the last dose.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/Modified
- **Validated Test Modifications:** Removed pH testing per communication from manufacturer. Increased room temperature specimen storage to 4 hours per on-site specimen stability validation (SGAH.VC350v0).

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.

Concentration	**S.D.**
300 ng/mL	47 ng/mL
500 ng/mL	86 ng/mL
1000 ng/mL	208 ng/mL

14. LIMITATIONS OF METHOD

- A positive result suggests the likely presence of amphetamines but does not indicate or measure intoxication.
- The presence of amphetamines in urine is only an indication of recent exposure to or use of amphetamines.

- The psychological and physiological effects of amphetamines do not necessarily correlate with urinary concentration.
- A positive AMPH result suggests the likely presence of drug and its metabolites. The AMPH method cannot fully quantitate the concentration of individual components.
- Interpretation of results must take into account that urine concentrations vary extensively with fluid intake, and other biological variables.
- There is a possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.
- NEGATIVE results for specimens with concentrations below the assay range may be accompanied by an "assay range" or by a "below assay range" message. These results should be reported as NEGATIVE.
- POSITIVE results for specimens with concentrations above the assay range may be accompanied by an "assay range" or by an "above assay range" message. These results should be reported as POSITIVE.

14.1 Analytical Measurement Range (AMR)

Qualitative Assay: 125 – 1800 ng/mL (for 1000 ng/mL cutoff)

14.2 Precision

Material	Mean ng/mL	Standard Deviation (%CV)	
		Repeatability	Within-Lab
Calibrator Control ng/mL			
225	248	19.1 (8)	20.1 (8)
300	320	11.3 (4)	18.5 (6)
375	391	21.4 (5)	28.0 (7)
500	545	20.5 (4)	26.2 (5)
625	684	40.3 (6)	50.2 (7)

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.

AMPH Flex® Reagent Cartridge is harmful to aquatic life with long lasting effects. Contains: 2-methyl-4-isothiazolin-3-one. Avoid release into the environment.

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 AMPH Flex® Reagent Cartridge K5091

17. REFERENCES

1. Package Insert, AMPH Flex® Reagent Cartridge K5091, Siemens Healthcare Diagnostics Inc., 05/05/2015.
2. Package Insert, UDAT CAL, Siemens Healthcare Diagnostics Inc., 05/2011.
3. Package Insert, Liquichek Urine Toxicology Controls, Bio-Rad Laboratories, 08/2016.

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
000	7/6/16		Update owner	L Barrett	R SanLuis
000	7/6/16	Header	Add WAH	L Barrett	R SanLuis
000	7/6/16	3.1, 3.2	Add urine collection kit	L Barrett	R SanLuis
000	7/6/16	4.2	Add safety instructions	A Chini	R SanLuis
000	7/6/16	5.2	Remove uncapped calibrator storage	A Chini	R SanLuis
000	7/6/16	6.4, 6.6	Replace LIS with Unity Real Time	L Barrett	R SanLuis
000	7/6/16	11.3	Add report comments	A Chini	R SanLuis
000	7/6/16	16	Update titles	L Barrett	R SanLuis
000	7/6/16	17	Update PI dates	A Chini	R SanLuis

Version	Date	Section	Reason	Reviser	Approval
000	7/6/16	Footer	Version # leading zero's dropped due to new EDCS in use as of 10/7/13.	L Barrett	R SanLuis
1	12/1/17	3.2	Add room temp storage for 4 hours, remove onboard stability	L Barrett	R SanLuis
1	12/1/17	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
1	12/1/17	7.2	Change low freezer temp from -70 to -50	L Barrett	R SanLuis
1	12/1/17	10.5	Move patient review from section 6	L Barrett	R SanLuis
1	12/1/17	13	Add reference to validation for specimen stability	L Barrett	R SanLuis
1	12/1/17	15	Update to new standard wording, move hazard statement from 4.2	L Barrett	R SanLuis
1	12/1/17	17	Update QC PI date	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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