

ADMINISTERING THE TREATMENT VALIDATION URINE SURVEY

1. PURPOSE

This document describes the process by which DeWorm3 study staff will administer the Treatment Validation Urine Survey to eligible participants. Results of the urine analysis will be used to validate the presence of albendazole metabolites in the urine of individuals confirmed to have been treated. This survey should be administered only after the DeWorm3 study staff receive the consent or assent of participants.

2. INTENDED USERS

This document is intended for use by data managers, field managers and field supervisors and any other DeWorm3 staff involved in administering the Survey.

3. RESPONSIBILITIES

All relevant DeWorm3 study staff should understand and follow this SOP prior to conducting the Survey. It is the responsibility of the site's Principal Investigator (PI) to ensure that all study staff comply with this SOP during the consenting of study participants who have been deemed eligible on the basis of the Screening/Eligibility criteria and the administration of the Survey.

4. DEFINITIONS

4.1. Treatment Validation Urine Survey: A survey conducted in a subset of individuals, within 8 villages selected from the intervention arm of the study, directly observed to have swallowed an albendazole tablet in the last 48 hours. Results of the urine analysis will be used to validate the presence of albendazole metabolites in the urine of individuals confirmed to have been treated.

4.2. Treatment Validation Urine Survey Participant Sample List: A list of 15 individuals from each village who are targeted to provide a urine sample. The sample will be an age-stratified sample: 3 preschool-age children (pre-SAC), 3 school-age children (SAC) and 9 adults.

4.3. Treatment Validation Urine Survey Replacement Sampling Lists: three lists of five reserve individuals (1 pre-SAC, 1 SAC and 3 adults) from each village who may be approached for inclusion in the Treatment Validation Urine Survey in the event that individuals from the Treatment Validation Urine Survey Participant Sample List are unavailable, ineligible or unwilling to participate.

4.4. Exclusion criteria are conditions which prevent participation in the Treatment Validation Urine Survey. Exclusion criteria include: individuals who could not be directly observed as treated with albendazole, who refuse consent/assent, is unavailable to provide a urine sample within the 48 hour post-treatment period or is unable to provide a urine sample within one hour of the supervisor visiting.

5. REQUIRED MATERIALS

5.1. Smartphone preloaded with SurveyCTO Treatment Validation Urine Survey

5.2. Study Information Sheets, in local language

5.3. Treatment Validation Urine Survey Participant sample list

5.4. Urine Survey consent form in local language

5.5. Urine Survey assent form in local language

5.6. Clipboard and black pen

5.7. Ink pad, and wiping cloth

5.8. Binder or folder for filing all completed consent and assent forms

5.9. One barcode per individual

5.10. Coloured permanent marker pens

- 5.11. Urine Collection Kits: 50ml containers (50ml polypropylene tubes with screwcap Item #6255 – Globe Scientific Inc), tissue, bag
- 5.12. Latex gloves
- 5.13. Permanent ink marker
- 5.14. GSK Albendazole tablets in required quantities with valid expiry dates
- 5.15. 10ml containers (10ml polypropylene transport tubes with screwcap Item #6102 – Globe Scientific Inc) for aliquoting
- 5.16. Freezerworks labels

6. PROCEDURE

6.1. Procedure overview

- a. Administration of the Treatment Validation Urine Survey will take place in two stages:
 - i. After obtaining consent using the urine consent form and confirming that the sampled individual meets the eligibility criteria to participate in the Treatment Validation Urine Survey, Field Supervisors will personally administer or observe administration of albendazole to sampled individuals and record this activity using the Treatment Validation Urine Survey SurveyCTO form.
 - ii. Field Supervisors will revisit sampled individuals between 2 to 48 hours after administration of albendazole to collect urine samples from participants. The sample will then be transported to the lab within 12 hours of being collected where they will be aliquoted into two 10ml containers and stored at -20°C.
- b. Only Field Supervisors accompanying a community drug distributor (CDD) are authorised to undertake the drug administration related to the Treatment Validation Urine Survey outlined in this SOP.
- c. The drug administration related to the Treatment Validation Urine Survey must be conducted prior to the school-targeted treatment and community-wide treatment so that the albendazole can be delivered by the same individual who will collect the urine within 48 hours.

6.2. Preparation for drug administration related survey

- a) In advance of drug administration and the survey, the site coordination team should conduct a sensitization visit or phone call to village leaders to ensure that they are aware of the survey activity in advance of the survey team's visit
- b) Sufficient quantities of GSK albendazole with valid expiry dates should be made available for transport to the field.
- c) The trial coordinator should ensure that the teams have the Treatment Validation Urine Survey Participant Sample List at the start of the activity. Treatment Validation Urine Survey Replacement Sampling Lists will be provided along with the original lists in advance of data collection activities creating a combined list of 30 individuals from which 15 must be sampled. Individuals on this combined list will be ranked according to their list of origin (stage 1=original sampling list, stage 2=1st reserve list, stage 3=2nd reserve list, stage 4=3rd reserve list). Field supervisors should work their way down these combined lists attempting to sample all individuals within an age stratification bracket in a stage before moving on to individuals from the following stages.
- d) Where an individual on the original sampling list must be replaced they should be done so by an individual on a reserve list within the same age stratification bracket.
- e) Urine-collection kits should be prepared in advance so that these can be ready to be taken to the field. To prepare the kits:

- i. Offer tissue and if requested tear off tissue roll, counting several squares per kit
 - ii. 50ml container
 - iii. Compile in a small opaque bag.
- f) The barcode stickers should be printed. One will be printed for each individual on the Treatment Validation Urine Survey Participant Sample List. The barcode stickers will display the 9-digit participant ID. The field supervisor should take the barcode stickers for the individuals they will be visiting that day.
- g) Field supervisors should ensure they have sufficient consent/assent forms as well as the latest version of the SurveyCTO Treatment Validation Urine Survey Form on their smartphone, and that the smartphone is fully charged.

Where necessary male field supervisors should make arrangements for female field workers to accompany them when collecting urine samples from female participants in order to minimize embarrassment caused to the participant and reduce refusal rates for depositing a urine sample.

6.3. Locating and approaching the individual for drug administration

- a. Locate the intended household using the Treatment Validation Urine Survey Participant Sample List. For each sampled participant, information collected at the census will be provided (Admin levels including village, Household ID, Household Head Name, Household Address/Information, Household Phone Number, Sampled Individual Name(s), Sampled Individual age, Sampled Individual sex, Sampled Individual ID.
- b. Open the SurveyCTO Treatment Validation Urine Survey. Proceed through the form selecting the administrative level you are in, followed by the correct field supervisor name and accompanying CDD. After selecting the village that the individual is located in you will be presented with a list of individuals and their corresponding households. Select the relevant individual from this list.
- c. Once you have confirmed that the participant's individual and household information is correct a Google map will be available to help guide you to the location of the household.
- d. Upon arrival at the household first confirm that the individual is present at the household. If they are not present arrange a time to return to the household when they will be available and then save and finalise the form.
- e. Following this, ask if the household's DeWorm3 Study Card is available. If the card is available ask to see it and scan the barcode on the card. If not, select [No] and indicate why the card is not available.
- f. If the card is not available, select the method of entry for the Household ID you will use. The preferred option is scanning the Household's copy of the consent form, then the extra sticker in the census log you have taken to the field, and the last option is entering the ID manually from the participant sample list you have taken to the field.

6.4. Drug administration

6.4.1. Eligibility and consent

- a. Once you have entered the household's ID and received confirmation this is correct proceed with assessing eligibility and seeking consent.

- b. Explain that you are arriving early to treat the selected individual separately from the rest of the household as they have been selected to participate in a post-treatment urine survey, in which they are treated and then asked to provide a urine sample at a revisit within two days. This is a single timepoint survey and the participant will be treated as usual for following MDAs and not asked to provide urine (unless they are sampled again). Explain that a field officer and CDD will be returning over the next few weeks to treat the rest of the family.
- c. It should be confirmed that the individual:
 - i. is older than 24 months of age
 - ii. does not have a history of adverse reactions to benzimidazoles
 - iii. is not pregnant in the first trimester
 - iv. is not severely ill
 - v. is not intoxicated (in a way that would impair swallowing or consent process)
 - vi. is able to swallow/chew an entire tablet without requiring it to be crushed
- d. The next question will ask if the individual agrees to participate in the treatment activity and urine collection activity. If the individual refuses to participate in this treatment and urine collection activity, select 'refused' and then record why the individual refused to participate. After this, save and finalise the form. They are still eligible to receive treatment in the standard MDA that will follow.
- e. If assent/consent is refused, the individual is not eligible for urine collection and will need to be replaced.
- f. If the individual agrees to participate present the Urine Survey Consent Form (and Assent Form as required).
- g. If the potential participant is 18 years or above, only they are required to be present to consent. If the potential participant is below 18 years a caregiver must be present to participate during the entirety of the consenting/assenting process.
- h. For participants of age between 2 and 7 years, the caregiver must provide informed consent for their participation. For participants of age between 7 and 11 years the child must provide verbal consent in presence of the parent/caregiver and the parent/caregiver must provide informed consent for their participation mentioning that their child has consented to participate. For participant between 12 and 17 years the child must provide informed written assent in addition to parental/caregiver consent.
- i. Participants/caregivers will be told that participation in the Treatment Validation Urine Survey is completely voluntary and if they do not feel comfortable, they need not participate. If the potential participant or their caregiver is interested in participating in the Urine sample coverage survey and is able to read, give him/her a Urine Survey Consent Form in their preferred language to review.
- j. Read the Consent Form to the participant/caregiver and answer any questions that the participant/caregiver has regarding the study or study participation.
- k. If the participant/caregiver agrees to participate, she/he will be invited to sign the Consent/assent Form.
- l. If the potential participant is less than 18 years of age, a caregiver must be present and participate during the entirety of the consenting/assenting process for the participant to be enrolled in the Urine sample coverage survey and provide consent.
- m. If the participant is child 7 to 11 years of age explain in simple language to the child about the study in presence of their parent/caregiver

- n. If the participant is a child 12 to 18 years of age, read the Assent Form to the participant. After reading the form, answer any questions that the child has. If the child agrees to participate in the survey, he/she will be invited to sign the Assent Form.
- o. After consent/assent is provided, sign the Consent and Assent Forms. Ensure that the parent/caregiver has already signed an informed consent form for the child to participate.
- p. If the participant has a significant intellectual disability or is deaf/dumb they take on the same status as a child less than 7. If they are able to assent please document this as well as consent from the primary caregiver and if unable to assent, collect consent from the primary caregiver. This applies whether the participant is a child or an adult. The primary caregiver will answer the questions on the participant's behalf. Document such a case in the notes section at the end of the survey.
- q. If the participant and/or caregiver is unable to sign the Consent or Assent Forms, she/he will apply a thumbprint using the inkpad. However, her/his name must be written on the same page by an impartial witness. The impartial witness must be a literate adult (aged 18 years or above) of the participant/caregiver's choice (not study staff) who has sat through the consenting process, can read the information provided and sign their own name.
- r. Provide two copies of the Consent and Assent Forms for the participant/caregiver to sign. The participant will be offered one copy and the other copy will be kept and placed in the binder for filing in the office
- s. If the potential participant/caregiver is reluctant to sign the Consent Form, then ask her/him if she/he has questions that need to be clarified.
- t. If the potential participant still indicates unwillingness to participate in the study, then thank her/him for their time and assure him/her that this will not affect their access to MDA in the future.
- u. **If the participant and/or the caregiver of the participant (if required) is *not present*** at the house to consent and to participate in the Treatment Validation Urine Survey select [No, unable to answer at this time] in the Treatment Validation Urine Survey. Save and finalise the form now. Schedule a time to return when the participant (and or their guardian) will be home. Mark on the Treatment Validation Urine Survey Sample List that the household has been visited for the first time and a repeat visit is required.
- v. **If the participant and/or the caregiver of the participant (if required) *refuses consent***. Save and finalise the Treatment Validation Urine Survey Form now
- w. **If the participant and/or the caregiver of the participant (if required) is *present*** select [Yes, consented] and continue with the survey

6.4.2. Delivery of albendazole

- a. Individuals over 24 months should be administered one 400mg albendazole tablet.
- b. If the tablet is spat out or vomited within 30 minutes of administration the tablet should be re-administered. This should be noted on the SurveyCTO form in the notes question at the end of the form.
- c. It is important that the administration of albendazole is directly observed for all individuals participating in the urine sampling. Tablets should not be left at the house for absent individuals. Study staff should return 3 times to try to reach individual who were absent at the time of drug administration.
- d. Once consumption of the albendazole by the respondent has been directly

observed they should be informed that a DeWorm3 team member will return within 48 hours to collect a urine sample. It should be emphasised that it is not necessary for them to produce a sample before this point. Record in the form notes any time over the next 48 hours when the respondent knows they will not be present at the house. After this thank the respondent for their time and save and finalise the form.

6.5. Urine sample collection

- a. Participants in the Treatment Validation Urine Survey will be revisited between 2 and 48 hours after drug administration and asked to provide a urine sample to be sent to the lab for storage for subsequent testing via HPLC.
- b. When returning to a household to collect a urine sample open the SurveyCTO Treatment Validation Urine Survey and follow the same steps as before to confirm the identity of the household. After selecting the correct household from the list indicate the purpose of the visit. If a DeWorm3 staff member has previously administered albendazole to the individual then the only option available will be [Collecting urine sample]. Select this and then proceed to the household, following directions if required.
- c. On returning to collect the urine sample within the window specified above, introduce the Urine Collection Kit materials to the participant (tissue roll, 50ml container, small opaque bag). Explain the contents of the Urine Collection Kit:
 - i. The tissue roll is for wiping any spillage
 - ii. The container will be used to carry the urine sample back to the laboratory
 - iii. The bag is to protect their privacy
- d. It is essential that the participant collect the urine sample at the time of the visit of the field supervisor. In situations where the participant is not able to do so, as a last resort, the field supervisor can leave the Urine Collection Kit with the participant and return after a maximum of one hour to collect the sample. The barcode must be placed on the container prior to giving it to the participant. The container cannot be left overnight.
- e. Confirm with the individual that they will be able to provide a urine sample immediately upon receipt of the container. If they are able to do so select [yes] when the form asks if the individual can produce a urine sample now.
- f. Apply the appropriate barcode sticker with the word "Urine" to the lid of the container **before you give the container to the participant.**
- g. Do not stick the barcode to the side of the 50ml container, as this is a curved surface and cannot be scanned. Do not stick it to the base of the pot, as if this is put down on a muddy/wet surface the barcode will be soiled.
- h. Write the participant's name on a sticker using permanent marker/ball point pen and paste it on the side of the urine container.
- i. Give the participant the following instructions:
 - i. Ask the participant to go to the place where they usually urinate, preferably a toilet facility. If not, wherever they would usually go.
 - ii. They should collect enough urine to fill at least two thirds of the 50ml container (you can mark a line on the container to indicate the amount required). Then they put the lid on tightly.
 - iii. Inform them to use the tissue roll for wiping any spillage
 - iv. Once the collection is complete they should dispose of tissue roll in the latrine facility if available.

- v. The collected urine in the container should be placed into the opaque bag and handed to you.
- j. A glove should be worn when receiving the urine from the participant, although there should be no direct contact with the urine as it will be in a container within a bag.
- k. Upon receipt of the container, scan the ID on the 50ml container into the Form. If the ID is soiled and cannot be scanned, enter the ID manually.
- l. If the ID does not match the ID of the participant logged in the survey, this will be flagged and you will not be able to proceed.
- m. When the participant hands over the container, discretely check the sample (without removing the lid). Note down any comments in the SurveyCTO Form.
- n. Once collected from the participant and logged, place the 50ml container in the cooler box ready to transport to the laboratory. Save and finalise the form.
- o. All samples should be delivered to the lab within 12 hours of being collected by the participant. Here they will be aliquoted into two 10ml containers and stored at -20°C.
- p. If an individual cannot provide a urine sample at the time of the visit by the field supervisor or within one of hour this visit they should be replaced by an individual from the reserve lists.

6.6. Returning to collect a urine sample later

- a. In situations where the participant is not able to provide a sample at the time of the field supervisor's visit, as a last resort, the field supervisor can leave the Urine Collection Kit with the participant and return after a maximum of one hour to collect the sample.
- b. To do this, select [no] when the form asks if individual can produce a urine sample now.
- c. Follow through the instructions on the form, applying the sticker to the container as outlined in section 6.5 points f) to i).
- d. scan the ID on the 50ml container into the Form. If the ID is soiled and cannot be scanned, enter the ID manually.
- e. If the ID does not match the ID of the participant logged in the survey, this will be flagged and you will not be able to proceed.
- f. Before leaving confirm with the individual that they understand that the urine must be fresh, not from another day (for those who do not have toilets and can identify a previously collected urine). Also emphasize the importance of the urine being collected being from the same individual who was sampled and was administered the albendazole.
- g. When returning to a household to collect a urine sample after leaving the container with the individual open the SurveyCTO Treatment Validation Urine Survey and follow the same steps as before to confirm the identity of the household. After selecting the correct household from the list indicate the purpose of the visit. If a DeWorm3 staff member has previously left a container for the individual to provide a urine sample then the only option available will be [Returning to collect urine sample]. Select this and then proceed to the household, following directions if required.
- h. When receiving the sample from the participant a glove should be worn, although there should be no direct contact with the urine as it will be in a container within a bag.

- i. When the participant hands over the container, discretely check the sample (without removing the lid). Note down any comments in the SurveyCTO Form.
- j. In the event that the participant is not present at this return visit, or has been unable to provide a urine sample they should be recorded as being unable to provide a sample and excluded from the survey. They will be replaced by an individual from within the same age stratification bracket from the next sampling stage.

6.7. Survey completion

- a. Save and finalise the SurveyCTO form.
- b. Ask the participants if they have any further questions and thank them for their participation.

6.8. Replacing Treatment Validation Urine Survey participants

- a. All participants must be visited before they can be replaced in the survey. In the case that an individual is not present at the household at the point of first contact they should be visited a further two times before they are replaced. A participant will be replaced if they are younger than 24 months of age, have a history of adverse reactions to benzimidazoles, are pregnant in the first trimester, are severely ill, are intoxicated, are unable to swallow or chew and entire tablet without requiring it to be crushed or fall under the exclusion criteria.
- b. In the case that an individual has to be replaced they should be done so by an individual within the same age stratification bracket from the next sample stage. For example if a pre-SAC on the original sample list (stage 1) has to be replaced they should be replaced by a pre-SAC from the 1st reserve list (stage 2). All sampled individuals from both the original and reserve lists will be given to the site teams at the same time in one combined list in advance of data collection activities.

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