CHAPTER 34. BASE 24-HOUR URINE COLLECTION – LITHOLINK CORE LAB

34.1 Background

Participants who are enrolled in the CKD BASE Study will collect urine over a 24-hour period at B0, W12 and W28. A 50 ml tube of urine will be shipped overnight to Litholink Corporation in Chicago, Illinois. Two additional tubes containing 10 ml of urine will be saved as back up and frozen at each local site.

For general collection and processing questions, call 1-800-338-4333. For additional supplies needed and shipment notification, contact Susan Donohue at donahus@labcorp.com and Ignacio Granja at granjai@labcorp.com. Contact information can be found in the CKD BASE Address Directory.

34.2 Schedule, Type and Volume of Urine Required

<table>
<thead>
<tr>
<th>Tube Size</th>
<th>Collection Periods, Quantity Required, Storage and Shipping</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 ml – provided by Litholink</td>
<td>B: 1 x 50 ml urine, Storage: room temperature</td>
</tr>
<tr>
<td>15 ml – provided by local sites</td>
<td>2 – 10 ml urine, Storage: In -20º or colder freezer locally</td>
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34.3 Training Requirements for Personnel Sending Samples

Each person shipping diagnostic specimens should be trained according to DOT and IATA regulations. Someone at each BASE site will be responsible for training the appropriate personnel.

34.4 Logistics for Litholink

Overview: The Litholink Corporation will provide 24-hour urine collection kits – see section 34.5 for specific contents. Participants will collect their urine over the course of 24-hours and bring in the urine collection container(s) for processing by the study coordinator or other designated person. The labels to be used locally for the backup tubes will be supplied to the sites by the DCC with detailed completion instructions provided. The tube labels include space to write in the BASE participant’s 6 digit-identification number. The labels will also include two spaces in which the study staff should mark the participant’s alphanumeric code, which will be used as an alternative ID. Tubes should be labeled immediately prior to when urine from the participant is poured into the tubes.
34.5 Kits and Shipping Materials

Litholink Kit Contents include:
1–Orange urine collection container
1–Sealed tube of liquid urine preservative (contains Gentamicin 20 mg, Germall II 1.25 g, Potassium Fluoride 306 mg)
1–Green-topped 50 ml tube
1-Safeguard Specimen (biohazard) Bag with absorbent material
1-Pre-addressed shipping box (printed with appropriate DOT labels)
1-Preprinted Fedex Priority Overnight label (See address directory for name of individual at Litholink who will receive the specimen box)
1-Customer service card with toll-free phone number

Note: Litholink will send female collection aids (‘hats’) in one bulk shipment.

Local Site provides:
Extra 15 ml tubes (for storing and freezing two additional tubes containing 10 ml/tube of backup urine)
Tube labels (provided to each site by DCC)
Freezer rack/storage box to hold frozen urine tubes ‘backup’
-20° or colder freezer

34.6 Instructing the Participant on Collecting Urine

Provide the participant with items needed for urine collection including: orange urine collection container, sealed tube of liquid urine preservative, ‘how to’ instructions, and if female, urine collection aid ‘hat’. (It is suggested that the urine jug be marked with some identifying information to separate multiple samples in the event that more than one participant comes in for a study visit on the same day.). For the initial collection, it is recommended that the participant be given two jugs since each 4 liter jug should not be filled more than 4,000 mls of urine. In the event that the participant’s output exceeds the 4,000 mls, the second jug could then be used to complete the collection. Note, any collections of over 4,500 mls in a jug will need to be repeated. If the participant does not use the second jug for the collection, the participant should return the unused jug to the site and the site could use it for another participant. However, if the participant does use the second jug or the urine volume is close to 4,000 mls, a second jug should be given at subsequent visits where a 24-hour collection is needed.

Thoroughly review the instructions with the participant (and caregiver, if he or she is accompanying the study participant). Urine collection should start the date prior to the in-person study visit* and should be written on participant’s instruction sheet. Be sure to provide the participant with study personnel contact information and an emergency contact, if needed. Remind the participant that all urine is collected even if there is nighttime urination. Collections should be as close to 24-hours as possible prior to the in-person study visit. Urine jug can be stored at room temperature. Collection time should be between 20 and 28 hours. If during Baseline, the collection is <20 or >28 hours, an additional collection is required for randomization.
*For in-person visits requiring 24-hour urine collection (B1, W12 and W28), it is helpful to schedule in-person visits on a Monday so urine can be collected over the weekend and brought in to the visit.

Participant Instructions sheets on collecting their urines are provided in this chapter’s appendices. Appendix A includes two IRB-reviewed participant instructions for females and for males prepared by University of Utah. Appendix B provides a generic template that can be modified accordingly. Any participant urine collection instructions must be submitted to your local IRB.

For female participants, instruct the participant to try to avoid collecting the sample during their menstrual cycle. If they happen to do the collection during this time, the sample should still be sent to Litholink with a note stating that the sample was collected during the participant’s menstrual cycle.

If the participant comes in for the W28 visit, does not bring in a 24-hour urine collection, and study medications are stopped, the 24-hour urine collection for W28 will be missing and should not be recollected. If the 24-hour urine was collected after the participant stopped study medications at W28, the urine results would not provide the pharmacodynamics data that is needed since the pharmacodynamic effect is expected to dissipate within a day or so of stopping BASE study medications.

### 34.7 Litholink Urine Sample Processing Information

Participant will return urine collection jug and instruction sheet where actual dates and times of start/stop urine collection are written in by the participant. Record this information on Form 326 (start and end date of urine collection and start and end time of urine collection).

Process any urine regardless of under or over collection. If during baseline, if the collection is < 20 hours or > 28 hours, the collection will need to be repeated in order for the participant to be randomized. Also, filling a 4-liter jug with more than 4,000 mls of urine may compromise results from Litholink. Any collection that exceeds 4,500 mls in one jug will need to be repeated.

#### 24-Hour Urine Collection processing – (for 1 or 2 jugs)

1. Before measuring urine volume, it is important to tighten the lid.
2. Place the collection container on a flat surface turning the jug upright so the handle is vertical.
3. Use the measuring tool along the side of the container (jug lines) to read how much fluid is inside the container. Estimate to the nearest 100 mls and record on Form 326 item 14a (Estimated volume of this 24-hour urine collection to the nearest 100 mls). If a second jug was used, estimate the second jug to the nearest 100 mls and record on Form 326 item 14b (Estimated volume of additional urine (second jug) collected to the nearest 100 mls).
4. Weigh the urine collection (includes the urine, jug with lid and the preservative). Enter value on Form 326 item 15a (Weight of the 24-hr urine collection jug). If a second jug was used, weigh the second jug urine collection (includes the urine, jug with lid and the
preservative). Enter the value on Form 326 item 15b (Weight of the second 24-hr urine collection jug).

5. Thoroughly mix or shake the urine collection container(s).

6. Fill the green-topped tube marked Collection 1 about ¾ full with the urine sample. If a second jug was used, fill a second green-topped tube marked Collection 2 about ¾ full with the urine sample.

7. Twist green top(s) tightly to seal. Make sure that the top(s) is on secure and evenly so this does not leak when shipping to Litholink. Be sure the 50 ml tube(s) used for shipping is labeled with the BASE study participant identification number and alphacode, start date/time of urine collection, and visit type. Do not spin the tube(s). Tube(s) can sit at room temperature until ready to ship.

8. Proceed to processing the backup tubes in Section 34.8.

Complete a paper copy of Litholink 24-Hr Urine Mailing form (Form 326) and make sure a copy is made of the completed document so it can be included in the shipment to Litholink. The information on the form must also be entered in the database.

All efforts should be made to ship the 50 ml tube of urine to Litholink the day the collection ends. The urine collection will no longer be good if the urine collection is received at Litholink > 96 hours after the time the urine collection ended as documented on Form 326 (Litholink 24-hr Urine Mailing Form). Specimens older than four days (96 hours) yield suboptimal results that could impact the quality of study data thus the participant should be instructed to re-collect the sample.

In Baseline, the following criteria must be met in order for the 24-urine to meet randomization eligibility criteria:

- Form 326 shows preservative observed in urine container (Q9=1) ................................................. Yes
- Form 326 shows preservative added (Q10=1 or 2)................................................................. Yes
- Form 326 shows that collection was complete (Q11=1) ................................................................. Yes
- Form 326 shows tube sent to Litholink (Q16=1 or 2) ................................................................. Yes
- Collection was between 20 and 28 hours? ................................................................. Yes

At least one Litholink urine results Form 355 with ammonium results ......................... YES

### 34.8 Processing Backup Tubes for Freezing

1. Complete and attach the participant ID labels provided by the DCC to the urine tubes prior to filling. Place the label lengthwise on the tubes – do not overlap. DO NOT write the participant’s name or any other personal identification information (e.g., SS#, DOB) on the tubes.

Sample label:

<table>
<thead>
<tr>
<th>BASE Study-Litholink</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID: __ __ __ __ __ __ __ __ __ __ __ __ __ __</td>
</tr>
<tr>
<td>Visit: Baseline W12 W28</td>
</tr>
<tr>
<td>Start Date: __ <strong>/</strong>__ <strong>/</strong> __ __ __</td>
</tr>
</tbody>
</table>
The tube labels include 8 spaces on which the study team member will write in the CKD BASE Participants’ 6 digit ID and alpha code with a fine-tipped permanent marker (like a Sharpie). Circle the visit: Baseline, W12 or W28. Write the start date of the urine collect.

2. Pour 10 ml of urine into each tube and make sure seal is closed tightly. Place tubes in storage container (rack/box) in the designated -20°C or colder freezer. Every effort should be made to freeze the back-up samples within 48 hours from the time the urine collection ended as documented on Form 326 (Litholink 24-hr Urine Mailing Form). Note, if two urine collection jugs were used by the participant, than two back up samples are needed from each jug for a total of four back-up samples.

3. Dispose of any remaining urine and urine jug according to your site’s local disposal policy.

4. Do not ship tubes to Litholink unless told to do so. Await word from either Litholink or the DCC indicating the status of the original 50 ml urine tube.

5. After receiving successful receipt and status information on the 50 ml urine tube from either Litholink or the DCC, complete Form 15 - Back-up Litholink Sample Discard Form. This form documents the disposition of the two frozen tubes for the urine collection.
   a. If the 50 ml sample was analyzed and results reported, dispose of the frozen tubes according to your site’s local policy and by completing Form 15.
   b. If the original sample could not be analyzed sufficiently, Litholink will contact your site to ship the tubes that were frozen previously. Complete Form 327-Litholink Back-up Mailing Form indicating that frozen tubes are being shipped.

6. If shipment to Litholink is required, remove frozen tubes from freezer. Verify ID and alphacode and other information that appears on the tubes’ labels. Do not thaw out the urine. Place frozen tubes into the biohazard bag with the absorbent material included. Ship at room temperature. (Do not ship on a cold pack.)

7. Complete Form 327 Litholink Back-up Mailing Form and make a copy for your files. Place the completed F327 inside the shipping box and send by FedEx to Litholink.

   Note: If frozen urine is requested on a Friday, keep the tubes in the freezer and ship on Monday.
34.9 Shipping Instructions

Shipping Instructions

1. Place the green-topped tube(s) in the biohazard bag with the absorbent paper and seal the bag.

2. Endorse the following into your Litholink Patient Sample Shipping Box:
   1) Sealed biohazard bag
   2) Completed Collection Data

3. Complete the return address portion on the right-hand side of the FedEx form.

4. Peel the backing off the back of the FedEx form and stick the form to the top of the box.

5. Remove the adhesive strip under the front flap of the Litholink Patient Sample Shipping Box and seal.

6. Call 1-800-GoFedEx (1-800-463-3339) to schedule a pickup or to find a FedEx drop box near you.
Base Study
Instructions for Collecting the Urine Sample - Female

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:

Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:
- 1 large orange collection jug
- 1 collection aid (aka “hat”)
- 1 tube of liquid urine preservative
- Pen or pencil

Instructions:

- The urine collection will start the day before your study visit.

  My urine collection will begin on ________________

- When you wake up in the morning, flush your first urine in the toilet. DO NOT collect this urine.

  Please write down the exact time: ________________

- Open the tube of urine preservative and empty it into the collection container.
Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important:** When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.

Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. To perform the collection, place the collection aid ("hat") over the toilet and then carefully pour the urine into the orange collection container. The first urine collected the following morning is your stop time.

Please write down this exact time: ____________________

Bring the orange jug with the lid firmly attached to your study visit.

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**Appointment Information:**

Date: ____________________

Time: ____________________

Location: Center for Clinical and Translational Science (CCTS) on the 5th floor of the hospital.
BASE Study
Instructions for Collecting the Urine Sample - Male

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:

Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:
- 1 large orange collection jug
- 1 tube of liquid urine preservative
- Pen or pencil

Instructions:

- The urine collection will start the day before your study visit.

  My urine collection will begin on _________________

- When you wake up in the morning, flush your first urine in the toilet. DO NOT collect this urine.

  Please write down the exact time: _________________

- Open the tube of urine preservative and empty it into the collection container.
- Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important:** When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.

- Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. The first urine collected the following morning is your stop time.

  Please write down this exact time: ____________________

- Bring the orange jug with the lid firmly attached to your study visit.

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**Appointment Information:**

Date: ____________________

Time: ____________________

Location: Center for Clinical and Translational Science (CCTS) on the 5^th^ floor of the hospital.
Appendix B: Template Consent Form

BASE Study - Instructions for Collecting the Urine Sample

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for persons with kidney conditions like you.

If you have any questions about how to collect the sample, please call one of the following people:

BASE Study Team Contacts:
Coordinator: ______________  xxx-xxx-xxxx
Coordinator: ______________  xxx-xxx-xxxx
Study Nurse: ______________  xxx-xxx-xxxx
Study PI: ______________  xxx-xxx-xxxx

Before starting:

Check to be sure you have:
- 1 large orange collection jug
- 1 tube of liquid urine preservative
- 1 collection aid, if needed (“hat” for females, urinal for males, if requested)
- Pen or pencil
- This instruction sheet

Instructions:

- The urine collection will start the day before your study visit.
  
  **My study coordinator says to start on this day** *(write in day, date): _______*

  **My actual urine collection began on** *(write in day, date): _______*

- When you wake up in the morning, flush your first urine in the toilet. **DO NOT** save this urine.

  **This is the time I first went to the bathroom after waking up:**

  _____________  Circle one:  am  pm

- Open the tube of urine preservative and empty it into the collection container.
Drop the urine preservative tube and lid into the orange jug. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If these two items are not in the jug, you will be asked to repeat the urine collection.**

Collect all of your urine into the container over the next 24 hours. Keep the jug at room temperature (no need to refrigerate it). To perform the collection, place the collection aid (“hat”) over the toilet and then carefully pour the urine into the orange collection container.

Collect all urine produced during the night. The last time you collect your urine in the jug is the very first urine the following morning. **The first urine collected the following morning is your stop time.**

**This is the time I first went to the bathroom after waking up the next day:**

Circle one: am pm

Bring the orange jug with the lid firmly attached to your study visit instruction sheet.

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**Appointment Information:**

Date: ____________________

Time: ____________________

Location: ____________________