MEDICAL AND MEDICATIONS GUIDE

For full guidance on visit procedures and CRF completion see: SSP section 6 and CRF Completion Guidelines (CCGs)

MATERNAL MEDICAL EVENT, CONDITIONS, AND MEDICATIONS

What to Document

- Significant historical and current medical events: record on the maternal **Medical Events/Conditions CRF** (one medical condition per CRF). Generally, include:
    - Past and current (this pregnancy) obstetric complications
    - Chronic medical conditions that are ongoing or took place during a past pregnancy
    - Prior medical conditions requiring surgery or hospitalization (admission to hospital)
    - Clinically significant medical conditions during pregnancy that required more than 2 weeks of medication
    - Lab or point-of-care (POC) testing resulting in a diagnosis
    - Common transient events during pregnancy, such as an episode of emesis or pelvic pressure, need not be captured unless they require medication for more than 2 weeks.
- All medications used during pregnancy and postnatal period (through study exit): record on the maternal **Medications CRF.**
    - Include any prescribed/provider directed medications, including over the counter medications.
    - Exceptions include:
        - PrEP (as this will be recorded on the PrEP Use CRF)
        - Common medications used episodically to treat common pregnancy complaints such as pelvic pressure, reflux, or nausea. ONLY include if used for more than 2 weeks.
    - Include herbal medications and supplements (any route of administration), pre-natal vitamins, malaria prophylaxis, etc.

General Guidance

- Elicit complete and accurate information from the participant.
- Report based on participant self-report, medical records (handheld or abstracted), and lab/POC Test results
- If unsure whether an event is significant enough to record on **the Medical Events/Conditions CRF**, record. Submit a query to the Safety Sub-committee for advisement as needed.

REPORTABLE MEDICAL EVENTS/CONDITIONS AND MEDICATIONS EXAMPLES		
Source information	**Medical Events/Conditions CRF**	**Medications CRF**
Participant reports that her last child was born at 32 weeks, "Prior preterm delivery"	Document as 'Prior preterm delivery"	No entry
Participant reports use of cigarettes during pregnancy	Document as "tobacco use disorder" indicate the type of drug and frequency in the description section in CRF Notes such as "cigarettes smoked 2-3 times per day." Mark as ongoing.	No entry
Participant reports ongoing use of cannabis use during pregnancy	Document as "substance use disorder," indicate the type of drug and frequency in the description section in CRF Notes such as "cannabis smoked 2-3 times per week." Mark as ongoing.	No entry
Participant reports alcohol use during first 3 months of pregnancy	Document as "alcohol use disorder," indicate the type of drug and frequency in the description section in CRF Notes such as "1-2 drinks per week during first 3 month of pregnancy." Provide stop date.	No entry
Study-performed syphilis test outcome is positive. ANC provider confirms diagnosis and treats with penicillin	Document as "positive syphilis screen," indicate as ongoing after the study performed test. If the diagnosis is confirmed, update the description to "syphilis diagnosis" and indicate treatment in CRF Notes (also record treatment medications on the Medications CRF).	Document "Penicillin"
Participant ANC card documents "Rh negative" and participant reports receiving shot during this pregnancy	Document as "Rh negative," and indicate if participant received RhoGAM shots in prior pregnancies in CRF Notes.	Document "RhoGAM" from current pregnancy. Note: date of injection is the

		medication stop and start date
Participant reports receiving contraceptive implant 6 weeks after birth	No entry	Document "etonogestrel" Note: date of insertion is start date; date of removal is stop date
Participant reports herbal medication to treat UTI	Document "urinary Tract Infection"	Document "Herbal medication to treat UTI," indicate any known ingredients in CRF Notes
HIV testing results confirm seroconversion and ART initiation documentation available	Document "seroconversion"	Document full ART regimen (names of drugs) as one CRF entry.
EPDS score ≥10	Document "positive depression score," indicate score and referrals in the CRF Notes	
Participant reports use of facility-based or community-based IPTp-SP	No entry	Document "sulfadoxine-pyrimethimine" with indication as "malaria prophylaxis"
Treatment for postpartum hemorrhage is documented in patient record as "E-MOTIVE" or "WHO bundle" or "MOTIVE bundle"	Document postpartum hemorrhage	Document oxytocin (or misoprostol) and tranexamic acid, if these are specifically listed – otherwise document as "WHO bundle"

Establishing medical events and medications at baseline- Enrollment

1. Record any noted past pregnancy complications or relevant medical events and medication from the **Obstetric Care and History CRF** on the respective **Medical Events/Conditions CRF,** and **Medications CRF,** as applicable.
2. Obtain general medical history – model after typical clinical approach by asking:
    - How are you doing today?
    - Do you have any health concerns today?
    - Do you have any chronic medical conditions outside of pregnancy such as asthma, depression, high blood pressure, genital herpes?
    - Have you ever had surgeries?
    - Have you have been hospitalized?
    - Since you've been pregnant have you taken medication for more than 2 weeks? Why?
    - What medications are you taking now?
3. Complete a new **Medical Event/Conditions CRF** and **Medications CRF** as needed

Follow up medical events and medications- Follow-up Visits

1. Document any new conditions/events or medications reported when administering the **Antenatal Care CRF, Pregnancy Outcome CRF,** or **Post-natal Care CRF** on the relevant **Medical Event/Conditions CRFs** or **Medications CRFs**
2. Review the **Medical Event/Conditions CRFs** for conditions without an outcome date and **Medications CRFs** for any medications without a stop date.
3. Consider the following questions:
    - Have there been any changes to X? Is it still an issue for you? (referring to ongoing medical conditions noted in the log)
    - Are you still taking X? (referring to a medication previously reported as continuing)
    - Since your last visit, have you had any new medical problems?
    - Since your last visit, have you had any surgeries?
    - Since your last visit, have you been to the casualty/ emergency department?
    - Are you taking any new medications since your last visit? Why?
4. For medical events that had been previously reported but are now resolved, the end/resolution date on the **Medical Events/Conditions CRF** should be updated. For medications that are no longer being taken, the stop date on the **Medications CRF** should be updated.
5. For new medical events and medications, the guidance provided above applies. Only significant medical events need be recorded on the **Medical Events/Conditions CRF**.

Maternal Pregnancy Outcome

Collect data based on participant report and medical record abstraction. Capture on the maternal **Pregnancy Outcome CRF**, with medical events/conditions detailed on the **Medical Events/Conditions CRF** and medications on the **Medications CRF.**

Pregnancy Primary Outcomes

- Full term live birth: ≥37 0/7 weeks of gestation
- Premature live birth <37 0/7 weeks of gestation
- Pregnancy loss before 20 0/7 weeks of gestation*
- Pregnancy loss at or after 20 0/7 weeks of gestation*

**Elective terminations should be documented as pregnancy loss; no further details should be included in study documentation.*

Pregnancy complication (secondary outcomes)
In reviewing medical records/charts, there are two scenarios for identifying complications:

1. Record states the complication by name → it should be marked on the **Pregnancy Outcome CRF** and entered onto the **Medical Events/Conditions CRF** as recorded in the medical chart. Indicate in the CRF notes that the condition is identified by name in the chart.
2. Record does not explicitly state a complication but the clinical scenario of the complication is described → select the presumed complication on the **Pregnancy Outcome CRF** with a description of the complication in the CRF Notes and complete the **Medical Events/Conditions CRF** with the same name of the complication.

The following definitions of pregnancy complications are intended to provide some guidance when reviewing medical records.

- **Maternal death:** Death of a CARE PrEP participant related to or aggravated by the pregnancy or its management. If death was within 24 hrs of the pregnancy outcome, attempt to ascertain time of outcome (birth) and time of death.
- **Hypertensive disorders of pregnancy:**
  - Gestational hypertension: Pregnancy >20 weeks and NEW diagnosis of hypertension (≥140 mmHg systolic and/or ≥ 90mmHg) usually sustained over 4 hours WITHOUT severe features of pre-eclampsia or proteinuria
  - Pre-eclampsia WITHOUT severe features: Pregnancy >20 weeks and NEW diagnosis of hypertension (≥140 mmHg systolic and/or ≥ 90mmHg) usually sustained over 4 hours AND proteinuria BUT no severe features which include
    - Severely elevated blood pressures, with systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg, which is confirmed after only minutes (to facilitate timely antihypertensive treatment)
    - Development of a severe headache (which can be diffuse, frontal, temporal or occipital) that generally does not improve with over-the-counter pain medications (such as acetaminophen/paracetamol)
    - Development of visual changes (including photopsia, scotomata, cortical blindness)
    - Eclampsia, or new-onset grand mal seizures in a patient with preeclampsia, without other provoking factors (such as evidence of cerebral malaria or preexisting seizure disorder). Seizures are often preceded by headaches, visual changes, or altered mental status
    - New onset thrombocytopenia, with platelet count <100,000
    - New onset of nausea, vomiting, epigastric pain
    - Transaminitis (AST and ALT elevated to twice the upper limit of normal)
    - Liver capsular hemorrhage or liver rupture
    - Worsening renal function, as evidenced by serum creatinine level greater than 1.1 mg/dL or a doubling of the serum creatinine (absent other renal disease)
    - Oliguria (urine output <400 mL/24 h)
    - Pulmonary edema (confirmed on clinical exam or imaging)
  - Pre-eclampsia WITH severe features: Pregnancy >20 weeks and NEW diagnosis of hypertension (≥140 mmHg systolic and/or ≥ 90mmHg) usually sustained over 4 hours AND proteinuria WITH one of the features listed above
  - Superimposed Pre-eclampsia: Meets the definition of Pre-eclampsia (with or without severe features) in a participant with a history of chronic hypertension
- **Chorioamnionitis:**
  - Maternal temperature >38 degrees Celsius on one occasion
  - + 1 or more of the following

- Baseline fetal tachycardia (FHT >160 bpm for 10 minutes or longer, excluding accelerations, decelerations and periods of marked variability; or a FHR >160 BPM during and after at least 3 consecutive contractions
- Maternal WBCs ≥ 15,000/mm3 in the absence of corticosteroids
- Definite purulent fluid from the cervical os
- AND, no alternative explanation

- **Puerperal sepsis:**
  - Maternal temp ≥38°C in the peripartum period and
  - Life-threatening infection related to delivery and
  - Signs of systemic involvement (for example)
    - Blood pressure <90/60
    - Renal or liver impairment
    - Respiratory distress
- **Endometritis:**
  - Livebirth or stillbirth within 42 days, and
  - Maternal fever ≥ 38°C during pregnancy, and
  - Fundal tenderness or purulent vaginal discharge ore pelvic pain or delay in the rate of reduction of the size of the post-partum uterus (localizing infection to the uterus)
- **Antepartum hemorrhage:**
  - Bleeding in the second or third trimester of pregnancy, and
  - Bleeding is either documented vaginally or suspected to be occurring intrauterine, intraperitoneally, or (rarely) retroperitoneally, based on clinical signs and symptoms
- **Postpartum hemorrhage:** >500cc of blood loss during pregnancy or labor. NOTE: if postpartum hemorrhage is documented in the patient record and postpartum treatment was provided, BUT documented blood loss is less than 500cc, document as postpartum hemorrhage.
- **Preterm premature rupture of membranes (PPROM):** Rupture of membranes before 34 weeks gestation and before contractions
- **Fever of undetermined etiology:** Maternal temperature >38 degrees Celsius with no source identified in the chart notes
- **Surgical site infection:** infection of the cesarean section or episiotomy incision

Infant Medical Events/Conditions and Medications

Assessment of the infant at all visits should include review of the infant's health, anthropometry, and feeding history.

What to Document

- Significant medical events: record on the infant* **Medical Events/Conditions CRF** one medical condition per CRF. Generally include:
    - Any significant medical events or conditions since birth, including congenital anomalies, abnormal growth, chronic medical conditions, developmental delays
    - Hospitalizations and surgeries (including prolonged nursery or NICU stay following birth)
    - Any diagnoses made by a medical provider
    - Abnormal lab results
    - Exclude common benign neonatal/infant findings such as milia, erythema toxicum, benign pustular melanosis, seborrhea ("cradle cap"), mild upper respiratory infection (common cold without fever).
    - Growth abnormalities. See SSP section 6.12.1 for tables to approximate growth percentiles.
- All medications from birth through study exit: record on the infant **Medications CRF.**
    - Including vaccines, antibiotics, oral rehydration salts, antimalarials, antiretrovirals, anti-fever medication use ≥5 days etc.
    - Exclude medications given for common benign infant findings such as diaper cream, saline solution for nose, etc.

** For non-enrolled infants, record events/conditions from in utero and delivery on the Medical Events/Conditions CRF under the maternal record in REDCap.*

The following relevant medical events/conditions may be evident in the chart but unrecognized by the parent:

- Resuscitation at delivery (needed help to start breathing/crying)
- Hypoglycemia (low blood sugar)
- Hypothermia (low temperature)
- Sepsis screening lab work (to check for infection)
- Heart murmur
- Elevated bilirubin (jaundice)
- Needed phototherapy
- Needed blood transfusion
- Breathing problems, (needed oxygen for help breathing)
- Needed antibiotics while in nursery
- Apnea (stopping breathing)
- Needed head ultrasound
- Needed seizure medication
- Needed ophthalmologic (eye) exam

General Guidance:

- Elicit history from the infant's mother, reviewing medical/delivery records/lab tests, and performing a physical exam.
- If unsure whether an event is significant enough to record on **the Medical Events/Conditions CRF**, record. Option to submit a query to the Safety Sub-committee for advisement

REPORTABLE MEDICAL EVENTS/CONDITIONS AND MEDICATIONS EXAMPLES		
Source information	**Medical Event/Conditions CRF**	**Medications CRF**
Well-baby card documents DTP3 vaccine	No entry	Document 'diphtheria, tetanus, and pertussis' vaccine. Note: date of injection is the medication stop and start date
Growth chart shows head circumference below 3rd percentile	Document 'microcephaly,' describe findings and any referrals provided	No Entry
A 6-day old newborn has lost 12% of his bodyweight since birth	document 'neonatal weight loss'	No entry
Hospital record indicated jaundice treated with phototherapy	Document 'jaundice,' describe the underlying diagnosis if available (physiologic, ABO incompatibility, sepsis, etc), treatment, and follow-up recommended in CRF Notes	No Entry
Infant diagnosed with pneumonia	Document 'pneumonia,'	Document antibiotics by name, include route, dosage, start and stop dates

Establishing medical history at Pregnancy Outcome Visit (1st Infant Visit)

1. At the PO visit, collect infant medical and medications history including delivery information and any issues that have arisen since delivery. Capture information at time of delivery on the **Infant Outcome CRF**, with medical events/conditions detailed on the **Medical Events/Conditions CRF** and medications on the **Medications CRF.**
2. Obtain general medical history – model after typical clinical approach by asking:
    - How is your baby doing today?
    - Has the infant been hospitalized for any reason other than their birth?
    - Has the infant ever had surgery?
    - Has the infant been to the casualty/emergency department?
    - If the baby is breastfeeding, does the infant have any issues with breastfeeding (e.g. trouble sucking or latching) or any special needs or medical problems that might affect feeding?
3. Perform infant physical exam to obtain growth measurements and identify congenital anomalies. **Infant Physical Exam CRF** will guide documentation of congenital anomalies. Congenital anomalies as well as other events or conditions attributed from physical exam findings on the infant **Medical Event/Conditions CRF**.

Follow up medical events and medications

1. Document any new conditions/events or medications reported when administering the **Post-natal Care CRF** on the relevant **Medical Event/Conditions CRFs** or **Medications CRFs**
2. Review the **Medical Event/Conditions CRFs** for conditions without an outcome date and **Medications CRFs** for any medications without a stop date.
3. Consider the following questions:
    - How is your baby doing today?
    - Have there been any changes to X? Is it still an issue for your baby? (referring to ongoing medical conditions noted in the log)
    - Is your baby still taking X (referring to a medication previously reported as continuing)
    - Since your last visit, has your baby had any new medical problems?
    - Since your last visit, has your baby had any surgeries or hospitalizations?
    - Since your last visit, has your baby been to the casualty/ emergency department?
    - Is your baby taking any new medications since your last visit? Why?
4. Perform physical exam to obtain current growth measurements and review previously reported or identify new medical events and conditions including congenital anomalies.

Congenital Anomalies

1. Check consent is on file to take infant photos/video. If yes, reconfirm consent verbally. Use the following counseling messages:
    - Provide as much information as possible about the diagnosed or suspected condition—*for example, whether the condition is considered minor or inconsequential to the infant's health, or if more serious, what the options might be for treatment. Reassure the parent(s) that referrals for further counseling and ongoing management of the condition will be provided.*
    - Because this is a research study, we would like to take some photos. The photos are voluntary.
    - The photos will help the doctors working on the study to evaluate the condition and decide if it is important to your baby's health.
    - There is no current evidence to suggest that exposure to the study products caused your baby's condition.
    - What questions or concerns do you have?

    Note: Do NOT take photos/video if no consent on file or the parent verbally declines.
2. Use GBD App and training slides as reference to guide documentation and taking of infant photos/video.
3. Complete the **Infant Physical Exam CRF** with as much information possible about the CA case.
4. After the visit, notify the Safety Sub-Committee of the CA case by submitting a query (upload Query Form to SharePoint and email the SSC). See SSP section 6 for notification guidance.