Laboratory Evaluation

General Instructions

The Laboratory Evaluation form captures results from laboratory tests performed throughout the trial.

The Laboratory Evaluation form is completed at every treatment and follow-up protocol visit, although the tests performed will vary by visit. Refer to the protocol for specific tests performed at each visit.

Fasting labs are required at several protocol timepoints and for all serum and urine tests performed per the Nephrotoxicity Guidelines specified in the protocol and manual of operations (below). Refer to the data collection timeline for information on fasting timepoints. Optimal fasting is 12 hours, minimal fasting is 8 hours.

Specific Instructions

Patient ID**:** Record the Patient ID in the top right hand corner.

Date of Evaluation: Record the date (month/day/year) the sample for the laboratory tests was collected.

Protocol Timepoint: Record the protocol timepoint that corresponds to the visit.

Laboratory Results Record the result for each test in the unit specified. If the result is not reported according to the unit specified, convert the laboratory result before recording the value. If the test was not performed, check "Not Done".

Results that are reported below the lower level of detection record "BLD" [-6].
Results that are reported above the upper level of detection record "ALD" [-7].

If the date of samples for a given test is not the same as the "Date of Evaluation" recorded at the top of the form, record the date of sample for that test.

For tests that are captured on the form but not required by protocol, record the result if the test is performed for clinical purposes.

Creatinine clearance should be calculated using the Modification of Diet in Renal Disease (MDRD) method. If the lab does not calculate via this method then the result must be recalculated by study personnel and the result via the MDRD method should be entered into the database and used to make study-related decisions.

The following is the IDMS-traceable MDRD Study equation (for creatinine methods calibrated to an IDMS reference method) available at
http://www.nkdep.nih.gov/lab-evaluation/gfr/estimating.shtml

$$GFR\ (mL/min/1.73\ m^2) = 175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$$

The equation does not require weight or height variables because the results are reported normalized to 1.73 m^2 body surface area, which is an accepted average adult surface area.

A MDRD calculator can be found at:

Conventional (mg/dL): http://nkdep.nih.gov/lab-evaluation/gfr-calculators/adults-conventional-unit.asp

SI unit (µmol/L): http://nkdep.nih.gov/lab-evaluation/gfr-calculators/adults-SI-units.asp

If a MDRD calculator is used then the result must be recorded in the patient chart to support any clinical decisions made as a result of that result. Include a printout from the MDRD calculator in

the study chart as source documentation. If creatinine clearance is reported as “Above 60” or “>60” then report the result using the special code for above the limit [-7].

If the creatinine result is reported as below the level of detection and creatinine clearance cannot be calculated, check “Not Done” for creatinine clearance.

Serum phosphate: The following are guidelines and clinical circumstances may alter the management at the discretion of the physician investigator:

Note: All additional and repeat tests per these guidelines should be performed on fasting samples.

If serum phosphate falls below 2.5 mg/dL and by at least 0.5 mg/dL from baseline, or if serum creatinine rises above 1.2 and by at least 0.3 mg/dL from baseline, the following additional tests will be requested at the time of the next scheduled clinic visit: fasting urinalysis, urine phosphate, creatinine and protein.

If serum phosphate:

Remains below 2.5 mg/dL (and at least 0.5 mg/dL lower than baseline) at the next 12 week visit, these tests will continue to be done at each regular visit. A serum vitamin D will also be requested at the discretion of the study investigator. If urine protein is elevated, a urine albumin level will be requested (and beta-2-microglobulin if possible). Dietary measures to increase intake of food rich in phosphorus will be recommended to the patient. ***Examples of phosphorous rich foods include:*** nuts and seeds (Brazil nuts, pumpkin seeds, sunflower seeds), low fat dairy (yogurt), cheese, fish (especially salmon), shellfish (scallops), pork, beef and veal, poultry, soy (tofu, edamame), beans and lentils, cereals, and garlic.

Falls below 2.0 mg/dL, oral supplementary phosphate will be prescribed in a dose of 250 mg three times daily (Neutra-Phos) and will be asked to return within 2 weeks for a repeat test. If serum phosphate remains below 2.0 mg/dL despite phosphate supplementation and no other cause of hypophosphatemia is identified, tenofovir will be stopped.

Falls below 1.4 mg/dL or if the patient complains of symptoms suggestive of hypophosphatemia (muscle weakness) and serum phosphate is 1.5 to 2.0 mg/dL, the patient will be started immediately on supplementary phosphate at a dose of 250 mg three times daily (Neutra-Phos) and will be asked to return within 72 hours, but definitely within 1 week, for a repeat test. If serum phosphate is <1.4 mg/dL on repeat testing, urine and serum phosphate and creatinine will be determined to assess maximal phosphate tubular reabsorption. If the serum phosphate remains below 1.5 mg/dL or symptoms persist with phosphate less than 2.0 mg/dL), tenofovir will be stopped and the patient treated with phosphate supplementation until normalization of the serum phosphate.

If serum phosphate falls below 1.0 mg/dL, the patient will be asked to return immediately and be admitted for phosphate therapy and evaluation.

If serum phosphate is 1.0-1.4 mg/dL, drug dosing may be interrupted, and phosphate supplementation provided. Repeat testing within 72 hours will be performed in conjunction with electrolytes (potassium, calcium and bicarbonate), BUN and creatinine. Aggressive supplementation with intravenous (if symptomatic) or oral (if no symptoms) phosphorus should be used. Repeat phosphate testing weekly until corrected to lower limit of normal range. If this intervention does not correct phosphate level in 2 weeks, Tenofovir DF should be permanently discontinued.

Glucose: check “Yes” or “No” to indicate whether a fasting sample was used for testing.