Infectious Disease Toolkit Guideline v2.0

Instruments

Toolkit Purpose

A collection of measures to capture essential phenotypes associated with Infectious Disease related biomedical research.

Guideline Description

The Infectious Disease toolkit can be used to collect essential phenotypes associated with Infectious Disease related research, including information related to Malaria, Trypanosomiasis / Sleeping Sickness and Tuberculosis (TB). The following document establishes guidelines (particularly applicable in Africa) on how to use the toolkit and collect detailed, relevant and harmonized phenotype and exposure data for research.

As listed below, the Infectious Disease toolkit consists of 24 Instruments, labelled Instruments 1 to 24:

Instrument	**Phenotypes**	**Instrument**	**Phenotypes**
1	Malaria Signs and Symptoms	13	STD Signs and Symptoms
2	Malaria Exposure	14	Sexually Transmitted Diseases
3	Malaria Control	15	HIV Signs and Symptoms
4	Malaria Treatment	16	Sexual Behaviour
5	Sickle Cell Disease	17	Blood Transfusion
6	Malaria Testing	18	PEP/PREP Treatment
7	Trypanosomiasis Signs and Symptoms	19	HIV Detection Test
8	Trypanosomiasis Testing	20	HIV ARV Treatment
9	TB Signs and Symptoms	21	CD4 Count and Percentage
10	Clinical TB History	22	Quantitative Viral Load
11	TB Testing	23	Complete Blood Cell Count
12	Current TB	24	Liver Function Assay

Important Notes

1. The toolkit employs branching logic, therefore, we recommend that it is completed in order, as some variables may or may not appear OR accept input based on the input of previously listed variables.

2. Some branching logic (specifically related to date of birth/age and current pregnancy) affects the display of items relevant to adult or paediatric participants across multiple instruments.

3. Any addition or removal of variables may also affect branching logic so editing of variables should be carefully positioned so as not to interrupt branching logic conditions with related variables.

4. All instruments in the toolkit are specified as optional, so that users are able to specify the focus of infectious disease research.

5. The toolkit is recommended to be used in conjunction with the Core Phenotypes toolkit (https://github.com/h3abionet/h3aphenstds).

6. Although not highlighted below, each instrument requires a collection date, which can be collected either manually or automatically.

7. Consistent codes are recommended for the identification of missing data, and these are incorporated into all Instruments discussed below. We recommend the use of 'Temporarily unavailable' for pending results in Instrument 5, 7, 10, 16, 18, 19, 20, and 21.

8. Codes for Missing Data are specified below:

Code	Value Label
-991	No information
-992	Asked but unknown
-993	Temporarily unavailable
-994	Not asked
-995	Refused
-998	Not applicable

9. We recommend that when a participant responds with an "I don't know" to a question that the interviewer firstly ensures that the participant understands the question clearly and secondly is gently encouraged to reconsider their response if possible. If "I don't know" is still the response we make use of the 'Asked but unknown' missing code. Questions where "I don't know" is a highly anticipated and valid response will have a checkbox for Unknown

included - it should be noted that this will not be recognised as missing data in statistical software.

Recommendations - Malaria

Instrument 1: Malaria Signs and Symptoms

The instrument enables the self-report collection or recording or assessment of information related to a research participant's Malaria signs and symptoms.

Questions	Date of symptoms collection/recording: Signs and Symptoms: **Response:** Yes (ongoing); Yes (previously); No; Don't Know Signs and Symptoms Included: - Abdominal pain - Chills - Cough (specify type) - Diarrhea - Fatigue - Fever - Headache - Jaundice - Malaise - Muscle Pain - Myalgia - Nausea - Tachypnoea - Tachycardia - Other (specify)
Notes	- Dates should be collected in the following format - DD-MM-YYYY - The symptom ontology can be consulted for specific symptom definitions: - https://www.ebi.ac.uk/ols/ontologies/symp - Unlike other instruments, a missing code should not be applied here, and instead the designated response option should be selected if a symptom is unknown.

Instrument 2: Malaria Exposure

The instrument enables the self-report collection of information related to a research participant's malaria exposure history.

Questions	Does the participant live in a malaria-endemic region?

	Response Options: Yes; No How often does the participant use a mosquito net or insecticide? **Response Options**: Consistently; Intermittently; Not Often; Not Applicable
Notes	- **Malaria** - A life-threatening parasitic disease caused by Plasmodium parasites that are transmitted by Anophles mosquito bites to humans and is typically clinically characterized by attacks of fever, headache, chills and vomiting. - **Malaria endemic regions**: https://www.who.int/news-room/fact-sheets/detail/malaria - **Insecticide** - Strictly, a substance intended to kill members of the class Insecta. In common usage, any substance used for preventing, destroying, repelling or controlling insects.

Instrument 3: Malaria Control

The instrument enables the self report collection of information related to a research participant's malaria control strategies.

Questions	Has the participant previously taken malaria chemoprophylaxis? **Response Options**: Yes; No (If Yes) What type of malaria chemoprophylaxis was taken? **Response Options**: Atovaquone-Proguaril; Chloroquine; Doxycycline; Mefloquine; Primaquine; Other (If Other) Specify other malaria chemoprophylaxis taken:
Notes	- **Chemoprophylaxis**: the administration of a medication for the purpose of preventing disease or infection.

Instrument 4: Malaria Treatment

The instrument enables the self report collection of information related to a research participant's malaria treatment history.

Questions	[Has the participant previously taken treatment for malaria? Is the participant currently on malaria treatment?] **Response Options**: Yes; No

Notes	- The most **common antimalarial drugs** include:
	  - Chloroquine phosphate
	  - Artemisinin-based combination therapies (ACTs)
	  - Atovaquone-proguanil (Malarone)
	  - Quinine sulfate (Qualaquin) with doxycycline (e,g, Oracea, Vibramycin)
	  - Primaquine phosphate

Instrument 5: Sickle Cell Disease

The instrument enables the self-report collection and(or) recording of Sickle Cell Disease (SCD) status from research participants or medical records, respectively.

Questions	Is the participant a SCD carrier? **Response Options**: Yes; No; Don't Know Has the participant been diagnosed with SCD? **Response Options**: Yes; No
Notes	- **SCD** - A pleiotropic inherited disorder of the blood, characterised by the appearance of sickle-shaped red blood cells and anemia. - **SCD carrier** - If you're a carrier of sickle cell, it means you carry one of the genes that causes sickle cell disease, but you do not have the condition yourself.

Instrument 6: Malaria Testing

The instrument enables the recording of a research participant's laboratory results with regards to Malaria Testing.

Questions	Test Date Test Type **Response Options**: Smear; PCR; RDT Test Result **Response Options**: Falciparum; Malariae; Ovale; Vivax; Other species; Negative; Not Determined (if Other species) Specify other malaria species:
Notes	- **Vivax**: Malaria in humans caused by Plasmodium vivax. - **Falciparum**: Plasmodium falciparum is a unicellular protozoan parasite of humans, and the deadliest species of Plasmodium that causes malaria in humans. - **Malariae**: Plasmodium malariae is a parasitic protozoan that causes malaria in humans. - **Ovale**: Plasmodium ovale is a species of parasitic protozoa that causes tertian malaria in humans.

Recommendations - Trypanosomiasis

Instrument 7: Trypanosomiasis Signs and Symptoms

The instrument enables the self-report collection or recording or assessment of information related to a research participant's Trypanosomiasis signs and symptoms.

Questions	Date of symptoms collection/recording: Signs and Symptoms: **Response:** Yes (ongoing); Yes (previously); No; Don't Know Signs and Symptoms Included: - Confusion - Fatigue - Fever - Headache - Insomnia - Irritability - Muscle Pain - Myalgia - Sleepiness - Sore/Swollen Lymph Nodes - Rash (specify type) - Other (specify)
Notes	- Dates should be collected in the following format - DD-MM-YYYY - The symptom ontology can be consulted for specific symptom definitions: - https://www.ebi.ac.uk/ols/ontologies/symp - Unlike other instruments, a missing code should not be applied here, and instead the designated response option should be selected if a symptom is unknown.

Instrument 8: Trypanosomiasis Testing

The instrument enables the recording of a research participant's laboratory results with regards to Trypanosomiasis Testing.

Questions	Test Date: Test Type: **Response Options**: Card agglutination test for trypanosomiasis (CATT); RDT; Lymph Examination; HCT (Woo Test); PCR;

	MSC/Double Centrifugation] Test Result: **Response Options**: Positive; Negative
Notes	- Dates should be collected in the following format - DD-MM-YYYY - **Trypanosomiasis** - A parasitic disorder caused by protozoa of the Trypanosoma brucei species. It is transmitted by flies and is endemic in various regions of Sub-Saharan Africa. Signs and symptoms include fever, joint pain, headache, and significant swelling of the lymph nodes. If left untreated, the parasitic infection causes anemia, heart, kidney, and endocrine failure, and neurologic damage. Subsequently patients develop confusion, disruption of the sleep cycle, and mental deterioration. - **Card agglutination test for trypanosomiasis**: It's a method developed for the detection of T b gambiense specific antibodies,10 is a simple tool for rapid screening of high patient numbers under field conditions using whole blood.

Recommendations - Tuberculosis

Instrument 9: Tuberculosis Signs and Symptoms

The instrument enables the self report collection or recording of information related to a research participant's current TB and TB treatment status.

Questions	Date of symptoms collection/recording: Signs and Symptoms: **Response:** Yes (ongoing); Yes (previously); No; Don't Know Signs and Symptoms Included: - Chest pain - Chills - Cough (specify type) - Fatigue - Fever - Loss of appetite - Night sweats - Unintentional weight loss - Other (specify)
Notes	- Dates should be collected in the following format - DD-MM-YYYY - The symptom ontology can be consulted for specific symptom definitions: - https://www.ebi.ac.uk/ols/ontologies/symp - Unlike other instruments, a missing code should not be applied here, and instead the designated response option should be selected if a symptom is unknown.

Instrument 10: Tuberculosis History

The instrument enables the self report collection of information related to a research participant's TB and TB treatment history.

Questions	[Has the participant ever been vaccinated for TB? Has the participant ever been in contact with someone who was diagnosed with TB?] **Response Options**: Yes; No (If Yes) Indicate the type of contact: **Response Options**: Household; Family/ Partner/ Friend outside the household; Place of work/ study/ prayer/ recreation When did the contact occur? **Response Options**: Current; Within the last 6 months; Within the last 6-24 months; Beyond the last 24 months
Notes	- **TB** - A chronic, recurrent infection caused by the bacterium Mycobacterium tuberculosis. Tuberculosis (TB) may affect almost any tissue or organ of the body with the lungs being the most common site of infection.
Questions	Has the participant previously been diagnosed with TB? **Response Options**: Yes; No (If Yes) Number of previous TB episodes: (If Yes) Site of previous TB episodes: **Response Options**: Pulmonary; Extrapulmonary TB; Pulmonary and extrapulmonary TB (If Extrapulmonary) Extrapulmonary sites involved: **Response Options**: Abdominal; Bone/joint; CNS Tuberculoma/s; Disseminated; Meningitis; Miliary TB; Pericardial effusion; Peripheral nodes; Pleural effusion; Spinal; Other (If Other) Specify extrapulmonary sites: Were any of these episodes rifampicin-resistant TB? Were any of these episodes multidrug resistant TB (MDR TB)? Were any of these episodes extensively drug resistant TB (XDR TB)? **Response Options**: Yes; No
Notes	- **Pulmonary TB** - A lung infection by Mycobacterium tuberculosis a slightly curved non-motile, aerobic, non-capsulated and non-spore forming strains of mycobacteria. - **Extrapulmonary TB** - A type of tubercular infection located outside of the lung, which is the most common location of tuberculosis, - **Meningitis** - Tuberculous Meningitis is a form of meningitis characterized by

	inflammation of the membranes (meninges) around the brain or spinal cord and caused by a specific bacterium known as Mycobacterium tuberculosis - **Miliary TB** - An extrapulmonary tuberculosis that results in formation of tiny lesions in all the organs. - **Pericardial effusion** - An extrapulmonary tuberculosis that is located_in pericardium resulting in acute pericarditis, chronic pericardial effusion, cardiac tamponade or pericardial constriction. - **Peripheral nodes** - A chronic, specific granulomatous inflammation of the lymph node with caseation necrosis, caused by infection with Mycobacterium tuberculosis or related bacteria. - **Pleural effusion** - TB pleural effusion is a buildup of fluid in the space between the lining of the lung and the lung tissue (pleural space) after a severe, usually long-term infection with tuberculosis. - **MDR TB** - A type of drug-resistant tuberculosis that is resistant to both rifampicin and isoniazid, the two most powerful anti-TB drugs. - **XDR TB** - A strain of Mycobacterium tuberculosis that is resistant to all of the following: isoniazid, rifampin, any of the fluoroquinolone antibiotics, and at least one of three injectable drugs (kanamycin, capreomycin, amikacin).
Questions	Has the participant ever previously taken preventive medication for TB? **Response Options**: Yes; No Duration of preventive treatment (In months) [Has the participant ever taken medication for a previous latent TB infection (LTBI)? Has the participant ever taken medication for a previous active TB infection? **Response Options**: Yes; No Last TB (latent or active) episode medication: **Response Options**: Ethambutol (EMB); Isoniazid (INH); Pyrazinamide (PZA); Rifampin (RIF); Fluoroquinolone (FQ); Amikacin (AMK); Kanamycin (KAN); Capreomycin (CM); Fixed combination of INH; Fixed combination of INH, RIF and PZA; Other (If Other) Specify other medication for last TB episode: Did the participant complete TB treatment for the last TB episode? **Response Options**: Yes; No (If Yes) Date TB medication was completed for last TB episode: Outcome of last TB episode: **Response Options**: Defaulted; Medication failed; Recovered

Notes	- Dates should be collected in the following format - DD-MM-YYYY - **LTBI:** Latent tuberculosis infection is a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB. - **Defaulted Treatment**: treatment interruption of at least two months. - **Treatment failure**: Patients whose sputum culture remains positive after 4 months of treatment.

Instrument 11: Tuberculosis Testing

The instrument enables the recording of a research participant's laboratory results with regards to TB Testing.

Questions	TB Specimen Collection Date: TB Tests requested: **Response Options**: Smear; Culture; GeneXpert; LPA Smear Result: **Response Options**: Negative; Scanty positive; 1+ smear positive; 2+ smear positive; 3+ smear positive Culture Result: **Response Options**: MTB Detected; MTB Not Detected; Invalid; Contaminated; No result TB Resistance Result: **Response Options**: Interminate; Susceptible; Resistant; Not Done GeneXpert Result: **Response Options**: MTB detected; MTB not detected; Indeterminate
Notes	- Dates should be collected in the following format - DD-MM-YYYY

Instrument 12: Current Tuberculosis

The instrument enables the recording of a research participant's laboratory results with regards to TB Testing. The instrument enables the self report collection of information related to a research participant's current TB treatment.

Questions	Does the participant currently have TB? **Response Options**: Yes; No Does the participant have active or latent TB? **Response Options**:

	Active; Latent Date participant clinically diagnosed with TB: Site of TB Disease: **Response Options**: Pulmonary; Extrapulmonary TB; Pulmonary and extrapulmonary TB; Unsure (If Extrapulmonary) Extrapulmonary sites: **Response Options**: Abdominal; Bone/joint; CNS Tuberculoma/s; Disseminated; Meningitis; Miliary TB; Pericardial effusion; Peripheral nodes; Pleural effusion; Spinal; Other (If Other) Specify other extrapulmonary site:
Notes	- **See Instrument 9** for further descriptions on TB disease sites.
Questions	[Is the participant currently taking preventive medication for TB? Is the participant currently on medication for TB (latent or active)?] **Response Options**: Yes; No (If Yes) Specify medication: **Response Options**: Ethambutol (EMB); Isoniazid (INH); Pyrazinamide (PZA); Rifampin (RIF); Fluoroquinolone (FQ); Amikacin (AMK); Kanamycin (KAN); Capreomycin (CM); Fixed combination of INH; Fixed combination of INH, RIF and PZA; Other (If Other) Specify other TB medication: Medication Start Date:
Notes	- Dates should be collected in the following format - DD-MM-YYYY - **See Instrument 9** for descriptions of **LTBI**.

Recommendations - Sexually Transmitted Diseases

Instrument 13: STD Signs and Symptoms

The instrument enables the self-report collection or recording or assessment of information related to a research participant's STD signs and symptoms.

Questions	Date of symptoms collection/recording: Signs and Symptoms: **Response:** Yes (ongoing); Yes (previously); No; Don't Know Signs and Symptoms Included: - Abdominal Pain - Bumps (Genital/Oral/Rectal) - Fatigue - Fever - Genital discomfort - Headache - Jaundice - Loss of appetite - Muscle pain - Nausea - Night sweats - Pain during sexual intercourse - Painful urination - Swollen/Sore lymph nodes - Unusual discharge - Other (specify)
Notes	- Dates should be collected in the following format - DD-MM-YYYY - The symptom ontology can be consulted for specific symptom definitions: - https://www.ebi.ac.uk/ols/ontologies/symp - Unlike other instruments, a missing code should not be applied here, and instead the designated response option should be selected if a symptom is unknown.

Instrument 14: Sexually Transmitted Diseases

The instrument is optional and enables the self report collection of information related to a research participant's history of sexually transmitted diseases.

Questions	Has the participant ever been diagnosed with a sexually transmitted disease (excluding HIV/AIDS)? **Response Options**: Yes; No; Refused (If Yes) Specify diagnosed STD/s: **Response Options**: Chlamydia; Gonorrhea; Herpes Simplex; Human papillomavirus (HPV); Syphilis; Other

	(If Other) Specify other diagnosed STD/s:
Notes	- **Chlamydia** - A sexually transmitted infection (STI) that is normally passed on through sex without a condom or sharing sex toys with someone who has the infection. Chlamydia is often symptomless however if left untreated it can lead to long-term health problems. - **Gonorrhea** - A common sexually transmitted bacterial infection caused by Neisseria gonorrhoeae. It is transmitted through vaginal, oral, or anal intercourse. Infected individuals may be asymptomatic. Symptoms in males include burning sensation during urination, discharge from the penis, and painful swelling of the testes. Symptoms in females include painful urination, vaginal discharge, and vaginal bleeding between periods. - **Herpes Simplex** - A group of acute infections caused by herpes simplex virus type 1 or type 2 that is characterized by the development of one or more small fluid-filled vesicles with a raised erythematous base on the skin or mucous membrane. It occurs as a primary infection or recurs due to a reactivation of a latent infection. - **Human papillomavirus (HPV)** - Human papillomavirus (HPV) is the most common sexually transmitted infection (STI). Many people with HPV don't develop any symptoms but can still infect others through sexual contact. Symptoms may include warts on the genitals or surrounding skin. - **Syphilis** - A contagious bacterial infection caused by the spirochete Treponema pallidum. It is a sexually transmitted disorder, although it can also be transmitted from the mother to the fetus in utero. Typically, it is initially manifested with a single sore which heals without treatment. If the infection is left untreated, the initial stage is followed by skin rash and mucous membrane lesions. - Interviewers need to be sensitive to the participant's culture and religion and be aware that some participants may be reluctant to answer these questions truthfully. - Participants should be reassured that their answers will be kept confidential.

Recommendations - HIV

Instrument 15: HIV Signs and Symptoms

The instrument enables the self-report collection or recording or assessment of information related to a research participant's HIV/AIDS signs and symptoms.

Questions	Date of symptoms collection/recording: Signs and Symptoms: **Response:** Yes (ongoing); Yes (previously); No; Don't Know Signs and Symptoms Included: - Chills - Cough (specify type)

	- Diarrhea - Fatigue - Fever - Muscle pain - Myalgia - Night sweats - Pneumonia - Rash (specify type) - Sore throat - Swollen/Sore lymph nodes - Ulcers - Unintentional weight loss - Other (specify)
Notes	- Dates should be collected in the following format - DD-MM-YYYY - The symptom ontology can be consulted for specific symptom definitions: - https://www.ebi.ac.uk/ols/ontologies/symp - Unlike other instruments, a missing code should not be applied here, and instead the designated response option should be selected if a symptom is unknown.

Instrument 16: Sexual Behaviour

The instrument is optional and enables the self-report collection of information related to sexual behaviour from research participants.

Questions	[Has the participant ever had any kind of sex? Has the participant ever had vaginal sex? Has the participant ever performed oral sex on a woman? Has the participant ever performed oral sex on a man? Has the participant ever had anal sex with a woman? Has the participant ever had anal sex with a man?] **Response Options**: Yes; No; Refused How old was the participant the first time they had any kind of sex?
Notes	- **Vaginal Sex**: During vaginal sex (also known as penetrative vaginal sex, sexual intercourse and just sex) the penis goes into the vagina. - **Oral Sex**: Oral sex involves using your mouth or tongue to stimulate your partner's genitals or anus. - **Anal Sex:** anal penetration with a penis. - Interviewers need to be sensitive to the participant's culture and religion and be aware that some participants may be reluctant to answer these questions truthfully. - Participants should be reassured that their answers will be kept confidential.
Questions	In their lifetime, with how many individuals has the participant had any kind of sex (opposite and same sex individuals)? In the past 12 months, with how many individuals have you had any kind of sex

	(opposite and same sex individuals)? In the past 12 months, how often has the participant had sex without using safe sex practices? **Response Options**: Never; Less than half of the time; About half of the time; Not always - but more than half of the time; Always; Refused
Notes	- **Safe Sex Practices** primarily involves having sexual intercourse with a barrier such as condoms, internal condoms, and dental dams, but may also include using PREP (**See Instrument 15**) when having sex, or practicing outercourse.

Instrument 17: Blood Transfusion

The instrument enables the self-report collection of information related to a research participant's history of receiving blood transfusion.

Questions	Has the participant had a blood transfusion? **Response Options**: Yes; No; Refused (If Yes) At what age?
Notes	- **Blood Transfusion** - The process of transferring blood or blood-based products from one person into the circulatory system of another.

Instrument 18: PEP/PREP Treatment

The instrument enables the self-report collection of information related to the use of PEP and PREP from research participants.

Questions	[Has the participant been exposed to the blood of a known HIV+ individual? Has the participant been on Pre-exposure prophylaxis (PrEP) treatment? Has the participant ever been on Post-exposure prophylaxis (PEP) treatment?] **Response Options**: Yes; No; Refused
Notes	- **PrEP** is a prevention method used by people who are HIV-negative and at high risk for being exposed to HIV. - **PEP** is a short course of HIV medicines taken very soon after a possible exposure to HIV to prevent the virus from taking hold in your body.

Instrument 19: HIV Detection Test

The instrument enables the recording of information related to the diagnosis (or lack thereof) of HIV with regards to a research participant. Information recorded in this Instrument needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

Questions	HIV Test Type: **Response Options**: HIV-1 RNA/DNA NAAT; HIV-1 P24 Antigen; HIV-1 Culture; HIV-2 Culture; HIV-2 RNA/DNA NAAT HIV Test Result: **Response Options**: Positive; Negative; Indeterminate (If Positive) HIV Type: **Response Options**: HIV-1; HIV-2 HIV Subtype: **Response Options**: A; B; C; D; F; G; H; J; K
Notes	- Dates should be collected in following format - DD-MM-YYYY - All results should be collected from a qualified medical laboratory facility.

Instrument 20: HIV ARV Treatment

The instrument enables the self-report collection of information related to Antiretroviral Treatment history from research participants.

Questions	Is the participant currently on ART treatment for HIV? **Response Options**: Yes; No; Refused (If Yes) Treatment Start Date: Specify current ART regimen:
Notes	- **ART** - Treatment of retroviral infections with medications that target the virus directly, limiting the ability of infected cells to produce new virus particles.
Questions	Was the participant previously on ART for HIV? (including regimen changes and ART interruptions) **Response Options**: Yes; No; Refused (If Yes) Previous ART stop date? Reason/s for stopping treatment? **Response Options**: Abnormal fat redistribution; Adverse drug reaction, unspecified; Availability of more effective treatment; Concern for cardiovascular disease; Drug toxicity; Participant defaulted; Hypersensitivity reaction; Structured Treatment Interruption (STI); Treatment failure; Other

	(If Other) Specify other reason for stopping ART:
Notes	- **Abnormal Fat Redistribution**: a condition in which the amount and/or distribution of adipose tissue (fat tissue) in the body is abnormal. - **Defaulted:** Treatment default is defined as treatment interruption of at least two months - **STI**: A planned break from treatment, during which a person stops taking medications.

Instrument 21: CD4 Count and Percentage

The instrument enables the recording of a research participant's laboratory results with regards to CD4 Count and Percentage. Information recorded in this Instrument needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

Questions	Specimen Collection date: CD4 Count: CD4 Percentage:
Notes	- Dates should be collected in following format - DD-MM-YYYY - All results should be collected from a qualified medical laboratory facility. - CD4 count measured in cell/uL

Instrument 22: Quantitative Viral Load

The instrument enables the recording of a research participant's laboratory results with regards to Quantitative Viral Load. Information recorded in this Instrument needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

Questions	HIV Viral Load test type: **Response Options**: HIV-1 RNA/DNA NAAT; RT-PCR; bDNA; Other (If Other) Specify other HIV Viral Load test type: HIV Viral Load detectable? **Response Options**: Detectable; Undetectable Viral Load:
Notes	- Dates should be collected in the following format - DD-MM-YYYY - All results should be collected from a qualified medical laboratory facility. - Viral load measured in copies/mL

Instrument 23: Complete Blood Cell Count

The instrument enables the recording of a research participant's laboratory results with regards to Blood Cell Counts. Notably, the same instrument recurs in the Kidney Disease toolkit. Information recorded in this instrument needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

Questions	Red blood cell count (RBC) White blood cell count (WBC) Hematocrit (HCT) Haemoglobin Mean cell haemoglobin Mean Cell Hb Concentration (MCHC) Mean cell volume Red cell distribution width (RDW) Eosinophils (Absolute Value) Basophils (Absolute Value) Neutrophils (Absolute Value) Monocytes (Absolute Value) Lymphocytes (Absolute value)
Notes	- Dates should be collected in following format - DD-MM-YYYY - All results should be collected from a qualified medical laboratory facility. - **RBC** - The determination of the number of erythrocytes in a biospecimen. - **WBC** - The determination of the number of leukocytes in a biospecimen - **pCO2** - the partial pressure of carbon dioxide dissolved in a solution. - **HCT** - The volume of packed RED BLOOD CELLS in a blood specimen. The volume is measured by centrifugation in a tube with graduated markings, or with automated blood cell counters. It is an indicator of erythrocyte status in disease. - **Haemoglobin** - The red respiratory protein of erythrocytes, which transports oxygen from the lungs to the tissues where the oxygen is readily released. - **Mean cell volume** - the average volume of erythrocytes in a specimen - **Mean cell haemoglobin** - the average concentration of hemoglobin in a population of erythrocytes - **MCHC** - The amount of hemoglobin in a given volume of packed red blood cells and is often calculated by dividing the hemoglobin concentration by the hematocrit. - **RDW** - Red blood cell distribution width is a measure of the range of variation of RBC volume that is reported as part of a standard complete blood count. - **Eosinophils, Basophils, Neutrophils, Monocytes, and Lymphocytes** - five white blood cell types that protect your body from infections or respond to intruders like parasites, fungi and cancer cells

Instrument 24: Liver Function Assay

The instrument enables the recording of research participant's laboratory results with regards to Liver Function. Information recorded in this Instrument needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff.

Questions	Alanine aminotransferase Aspartate aminotransferase Alkaline phosphatase Bilirubin Albumin Total Protein Gamma-glutamyl transferase (GGT)
Notes	- Dates should be collected in following format - DD-MM-YYYY - All results should be collected from a qualified medical laboratory facility. - **Alanine aminotransferase** - A family of pyridoxal phosphate-dependent enzymes involved in cellular nitrogen metabolism, amino acid metabolism, and liver gluconeogenesis. - **Aspartate aminotransferase** - A family of pyridoxal phosphate-dependent enzymes involved in amino acid metabolism and in the urea and tricarboxylic acid cycles. - **Alkaline phosphatase** - An enzyme that catalyses the cleavage of inorganic phosphate non-specifically from a wide variety of phosphate esters and having a high (greater than 8) pH optimum. - **Bilirubin** - A dark orange, yellow pigment that is the product of the breakdown of iron in the blood; it is conjugated in the liver and excreted in the bile. - **Albumin** - the main protein in blood plasma. Low serum levels occur in conditions associated with malnutrition, inflammation and liver and kidney diseases. - **GGT** - An enzyme that is found in many organs throughout the body, with the highest concentrations found in the liver. GGT is elevated in the blood in most diseases that cause damage to the liver or bile ducts.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome
ART: Antiretroviral Therapy
ARV: Antiretroviral
CATT: Card-Agglutination Trypanosomiasis Test
CD4: Cluster of Differentiation 4
DNA: Deoxyribonucleic acid
EMB: Ethambutol
GGT: Gamma-glutamyl transferase
HCT: Haematocrit Centrifuge Technique
HIV: Human Immunodeficiency Virus
HPV: Human papillomavirus
INH: Isoniazid
LTBI: Latent Tuberculosis Infection
MCHC: Mean Cell Hb Concentration
MSC: Modified Single Centrifugation
MTB: Mycobacterium Tuberculosis
NAAT: Nucleic-Acid Amplification Test

P24: Protein 24
PCR: Polymerase Chain Reaction
PEP: Post-exposure prophylaxis
PREP: Pre-exposure prophylaxis
PZA: Pyrazinamide
RDT: Rapid Diagnostic Test
RBC: Red Blood Cells
RIF: Rifampin
RNA: Ribonucleic acid
SCD: Sickle Cell Disease
STI: Structured Treatment Interruption
STD: Sexually Transmitted Disease
TB: Tuberculosis
XDR TB : Extensively Drug-Resistant Tuberculosis
MDR TB : Multi Drug-Resistant Tuberculosis
WBC: White Blood Cells

Administration

Mode of Administration

	Instruments											
	1	2	3	4	5	6	7	8	9	10	11	12
Interview OR Self-administered questionnaire	X	X	X	X	X		X		X	X		X
Clinical assessment	X				X		X		X			X
Bioassay/Lab- based assessment						X		X			X	
	13	14	15	16	17	18	19	20	21	22	23	24
Interview OR Self-administered questionnaire	X	X	X	X	X	X		X				
Clinical assessment	X		X									
Bioassay/Lab- based assessment							X		X	X	X	X

Life Stage

	Instruments											
	1	2	3	4	5	6	7	8	9	10	11	12
Infancy (0 - 12 months)	X	X	X	X	X	X	X	X	X	X	X	X

Toddler (13 - 24 months)	X	X	X	X	X	X	X	X	X	X	X	X
Childhood (2-11 years)	X	X	X	X	X	X	X	X	X	X	X	X
Adolescence (12 - 18 years)	X	X	X	X	X	X	X	X	X	X	X	X
Adult (18 and older)	X	X	X	X	X	X	X	X	X	X	X	X
	13	14	15	16	17	18	19	20	21	22	23	24
Infancy (0 - 12 months)				X		X	X	X	X	X	X	X
Toddler (13 - 24 months)				X		X	X	X	X	X	X	X
Childhood (2-11 years)				X		X	X	X	X	X	X	X
Adolescence (12 - 18 years)	X	X	X	X	X	X	X	X	X	X	X	X
Adult (18 and older)	X	X	X	X	X	X	X	X	X	X	X	X

Personnel and Training Required

Instruments 1 - 5, 7, 9, 10, 12 - 18, and 20 may be implemented as either self-reported questionnaires or interviewer- administered questionnaires. If interviewer- administered, interviews should be conducted by trained or study coordinators or data collectors who speak the native/local language of the target population. Information can also be recorded from or verified using hospital and(or) patient records. Information recorded in **Instruments 6, 8, 11, 19 and 21 - 24** needs to be gained from qualified medical laboratory facilities, with trained and qualified laboratory staff. If this is not available, it should be recorded from verified hospital and(or) patient records.

References

The Infectious Disease toolkit is based on and aligned with several existing standards, to facilitate data harmonisation. These resources are listed below:

1. H3Africa Case Report Form Instruments
2. Sickle In Africa Core Data Elements (https://www.sickleinafrica.org/SIA_data_elements)
3. Allie, T., Jackson, A., Ambler, J., Johnston, K., Du Bruyn, E., Schultz, C., Boloko, L., Wasserman, S., Davis, A., Meintjes, G., Wilkinson, R. J., & Tiffin, N. (2021). TBDBT: A TB DataBase Template for collection of harmonized TB clinical research data in REDCap, facilitating data standardisation for inter-study comparison and meta-analyses. PloS one, 16(3), e0249165. https://doi.org/10.1371/journal.pone.0249165
4. Protocol - Sexual Risk Behavior - Male (https://www.phenxtoolkit.org/protocols/view/101701)
5. Protocol - Sexual Risk Behavior - Female (https://www.phenxtoolkit.org/protocols/view/101702)

6. Enhanced COVID-19 Notifiable Medical Conditions (NMC) Notification Form (SA)
7. WHO Global COVID-19 Clinical Platform: Rapid core case report form
8. Protocol - Complete Blood Count (CBC) (https://www.phenxtoolkit.org/protocols/view/220501)
9. Protocol - Liver Function - Assay (https://www.phenxtoolkit.org/protocols/view/190801)
10. HIV Cohorts Data Exchange Protocol (https://hicdep.org/)

Contributors

Phenotype Harmonisation WG - H3Africa
Joint Phenotype Harmonisation Project - H3ABioNet
Phenotype Standardisation Project - H3ABioNet
Liberata Mwita
Lyndon Zass
Milaine Sergaine
Nicki Tiffin
Samah Ahmed
Upendo Masamu

Contact Us

For queries related to this standard and guideline, users can log a ticket to the Phenotypes Standards queue in the H3ABioNet Helpdesk. User feedback and improvements on the current toolkit are welcome and encouraged. These can also be submitted through the Helpdesk, or on our GitHub Issues page.