Laboratory Procedure Manual

Analyte: **Sodium, Potassium, Chloride (Electrolytes)**

Matrix: **Urine**

Method: **Roche Ion-Selective Electrode**

Method No: 4047.03

Revised: March, 2016

As performed by:

Nutritional Biomarkers Branch
Division of Laboratory Sciences
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Important Information for Users

CDC periodically refines these laboratory methods. It is the responsibility of the user to contact the person listed on the title page of each write-up before using the analytical method to find out whether any changes have been made and what revisions, if any, have been incorporated.

Public Release Data Set Information

This document details the Lab Protocol for testing the items listed in the following table:

Data File Name	Variable Name	Description
HULT_H_R SSLT_H_R U1LT_H_R U2LT_H_R	URHCLMSI	Chloride, Urine AM Collection (mmol/L)
	URHKMSI	Potassium, Urine AM Collection (mmol/L)
	URHNAMSI	Sodium, Urine AM Collection (mmol/L)
	URHCLESI	Chloride, Urine PM Collection (mmol/L)
	URHKESI	Potassium, Urine PM Collection (mmol/L)
	URHNAESI	Sodium, Urine PM Collection (mmol/L)
	UR1NASI	Sodium, Urine – 1st Collection (mmol/L)
	UR1KSI	Potassium, Urine – 1st Collection (mmol/L)
	UR1CLSI	Chloride, Urine – 1st Collection (mmol/L)
	UR2NASI	Sodium, Urine – 2nd Collection (mmol/L)
	UR2KSI	Potassium, Urine – 2nd Collection (mmol/L)
	UR2CLSI	Chloride, Urine – 2nd Collection (mmol/L)
	SSUNASI	Sodium, Urine – MEC Collection (mmol/L)

	SSUKSI	Potassium, Urine – MEC Collection (mmol/L)
	SSUCLSI	Chloride, Urine – MEC Collection (mmol/L)

1. Summary of Clinical Relevance and Test Principle

A. Clinical relevance

Sodium measurements are used in the diagnosis and treatment of aldosteronism (excessive secretion of the hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease (caused by destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance.

Potassium measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels.

Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

The urine electrolytes sodium, potassium and chloride are principally used as nutritional indicators in healthy persons. They are infrequently measured in clinical settings, and when they are it is usually in Intensive/Critical care units. Their measured values are not diagnostic of any disease in and of themselves; rather they can in certain special situations be used to help support the diagnosis of several somewhat rare clinical conditions. The more important use of urinary electrolyte data is for public health studies. Urine sodium data is an important biomarker of dietary sodium intake.

B. Test principle

An Ion-Selective Electrode (ISE) makes use of the unique properties of certain membrane materials to develop an electrical potential (electromotive force, EMF) for the measurements of ions in solution. The complete measurement system for a particular ion includes the ISE, a reference electrode, and electronic circuits to measure and process the EMF to give the test ion concentration. The type of ISE used on the Hitachi ISE Module(s) is classified as liquid/liquid junction type. The sodium **[1, 2]** and potassium **[3]** electrodes are based on neutral carriers and the chloride **[4]** electrode is based on an ion exchanger. For determinations on the ISE Module(s), the sample is diluted 1:31 and a single 15 uL sample is taken for the three assays.

2. Safety Precautions

Consider all specimens potentially positive for infectious agents including HIV, hepatitis B and hepatitis C. We recommend that the hepatitis B vaccination series for all the analysts working with whole blood and/or serum. Observe universal precautions; wear protective gloves, laboratory coats, and safety glasses during all steps of this method. Discard any residual sample material by autoclaving after analysis is completed. Place all disposable plastic, glassware, and paper (pipette tips, vials, gloves, etc.) in a biohazard autoclave bag and keep these bags in appropriate containers until sealed and autoclaved. Wipe down all work surfaces with 10% bleach solution when work is finished.

Handle acids and bases with extreme care; they are caustic and toxic. Handle organic solvents only in a well-ventilated area or, as required, under a chemical fume hood.

Reagents and solvents used in this study are listed in Section 6. Material safety data sheets (MSDSs) for all chemicals are readily accessible as hard copies in the lab.

3. Computerization and Data System Management

A. During sample preparation and analysis, samples are identified by their sample ID. The sample ID is a number that is unique to each sample that links the laboratory information to demographic data recorded by those who collected the sample.

B. Calculation of Sodium, Potassium and Chloride concentrations are accomplished with the software on the Roche Mod P and generated data are transferred to the DLS network where it is saved. The results file is imported into a database for review of the patient data, statistical evaluation of the QC data, and approval of the results. See "**SOP Computerization and Data System Management**" for a step-by-step description of data transfer, review and approval.

C. NHANES data is transmitted electronically on a regular basis (approximately weekly for 3-week turnaround analytes). Abnormal values are confirmed by the analyst, and codes for missing data are entered by the analyst and are transmitted as part of the data file. NCHS makes arrangements for the abnormal report notifications to the NCHS Survey Physician.

D. The data file and results file from the instrument workstation are typically backed up daily to the Roche/Hitachi USB Memory Stick for long-term storage. This is the responsibility of the analyst under the guidance of the project lead person. Files stored on the DLS network are automatically backed up nightly by ITSO support staff.

4. Specimen Collection, Storage, and Handling Procedures: Criteria for Specimen Rejection

A. Use serum free of hemolysis and gross lipemia, collected by standard venipuncture technique **[5]**. Only lithium heparin plasma may be used. Do not allow serum to remain on the cells after centrifugation. Potassium from the red cells will diffuse into the serum, giving falsely elevated results. Urine should be collected without using preservatives and stored refrigerated during collection **[6]**.

B. The appropriate amount of serum/plasma/urine is dispensed into a Nalge cryovial or other plastic screw-capped vial labeled with the participant's ID.

C. Specimens collected in the field are frozen, and then shipped on dry ice by overnight mail. Frozen samples are stored at -70°C. When separated from erythrocytes and stored tightly stoppered at 2-8°C, chloride content is stable for several days **[6]**. Sodium and potassium are stable for 2 weeks at 15-25°C or 2-8°C **[7]**.

D. Centrifuge samples containing precipitate before performing the assay. Grossly lipemic specimens should be cleared by ultracentrifugation. Turbid urine samples should be cleared by centrifugation.

E. A 500-µL sample of serum/plasma/urine is required to allow for repeat analyses; a volume of 150 µL is required for pipetting into the sample cup for analysis.

F. Ensure patient samples, calibrators and QC are at ambient temperature (20-25°C) before measurement.

G. Because of possible evaporation effects, all samples, calibrators, and QC on the analyzer should be measured within 2 hours.

H. Specimens generally arrive frozen. Refrigerated samples may be used provided they are kept cold and brought promptly (within 2 hours) from the site of collection.

I. Specimen handling conditions are outlined in the DLS Policies and Procedures Manual. The protocol discusses collection and transport of specimens and the special equipment required. If there is more than one analyte of interest in the specimen and it needs to be divided, the appropriate amount of blood, serum or plasma should be transferred into a sterile Nalge cryovial labeled with the participant's ID.

J. Samples thawed and refrozen less than six times are not compromised. If there is more than one analyte of interest in the specimen and it needs to be divided, the appropriate amount of blood or plasma should be transferred into a sterile Nalge cryovial labeled with the participant's ID.

5. Procedures for Microscopic Examinations: Criteria for Rejection of Inadequately Prepared Slides

Not applicable for this procedure.

6. Preparation of Reagents, Calibration (Standards), Controls, and All Other Materials: Equipment and Instrumentation

A. Reagent Preparation

The reagents are available from Roche Diagnostics and are prepared as follows **[8]**:

1) ISE Reference Electrolyte (catalog #10820652216) is in liquid form, ready for use.
2) ISE Diluent Gen2 (catalog #04880480190) is in liquid form, ready for use.
3) ISE Internal Standard Gen2 (catalog #04880455190) is in liquid form, ready for use.

The reagents are stable up to the stated expiration date at 15–25°C.

NOTE: The caps on the ISE reagent lines are not an exact fit with the 2 liter bottle. Place the cap over the bottle, but do not tighten. Ensure that the reagent line filter reaches the bottom of the bottle without obstruction from the indentations in the bottle.

Sodium, Potassium, Chloride and Reference electrodes are stable until the expiration date on the label when stored at 7-40°C. The on-board stability for the Na^+, K^+ and Cl^- electrodes is 2 months or 9000 tests. The Reference electrode stability is at least 6 months. The electrodes should be replaced after this time period has expired; however, since the instrument is not run on a daily basis, the electrodes will be replaced when slope readings indicate it is needed.

Sodium	50 to 68 mV/dec
Potassium	50 to 68 mV/dec
Chloride	-40 to -68 mV/dec

The slope ranges for newly installed electrodes should be in the upper half of the recommended electrode slope range (excluding chloride).

B. Standards Preparation

Standards are available from Roche Diagnostics in liquid form, ready to use.

STD 1: ISE Standard Low. Cat. No. 11183974 216, Code 502.
STD 2: ISE Standard High. Cat. No. 11183982 216, Code 503.
STD 3: ISE Standard High. Cat. No. 11183982 216, Code 763.

An internal standard solution is measured during calibration and between each sample to correct the calibration for drift between calibrations.

The standards are stored at room temperature and are stable until the expiration date on the box.

C. Preparation of Quality Control Materials

1) Serum QC pools

For serum Na^+, K^+ and Cl^- , quality control material can be purchased from Roche Diagnostics in two levels (Precinorm U Plus and Precipath U Plus). The controls are lyophilized and require reconstitution. Carefully open one bottle 1, avoiding the loss of lyophilizate and pipette in exactly 3.0 mL of diluent (bottle 2). Carefully close the bottle and dissolve the contents completely by occasional gentle swirling within 30 minutes. Avoid the formation of foam. Stability of Na^+, K^+ and Cl^- in the reconstituted controls is 5 days at 2-8°C or 4 weeks at -15 to -25°C when frozen once. Unopened controls are stable at 2-8°C until the expiration date.

2) Urine QC pools

For urine Na^+, K^+ and Cl^- , commercially prepared quality control material is purchased from CLINIQA in two levels (LIQUID QC™ 1 and LIQUID QC™ 2). The controls are liquid and ready for use. Stability of the constituents at 2-8°C is 36 months or until the expiration date, whichever comes first.

D. Other Materials

The following materials are available from the manufacturer (Roche Diagnostics):

1) Sample trays
2) Sample cups (standard and micro)
3) Sodium cartridge
4) Potassium cartridge
5) Chloride cartridge
6) Reference cartridge

E. Instrumentation

1) MODULAR ANALYTICS E170® system (Roche Diagnostics, Indianapolis, IN)
2) Daigger Vortex Genie 2 (VWR, Suwanee, GA)
3) Eppendorf micropipet and tips (Brinkmann Instruments Co., Westbury, NY)

7. Calibration and Calibration Verification Procedures

For commercial kit assays, calibration procedures recommended by the manufacturer are followed.

Calibration requires the use of low and high standard solutions available from Roche Diagnostics. The low ISE Standard is used for STD 1 and the high ISE Standard is used for STD 2 and STD 3.

Full Calibration is recommended as follows:

- every 24 hours

- after ISE cleaning
- after change of reagent bottle
- after replacement of any electrode
- following any dispense system component replacement or any major maintenance performed on the instrument

Please refer to the Roche *Modular Analytics® Operator's Manual* and the "**SOP Modular PE Calibration**" for additional details.

Calibration verification is conducted at least twice a year using international reference materials. For details, see **4047_SOP Calibration and Calibration Verification Na K Cl**.

NIST SRM 2201 Sodium Chloride and **NIST SRM 2202 Potassium Chloride** are available for calibration verification.

We participate in the **College of American Pathologists (CAP)** Urine Chemistry (U) and Urine Chemistry CAL V/L (LN6) challenge twice a year. We also participate in the General Chemistry (C) survey three times a year and the Chem/Lipid/Enzyme Cal V/L (LN1) survey twice a year.

This method has been standardized against primary calibrators prepared gravimetrically from purified salts.

Method figures of merit are presented in **Appendix 1**.

As this assay must be performed according to the manufacturer's specifications, none of the parameters can be altered. Therefore, ruggedness testing cannot be performed for this assay.

8. Procedure Operating Instructions, Calculations, and Interpretation of Results

A. Preliminaries

1) Allow patient samples, calibrators and QC to reach ambient temperature.
2) Ensure that the amount of reagents is adequate for the amount of samples to be run.
3) Make sure the analyzer and the tests required are not masked.
4) Check to see if calibration is required for the tests to be run.
5) If running the same tests on all samples, go to the "Start" global button and set the "default profile".
6) Be sure to clear all previously programmed samples from the Data Review screen after backing up the data.
7) Perform the required maintenance on the ISE Module.

B. Instrument Maintenance

1) The ISE Module maintenance consists of daily, weekly and as needed maintenance.
2) Daily maintenance should be performed at the start of each 8-hour shift, or more frequently, if necessary. The "green rack" should be run to clean and condition the ISE module after all sampling is completed for the day.
3) For additional maintenance requirements, refer to the instrument maintenance logs. For detailed, step by step instructions, refer to the Roche Modular Analytics ® Operator's Manual **[9]**.

C. Preparing the Run

One run is defined as 100 patient samples or less. Controls are run at the beginning and the end of each run.

When performing small runs or confirmation (repeat) runs, all levels of QC pools must be run in duplicate.

NOTE: Be sure to backup all previous test results and clear the "data review" screen before starting a new run.

1) Thoroughly mix all calibrators, QC and patient samples before pipetting. Visually check for any unusual sample volume, specimen color or debris/precipitate.
2) Prior to loading samples on the instrument, ensure that no air bubbles are present in the sample cups. Break a wood applicator into pieces and use them to pop the bubbles if necessary.
3) For a calibration run, use **black** calibrator racks. Open the barcoded calibrators and place them in an unassigned **black** calibrator rack. Nonbarcoded calibrators must be pipetted into sample cups and placed in their assigned positions in **black** calibrator racks. When calibration is completed, the results will be printed.
4) To run QC, use the **white** QC racks. If using Roche QC, open the barcoded QC's and place them in the **white** assigned rack and position. For CDC QC, pipette 150 µL of each nonbarcoded QC into a sample cup and place atop the tube in the assigned control position of the **white** QC racks. When the instrument is started, it will automatically run the correct tests on the preprogrammed QC and print the results.
5) To run patient samples, use the **gray** sample racks. Place empty sample cups onto barcode labeled 13 X 75 tubes in **gray** sample racks and pipette 150 µL of the serum samples into the sample cup. Pipette 20-25 samples at a time and immediately place the racks on the input buffer tray. **Gray racks with yellow stickers are for urine samples only**. Patient results do not print until requested.

D. Initiating a Run

Do not load samples on the input tray if the green light is flashing.

When the instrument starts, it will run the default profile on all samples unless programmed differently prior to loading.

1) Once the calibrator, control or sample racks are loaded on the input tray, they should be measured within 2 hours because of possible evaporation effects. Calibration and QC checks must be completed before pipetting patient samples.
2) For detailed, step by step instructions, refer to "**SOP Modular PE Operation"** or the Roche *Modular Analytics® Operator's Manual.*

E. Processing and Reporting a Run

1) The Hitachi Modular PE Control Module is used to review data and check for samples that need to be diluted or repeated for confirmation. The LIMS database is used for additional levels of data review by the analyst, project lead, QA officer, and supervisor and for data reporting.

2) For more detailed information, refer to Section 3 and the "**SOP Computerization and Data System Management".**

F. Special Method Notes

The system can be completely turned off for the weekend or extended holidays or when indicated by maintenance procedure or error code. Refer to the Roche *Modular Analytics® Operator's Manual* for instructions.

G. Calculations

All calculations are performed by the Hitachi Mod PE® Software system using a machine-stored calibration curve.

H. CDC Modifications

The method is run exactly as stipulated by Roche Diagnostics; CDC has introduced no modifications.

9. Reportable Range of Results and Sample Dilution

Serum/Plasma	**Urine**
Na^+: 80-180 mmol/L	Na^+: 20-250 mmol/L
K^+: 1.5-10.0 mmol/L	K^+: 3-100 mmol/L
Cl^-: 45-140 mmol/L	Cl^-: 20-250 mmol/L

If manual dilution is necessary, dilute the specimen with deionized water and re-assay. Multiply the result obtained by the appropriate dilution factor.

10. Quality Control (QC) Procedures

A. Blind Quality Controls

Blind QC specimens can be inserted into the mix of patient specimens. These QC specimens are generally prepared at two levels that would be encountered in patient samples; the labels used are identical to those used for patient samples. One blind QC specimen randomly selected for concentration is included at a randomly selected location in every 20 specimens analyzed.

Alternately, open label blind QC specimens can be used where the analyst knows that the sample is a blind QC, but they do not know what pool the sample is from. Open label blind QCs are only used if one can choose from at least 6 different pools and the analyte concentrations are similar to those found in patient samples.

B. Bench Quality Controls

Commercially prepared QC specimens are used for bench QC. These pools are analyzed in duplicate as part of each run.

Two QC pools per run with two or more QC results per pool:

1) If both QC run means are within 2Sm limits and the individual results are within 2Si limits, then accept the run.
2) If one of the two QC run means is outside the 2Sm limit -reject run if:
   a) 3S Rule – Run mean is outside a 3 Sm limit.
   b) 2S Rule – Both run means are outside the same 2Sm limit.
   c) 10 X-bar Rule – Current and previous 9 run means are on same side of the characterization mean.
3) If one of the four QC individual results is outside a 2Si limit – reject run if:
   a) Extreme Outlier – Run mean is beyond the characterization mean +/- 4Sm
   b) R 4S Rule – Within-run ranges for both pools in the same run exceed 4Sw (i.e. 95% range limit).

Note: Since runs have multiple results per pool for 2 pools, the R 4S rule is applied within runs only.

Si = Standard deviation of individual results (the limits are not shown on the chart unless run results are actually single measurements).
Sm = Standard deviation of the run means (the limits are shown on the chart).
Sw = Within-run standard deviation (the limits are not shown on the chart).

The QC results are checked after each run using of a multi-rule quality control program **[10]**. A QC program written in SAS is available from the DLS Quality Assurance Officer and should be used to apply these rules to QC data and generate Shewhart QC charts. No results for a given analyte are to be reported from an analytical run that has been declared “out of control” for that analyte as assessed by internal (bench) QC. The initial limits are established by analyzing pool material in 20 consecutive runs and then are reevaluated periodically. When necessary, limits are updated to include more runs.

While a study is in progress, QC results are stored in a LIMS database. For runs that are not imported into the database (i.e., R&D, troubleshooting, research-type runs), QC results are stored electronically in the analyte-specific folder on the DLS network. A hardcopy of the QC results from each run is also maintained by the analyst.

11. Remedial Action if Calibration or QC Systems Fail to Meet Acceptable Criteria

A. Check to make sure that the hardware is functioning properly.
B. Recalibrate the instrument.
C. Check reference material.
D. If the steps outlined above do not result in correction of the "out of control" values for QC materials, consult the supervisor for other appropriate corrective actions.
E. Call the Roche “hotline” or service engineer.

F. Do not report analytical results for runs not in statistical control.

12. Limitations of Method; Interfering Substances and Limitation of the Procedures

Samples containing particulate matter should be centrifuged and the material removed before analysis. Grossly lipemic specimens should be cleared by ultracentrifugation.

Do not allow serum to remain on the cells after centrifugation. Potassium from the red cells will diffuse into the serum, giving falsely elevated results.

Hemolysis caused by the release of potassium from as few as 0.5% of the erythrocytes (from specimen collection) can increase the serum level of potassium by 0.5 mmol/L **[11]** and should only be reported at the discretion of the laboratory director. Hemolysis shows no significant interference to sodium or chloride.

Pseudo hyponatremia may be seen with lipemic specimens as a result of fluid displacement **[12]**.
Turbid urine samples should be cleared by centrifugation.

In very rare cases gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.

A list of substances and conditions known to affect the level of sodium, potassium, or chloride in vivo is given by Young et al [13] and Friedman et al [14]. No representation is made by Roche Diagnostics regarding the completeness of these lists or the accuracy of the information contained therein.

13. Reference Ranges (Normal Values)

Serum	**Plasma**
Na^+: 133-145 mmol/L	Na^+: 133-145 mmol/L
K^+: 3.3-5.1 mmol/L	K^+: 3.3-4.5 mmol/L
Cl^-: 96-108 mmol/L	Cl^-: 96-108 mmol/L

Expected values for serum and plasma were established from a study of 4,610 normal, healthy adults **[8]**.

Urine (24 hour) [15]

Na^+: Adult: 40-220 mmol/day (diet dependent)
Full term, 7-14 day old neonates have Na^+ clearance of about 20% of adult values
K^+: 25-125 mmol/day (diet dependent)
Cl-: Infant: 2-10 mmol/day
Child: 15-40 mmol/day
Thereafter: 110-250 mmol/day (diet dependent)

Reference ranges for urine electrolytes measured in spot urine samples will be established once NHANES data is available.

14. Critical Call Results ("Panic Values")

Serum critical limits are as follows:

- Sodium $\leq$120 and $\geq$158 mmol/L
- Potassium $\leq$2.8 and $\geq$6.2 mmol/L

- Chloride $\underline{<}$75 and $\underline{>}$126 mmol/L

Since survey data are transmitted several times weekly to Westat, abnormal reports are automatically forwarded to the NCHS survey physician for follow-up. For smaller, non-NHANES studies, abnormal values are identified to the study principal investigator. Emails sent concerning abnormal results are maintained by the supervisor for the duration of the study. Most of these studies are epidemiological in nature.

15. Specimen Storage and Handling during Testing

Specimens are allowed to reach room temperature during preparation. The unused portion of the patient specimen is returned to the freezer.

16. Alternate Methods for Performing Test; Storing Specimens if Test System Fails

If the analytical system fails, we recommend that the specimens be stored at ≤-20°C until the analytical system is restored to functionality.

17. Test Result Reporting System; Protocol for Reporting Critical Calls (If Applicable)

Test results that are not abnormal are reported to the collaborating agency at a frequency and by a method determined by the study coordinator. Generally, data from this analysis are compiled with results from other analyses and sent to the responsible person at the collaborating agency as an ASCII text file or Excel file, generally through electronic mail or via ftp site.

For NHANES 1999+, all data are reported electronically weekly to Westat who then transfer the results to NCHS. For some smaller studies, hard copies of a data report are sent, as well as the results in electronic format.

18. Transfer or Referral of Specimens; Procedures for Specimen Accountability and Tracking

The LIMS database is used to keep records and track specimens for NHANES 1999+. If analyses are performed for smaller, non-NHANES studies, records may be kept in Excel files on the DLS network.

We recommend that records, including related QA/QC data, be maintained for 10 years after completion of the NHANES study. Only numerical identifiers should be used (e.g., case ID numbers). All personal identifiers should be available only to the medical supervisor or project coordinator. Residual serum from these analyses for non-NHANES studies may be discarded at the request of the principal investigator, or may be transferred to the CDC CASPIR facility for use by other investigators. Very little residual material will be available after NHANES analyses are completed, and these vials may be routinely autoclaved.

The exact procedure used to track specimens varies with each study and is specified in the study protocol or the interagency agreement for the study. Copies of these documents are kept by the supervisor. In general, when specimens are received, the specimen ID number is entered into a database and the specimens stored in a freezer at -70°C. The specimen ID is read off of the vial by a barcode reader used to prepare the electronic specimen table for the analytical system. When the analyses are completed, result file is loaded into the database, and the analytical results are linked to the database by ID number. The

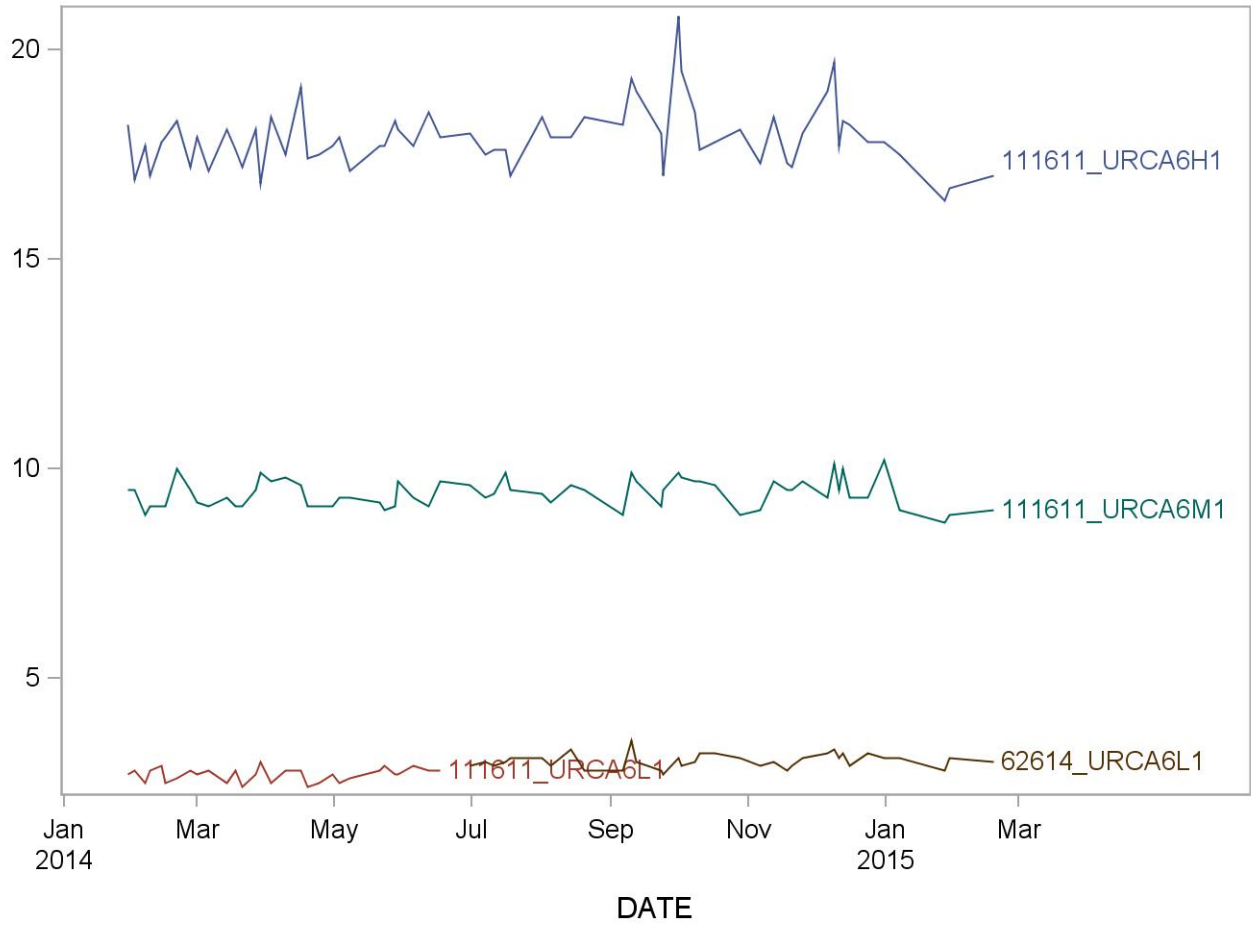
analyst is responsible for keeping a notebook containing the ID numbers of specimens prepared incorrectly, those with labeling problems, and those with abnormal results, together with information about these discrepancies.

19. Summary Statistics and QC Graphs

See the following pages.

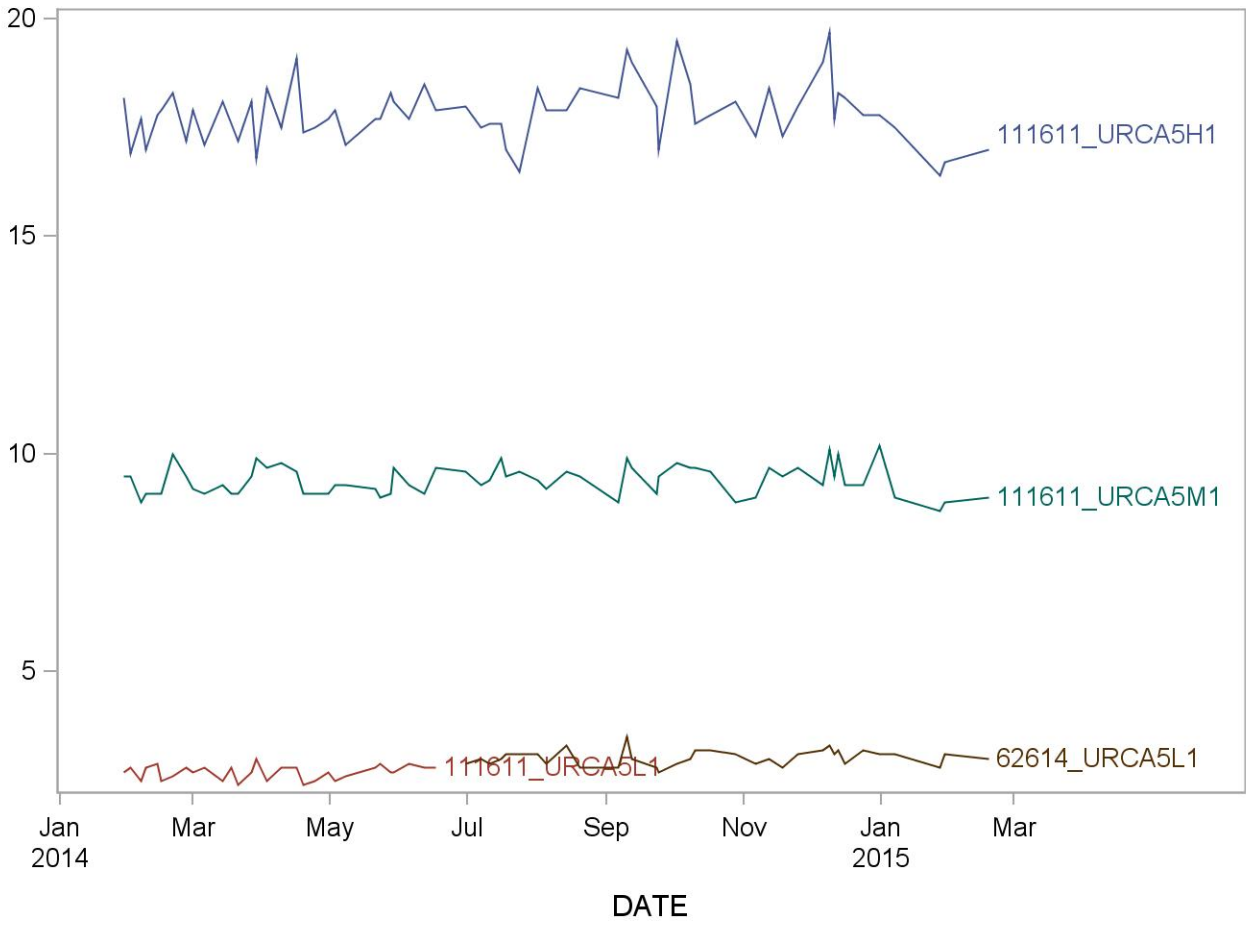
2014 Summary Statistics and QC Chart for Albumin, Urine AM Collection (ug/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
111611_URCA6H1	66	29JAN14	18FEB15	17.889	0.753	4.2
111611_URCA6L1	30	29JAN14	17JUN14	2.697	0.161	6.0
111611_URCA6M1	66	29JAN14	18FEB15	9.406	0.341	3.6
62614_URCA6L1	36	30JUN14	18FEB15	3.028	0.173	5.7



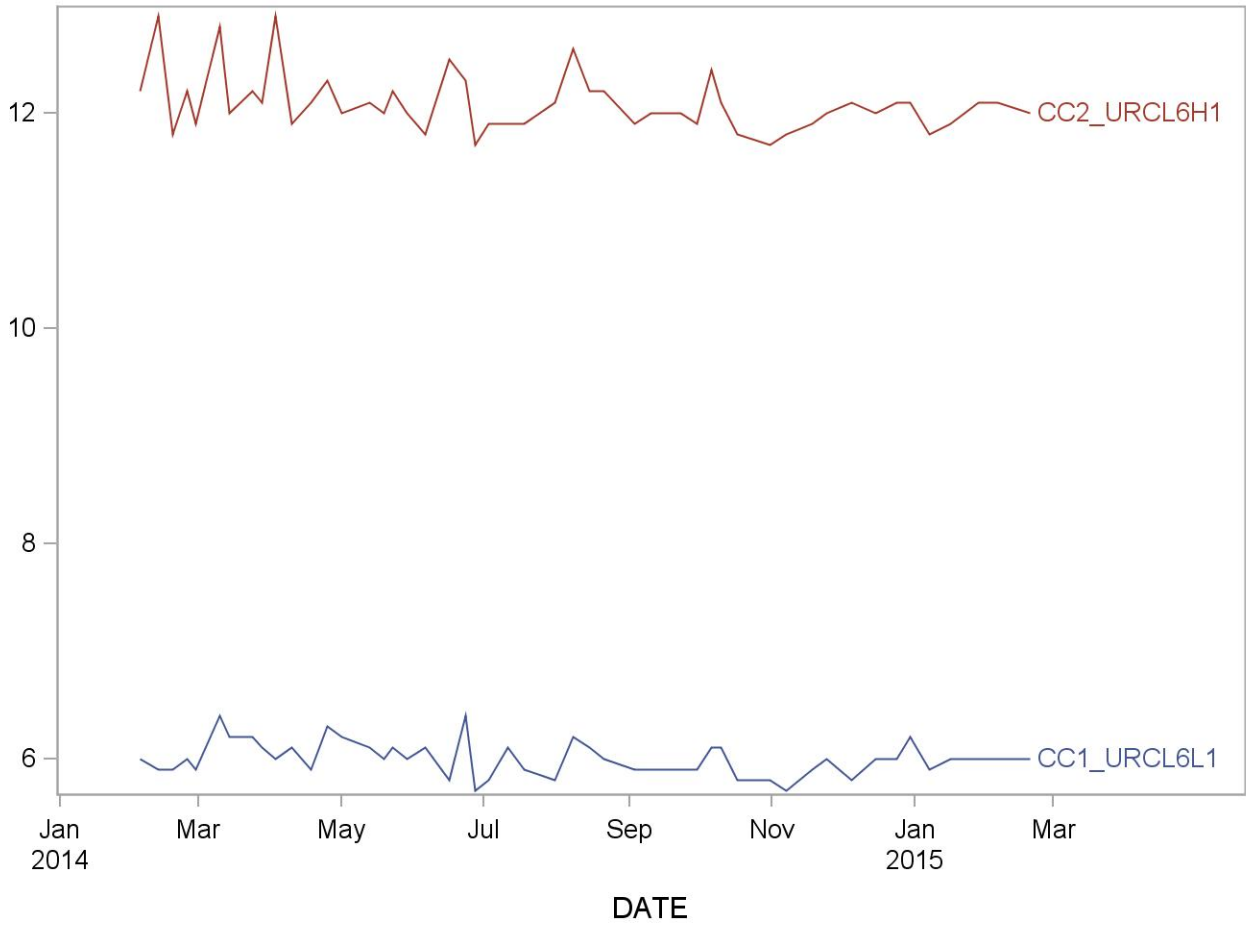
2014 Summary Statistics and QC Chart for Albumin, Urine PM Collection ug/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
111611_URCA5H1	65	29JAN14	18FEB15	17.834	0.680	3.8
111611_URCA5L1	30	29JAN14	17JUN14	2.697	0.161	6.0
111611_URCA5M1	65	29JAN14	18FEB15	9.400	0.339	3.6
62614_URCA5L1	35	30JUN14	18FEB15	3.031	0.175	5.8



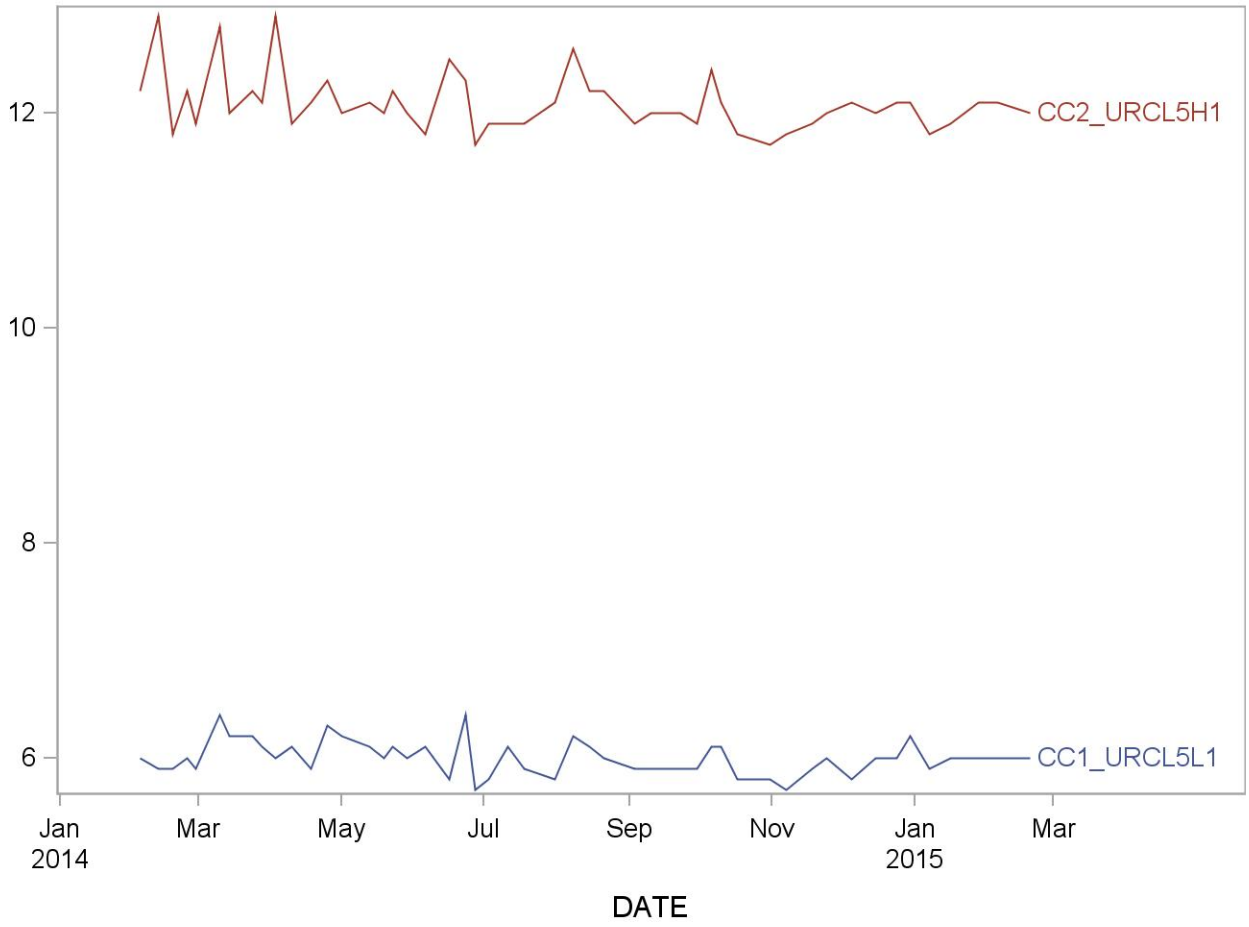
2014 Summary Statistics and QC Chart for Calcium, Urine AM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCL6H1	49	04FEB14	19FEB15	12.09	0.27	2.3
CC1_URCL6L1	49	04FEB14	19FEB15	6.00	0.16	2.7



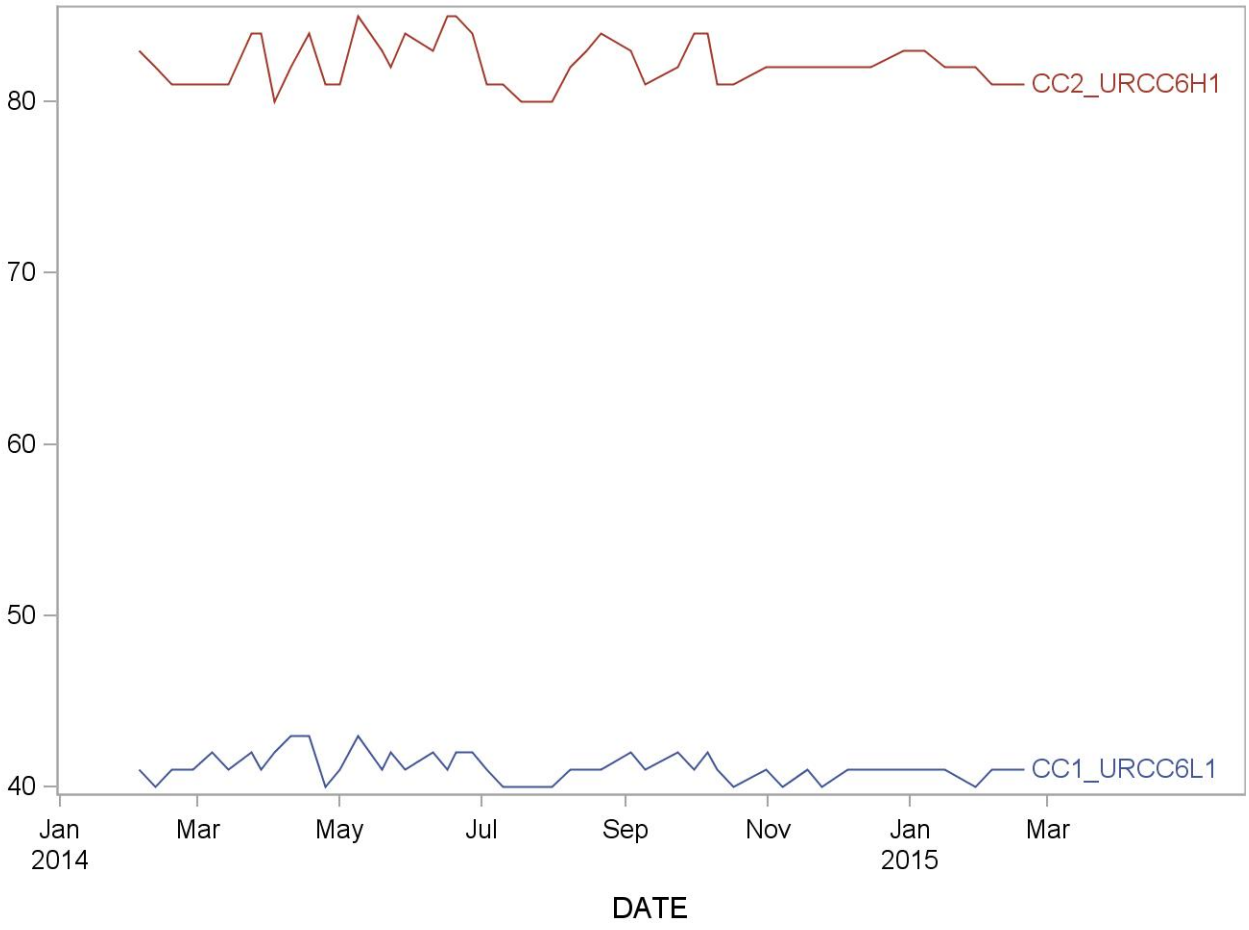
2014 Summary Statistics and QC Chart for Calcium, Urine PM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCL5H1	49	04FEB14	19FEB15	12.09	0.27	2.3
CC1_URCL5L1	49	04FEB14	19FEB15	6.00	0.16	2.7



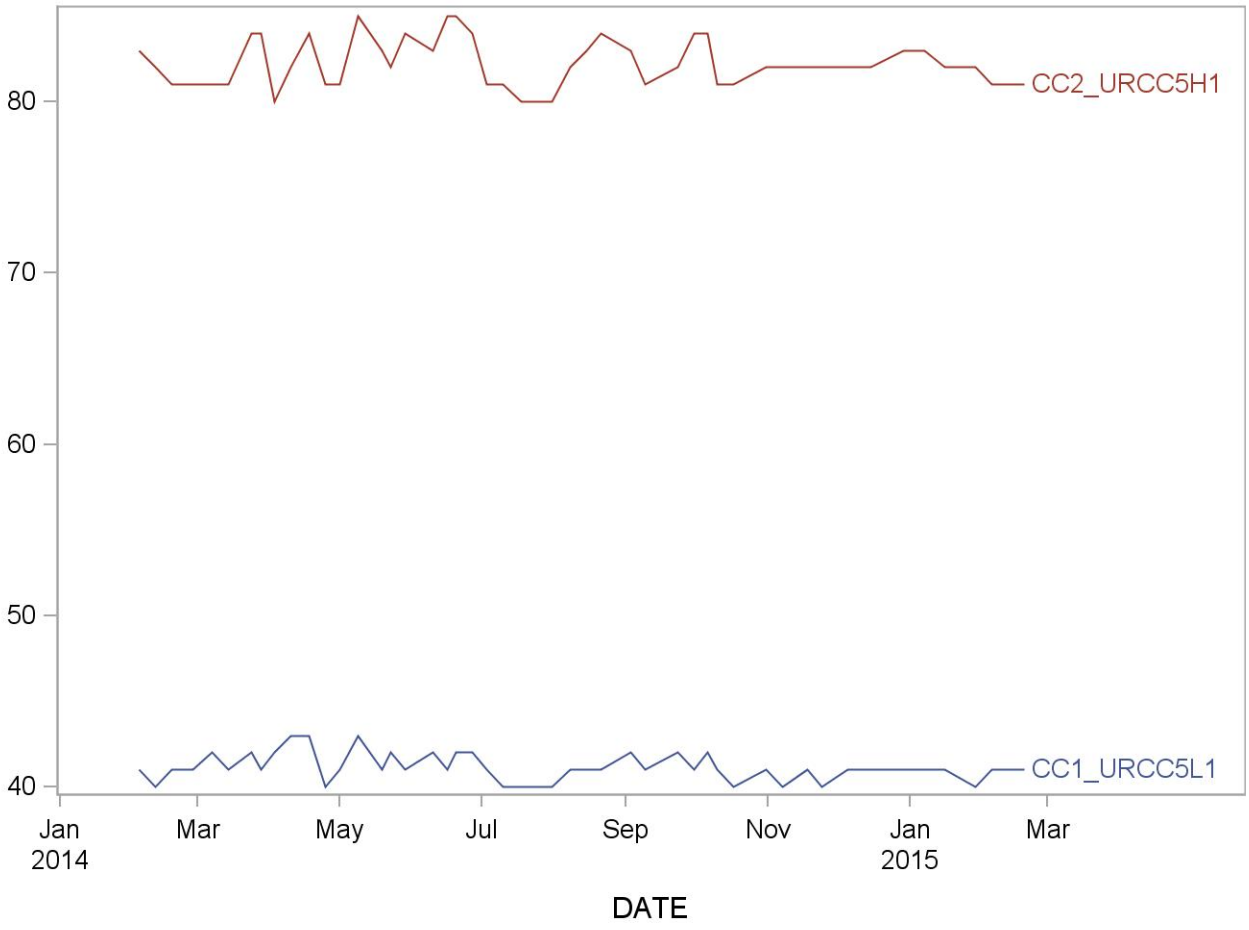
2014 Summary Statistics and QC Chart for Creatinine, Urine AM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCC6H1	48	04FEB14	19FEB15	82.3	1.4	1.7
CC1_URCC6L1	48	04FEB14	19FEB15	41.1	0.8	1.9



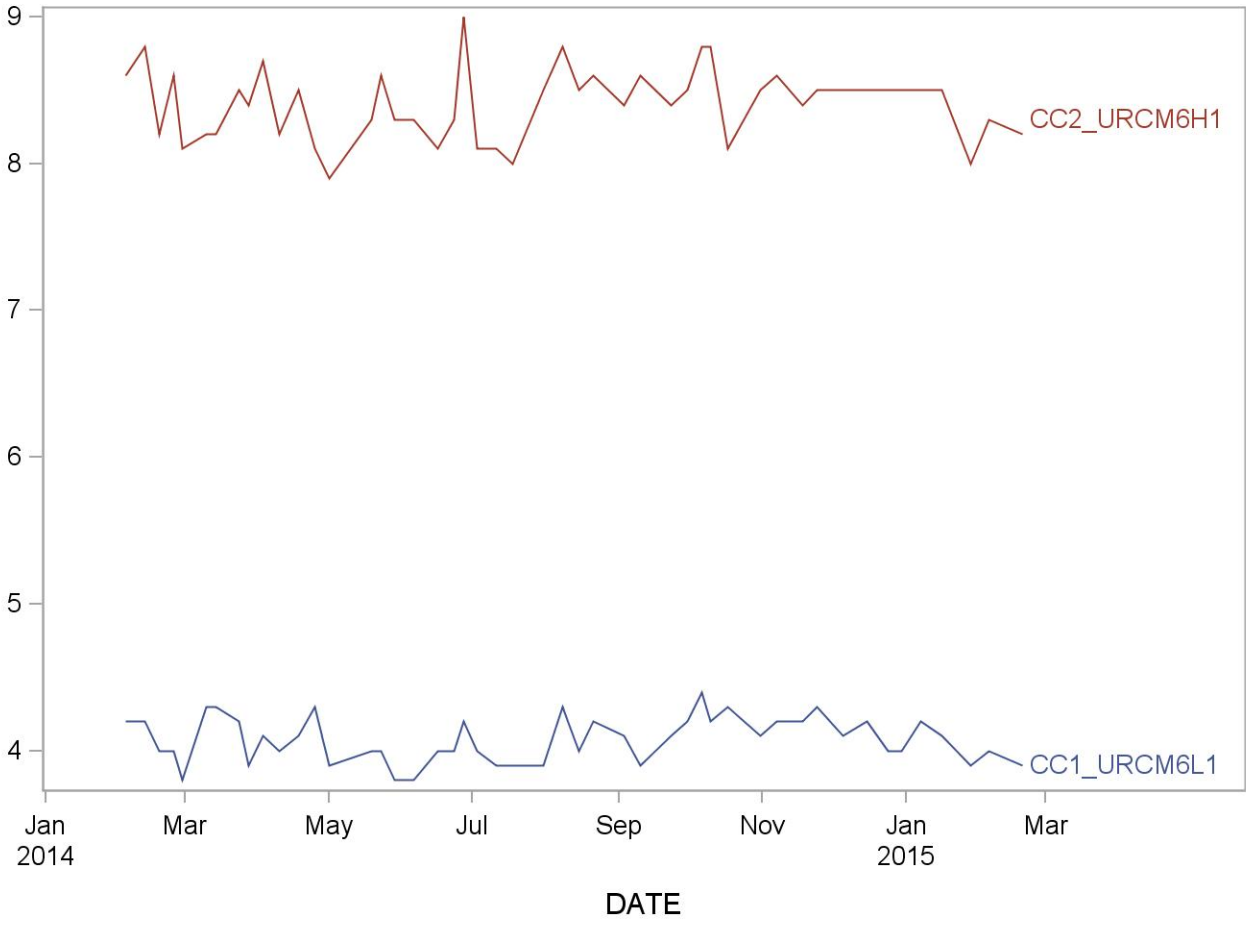
2014 Summary Statistics and QC Chart for Creatinine, Urine PM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCC5H1	48	04FEB14	19FEB15	82.3	1.4	1.7
CC1_URCC5L1	48	04FEB14	19FEB15	41.1	0.8	1.9



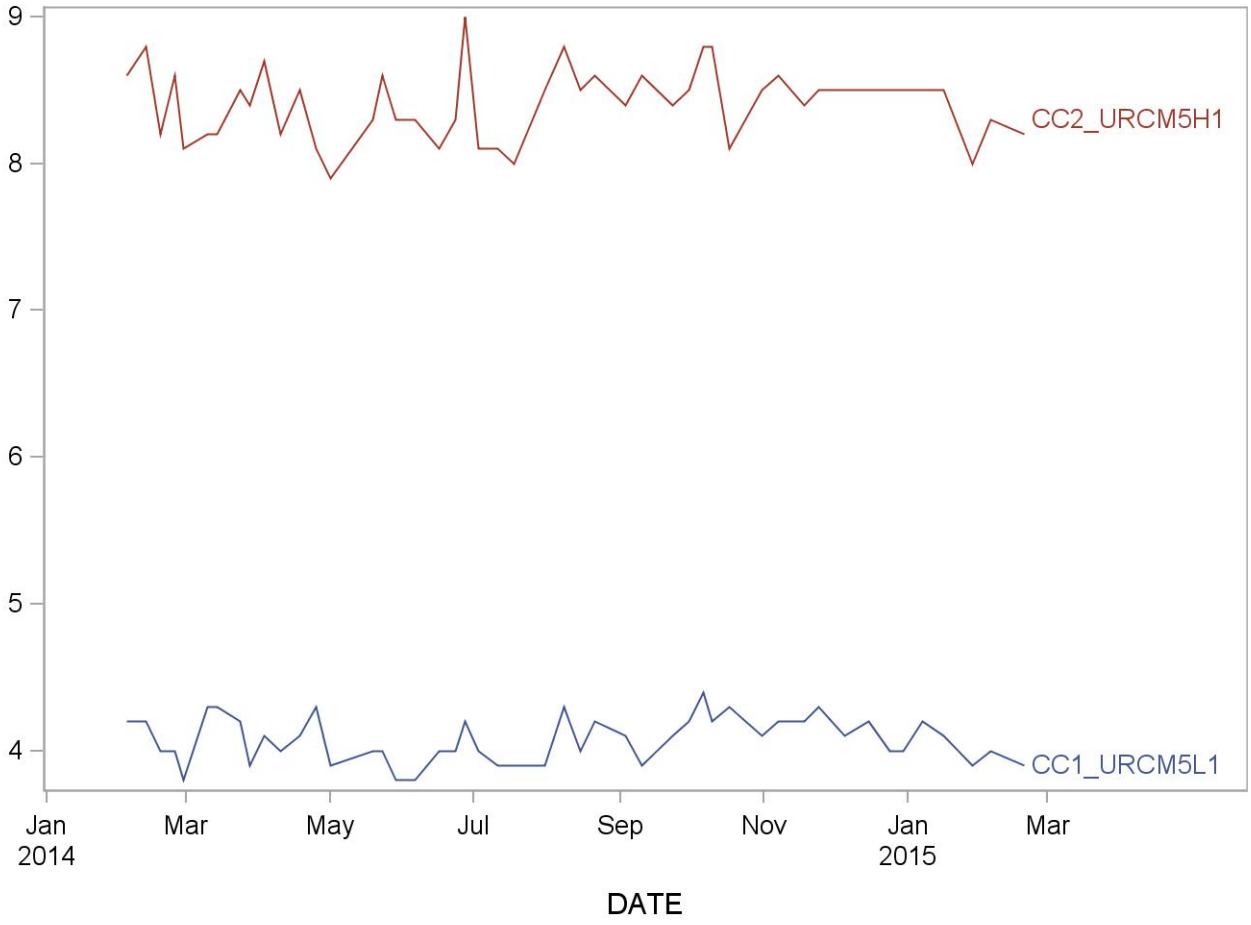
2014 Summary Statistics and QC Chart for Magnesium, Urine AM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCM6H1	48	04FEB14	19FEB15	8.41	0.24	2.9
CC1_URCM6L1	48	04FEB14	19FEB15	4.08	0.15	3.8



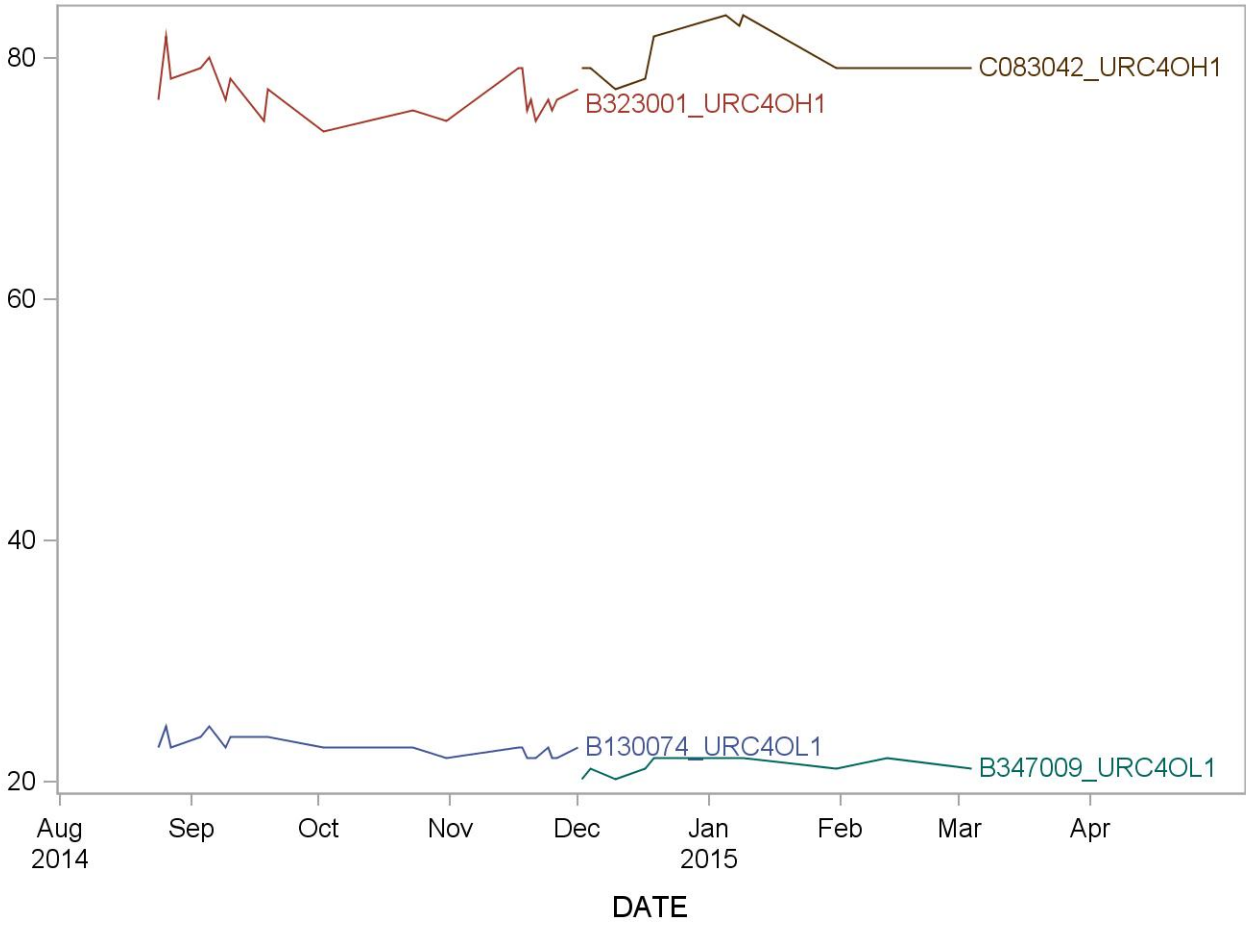
2014 Summary Statistics and QC Chart for Magnesium, Urine PM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCM5H1	48	04FEB14	19FEB15	8.41	0.24	2.9
CC1_URCM5L1	48	04FEB14	19FEB15	4.08	0.15	3.8



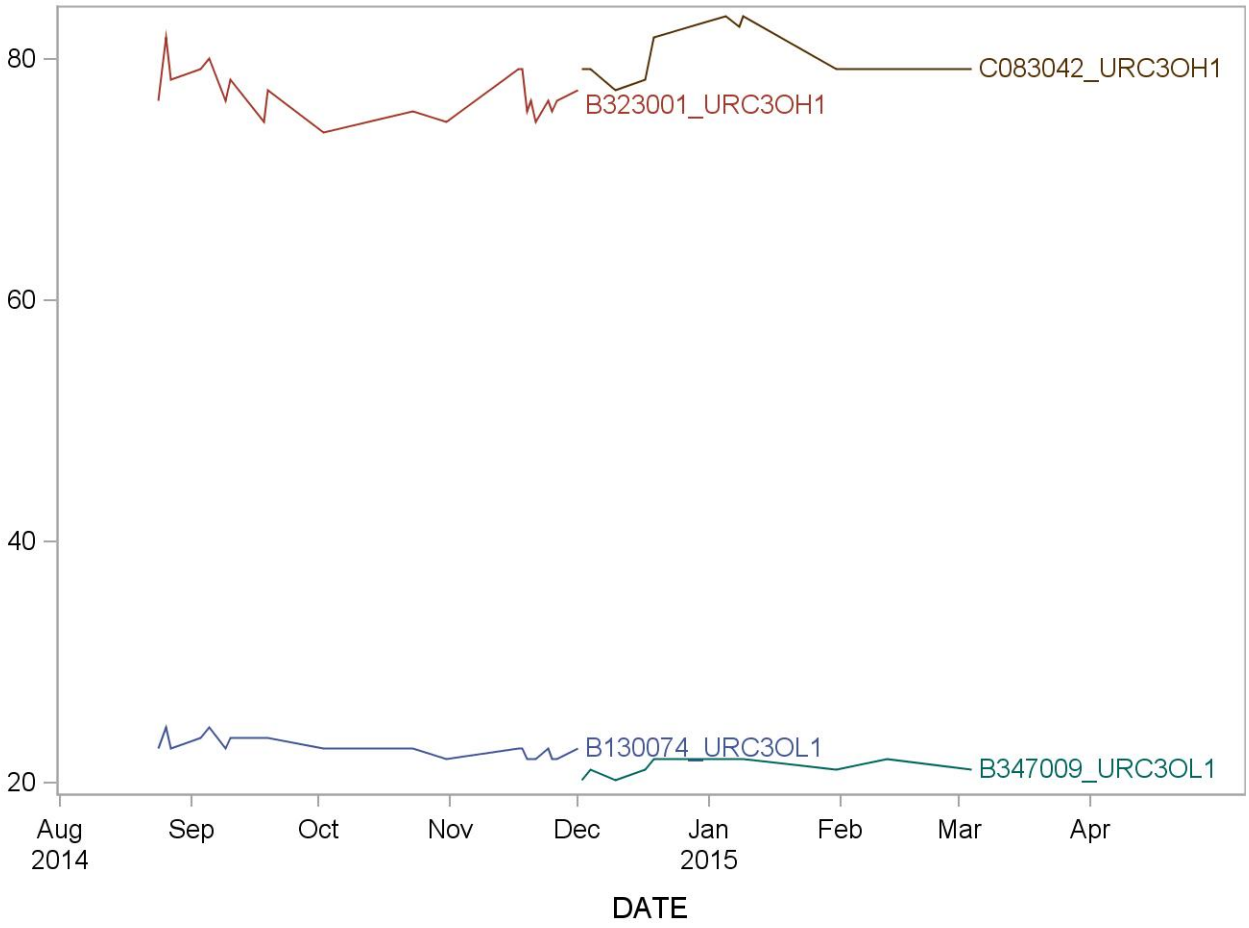
2014 Summary Statistics and QC Chart for Oxalate, Urine AM Collection (mmol/L)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
B323001_URC4OH1	21	24AUG14	01DEC14	77.105	2.016	2.6
B130074_URC4OL1	21	24AUG14	01DEC14	22.964	0.830	3.6
C083042_URC4OH1	11	02DEC14	04MAR15	80.320	2.194	2.7
B347009_URC4OL1	11	02DEC14	04MAR15	21.360	0.692	3.2



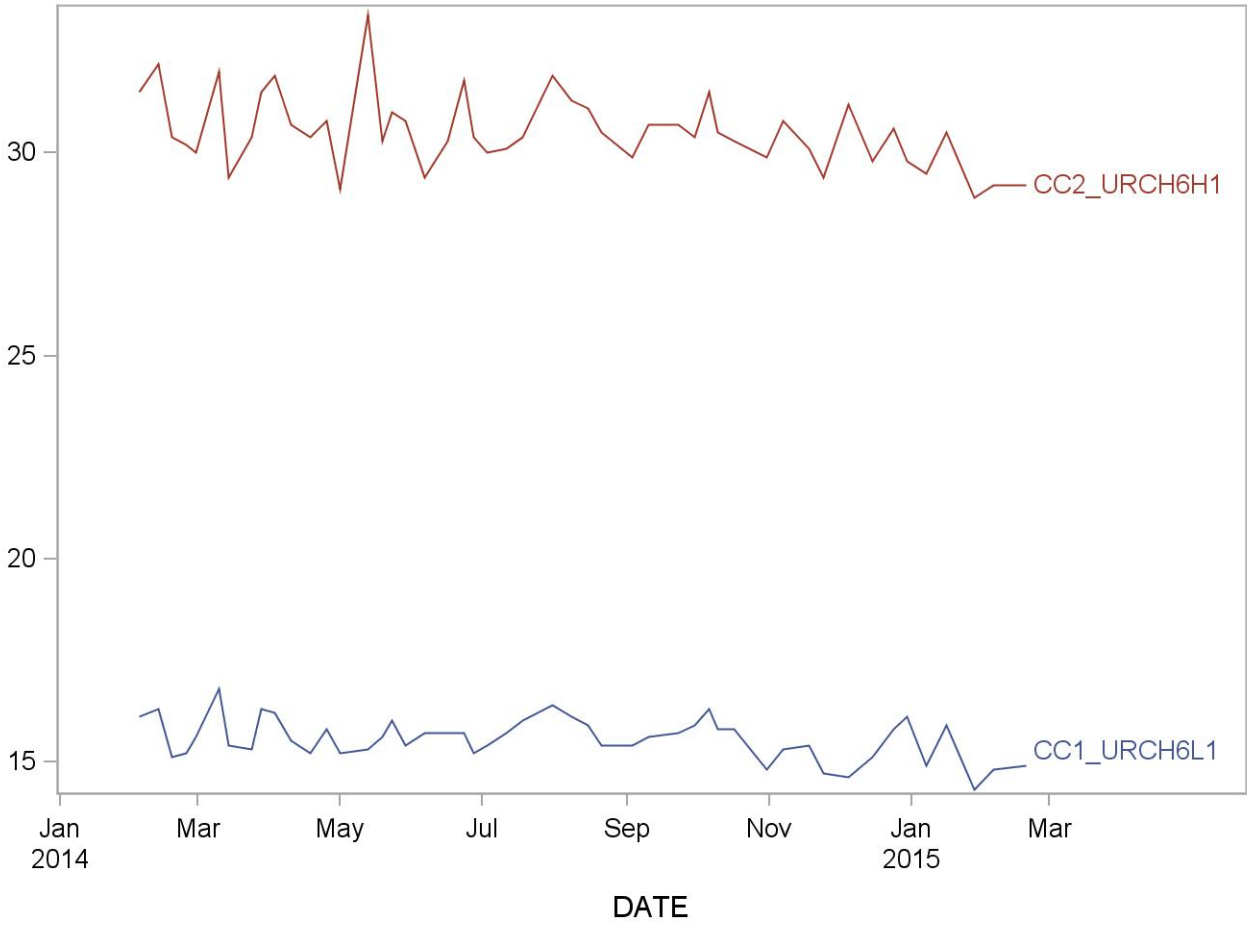
2014 Summary Statistics and QC Chart for Oxalate, Urine PM Collection (mmol/L)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
B323001_URC3OH1	21	24AUG14	01DEC14	77.1048	2.0159	2.6
B130074_URC3OL1	21	24AUG14	01DEC14	22.9638	0.8304	3.6
C083042_URC3OH1	11	02DEC14	04MAR15	80.3200	2.1944	2.7
B347009_URC3OL1	11	02DEC14	04MAR15	21.3600	0.6919	3.2



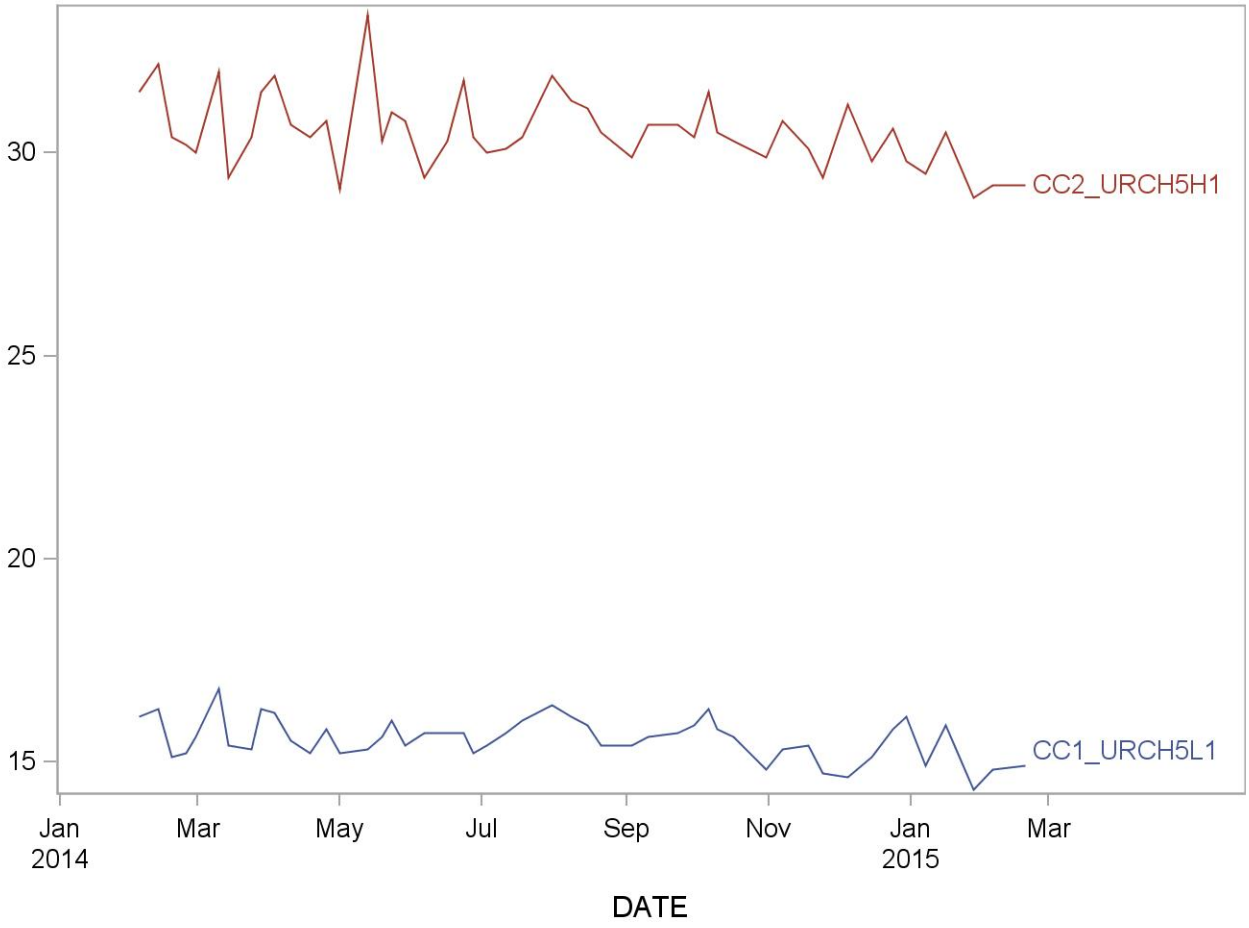
2014 Summary Statistics and QC Chart for Phosphorus, Urine AM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCH6H1	49	04FEB14	19FEB15	30.53	0.91	3.0
CC1_URCH6L1	49	04FEB14	19FEB15	15.56	0.52	3.3



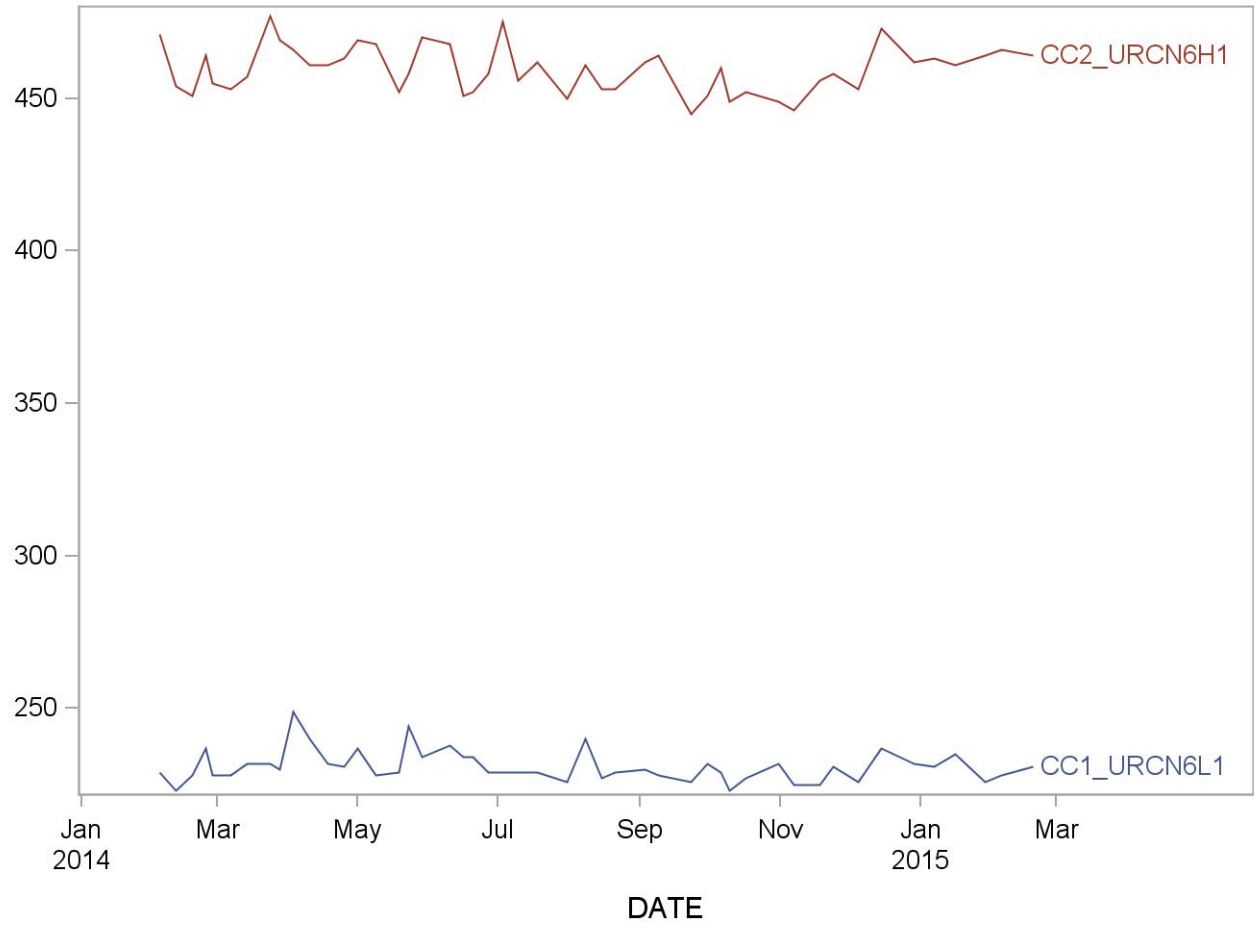
2014 Summary Statistics and QC Chart for Phosphorus, Urine PM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCH5H1	49	04FEB14	19FEB15	30.53	0.91	3.0
CC1_URCH5L1	49	04FEB14	19FEB15	15.56	0.52	3.3



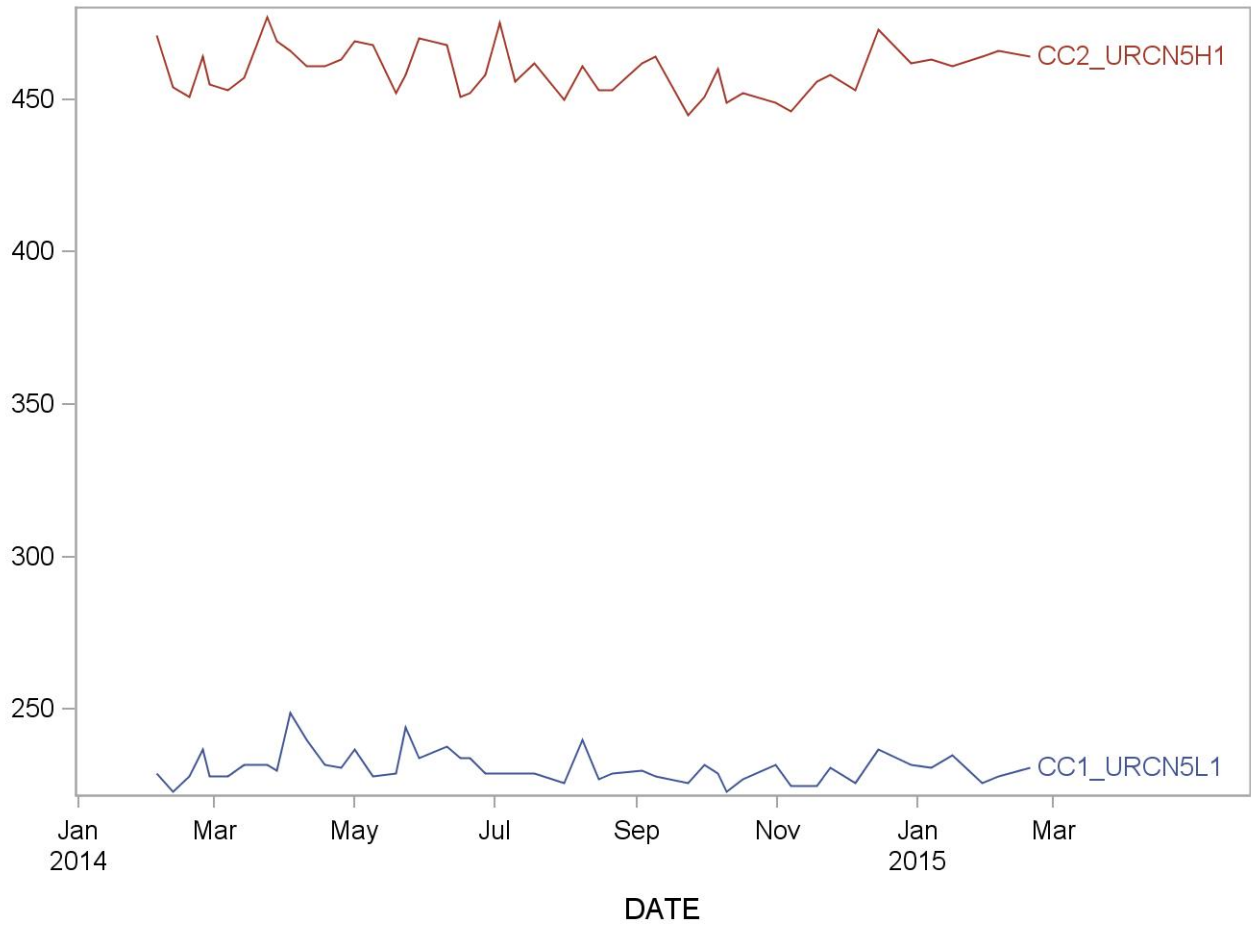
2014 Summary Statistics and QC Chart for Urea Nitrogen, AM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCN6H1	48	04FEB14	19FEB15	459.5	7.8	1.7
CC1_URCN6L1	48	04FEB14	19FEB15	231.0	5.2	2.3



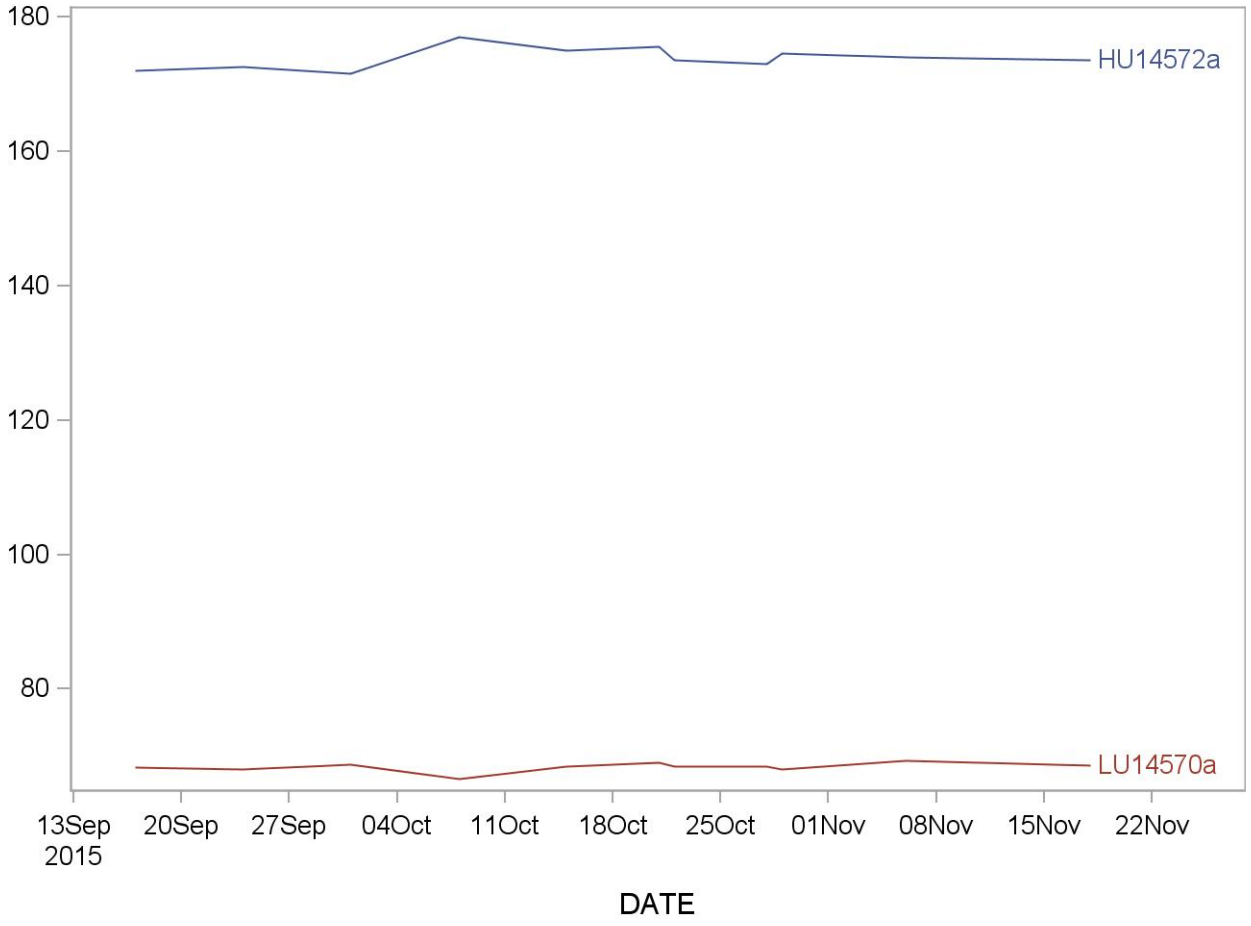
2014 Summary Statistics and QC Chart for Urea Nitrogen, PM Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
CC2_URCN5H1	48	04FEB14	19FEB15	459.5	7.8	1.7
CC1_URCN5L1	48	04FEB14	19FEB15	231.0	5.2	2.3



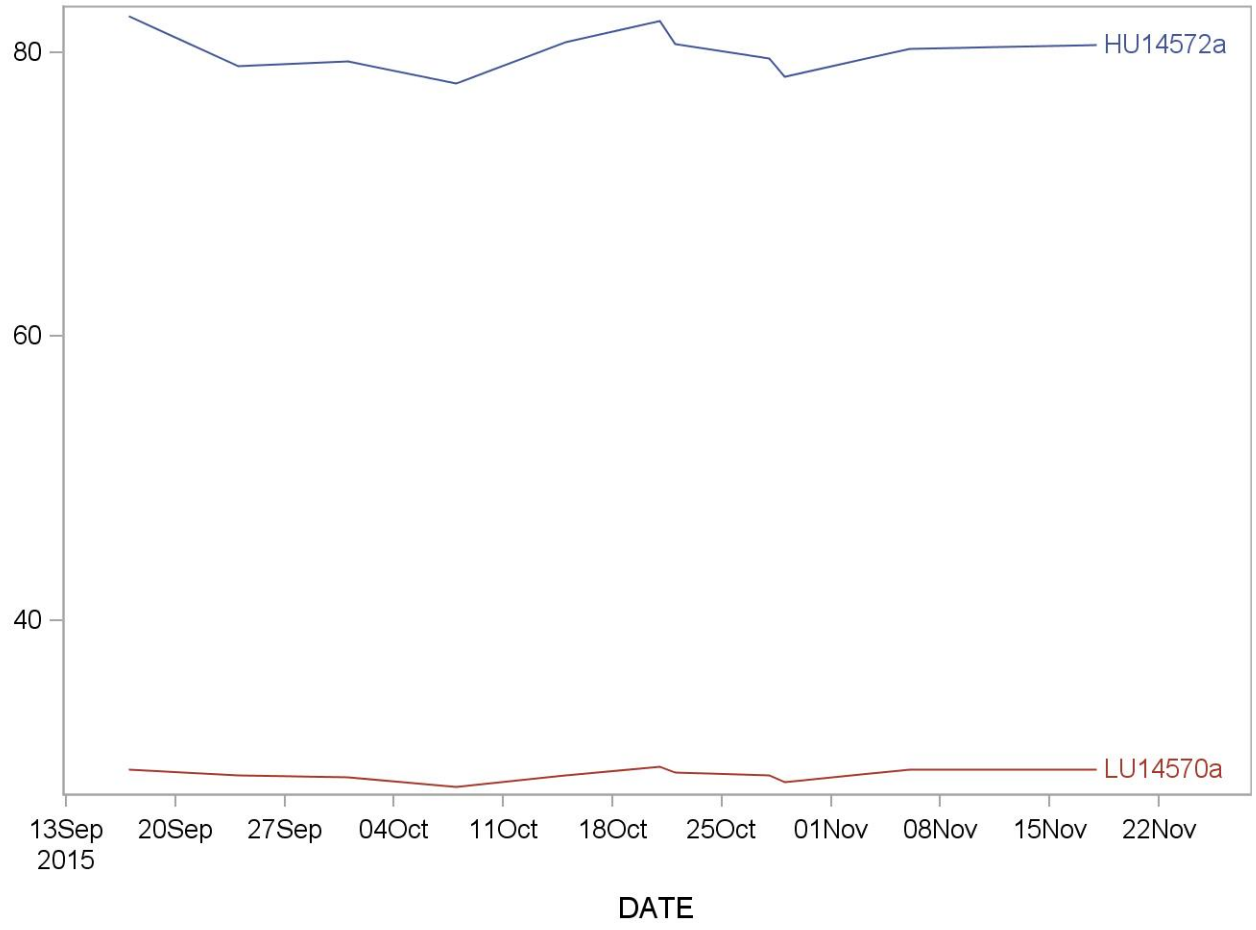
2014 Summary Statistics and QC Chart for Chloride, Urine - MEC Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
HU14572a	12	17SEP15	18NOV15	173.8750	2.0127	1.2
LU14570a	12	17SEP15	18NOV15	68.3542	0.8066	1.2



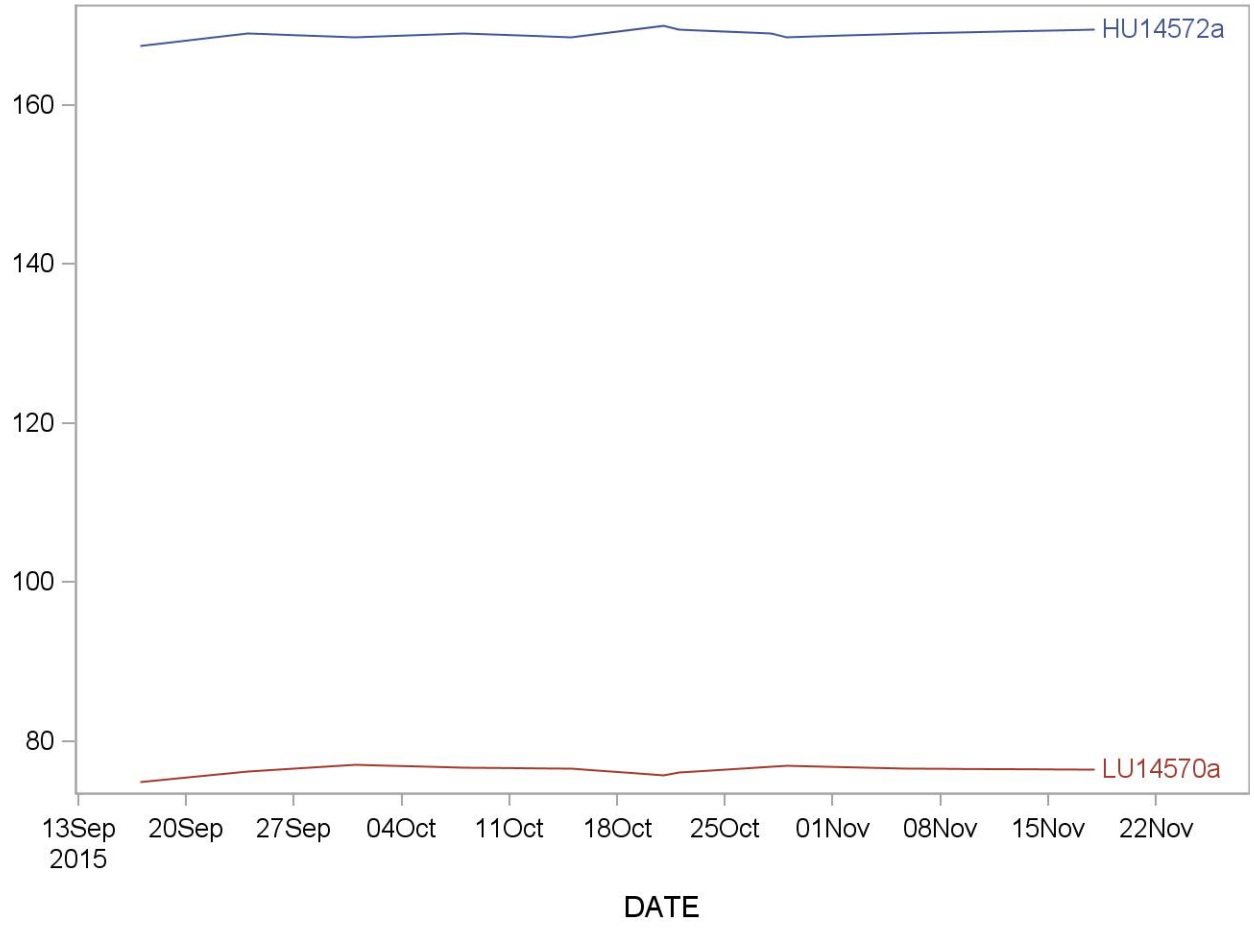
2014 Summary Statistics and QC Chart for Potassium, Urine - MEC Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
HU14572a	12	17SEP15	18NOV15	79.9292	1.5007	1.9
LU14570a	12	17SEP15	18NOV15	29.1250	0.4277	1.5



2014 Summary Statistics and QC Chart for Sodium, Urine - MEC Collection (mg/dL)

Lot	N	Start Date	End Date	Mean	Standard Deviation	Coefficient of Variation
HU14572a	12	17SEP15	18NOV15	168.8750	0.7724	0.5
LU14570a	12	17SEP15	18NOV15	76.4000	0.6227	0.8



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ACKNOWLEDGMENTS

We gratefully acknowledge the contributions of Donna LaVoie and Christine Pfeiffer who assisted in evaluating this assay and preparing the manuscript for this chapter.

Appendix 1 – Method Figures of Merit

Accuracy:

NIST 2201 sodium chloride (stock solution and dilutions prepared with water):

The Roche ISE assay shows a small bias (<5%) for sodium over a wide concentration range of 12.4-198.7 mmol/L using the NIST reference material. For chloride, the bias is <7% over a wide concentration range of 24.8-198.7 mmol/L.

NIST 2202 potassium chloride (stock solution and dilutions prepared with water):

The Roche ISE assay shows a shows a negative bias of <14% for potassium over a wide concentration range of 3.68 -99.4 mmol/L using the NIST reference material.

Precision:

The within-day imprecision (*n* = 10 replicates) of the Roche ISE Plus assay is <1% for urine sodium, <3.6% for urine potassium, and <2.2% for urine chloride.

The between-day imprecision (*n* = 57 days) is <3% for urine sodium (69-161 mmol/L), <6.5% for urine potassium (28-78 mmol/L), and <3% for urine chloride (82-191 mmol/L).

Dilution linearity:

Using the Validate UC1 urine material, we found good dilution linearity (r^2 >0.999) and the measured concentrations corresponded well (within ± 10%) with the expected concentrations.

Limit of detection (LOD):

The manufacturer does not specify LOD values.

In-house determined LOD using GEN1 reagents: 4 mmol/L for urine sodium, 0.2 mmol/L for urine potassium, and 0.4 mmol/L for urine chloride

Determination of the LOD by serially diluting the "low" QC pool with water and estimating the SD at a concentration of zero (σ_0) by extrapolating repeat analyte measurements (n = 9) made near the detection limit in these dilutions (LOD defined as 3 σ_0).

The manufacturer specified reportable range for GEN2 reagents starts at 20 mmol/L for urine sodium, 3.0 mmol/L for urine potassium, and 20 mmol/L for urine chloride.