Section 10. Clinical Considerations

This section presents information on the clinical procedures performed in MTN-016. Instructions for completing data collection forms associated with clinical procedures are provided in Section 13.

Clinical considerations for the pregnant participant and for her infant are described separately.

10.1 Baseline History: Woman

The complete baseline history should include the following information:

- Past medical history
- Previous pregnancy history
- History related to the index pregnancy
- Concomitant medications

A focused baseline medical history, which should include information about the index pregnancy, is obtained from potential study participants at the Screening and Enrollment Visit. Medications used by the participant also are ascertained and documented at this time. Family history of genetic issues on both the maternal and paternal sides should be captured as well. Past, recent or current drug use and exposures to toxic chemicals, substances, or materials such as work pollutants, contaminated water, pesticides, fertilizers, environmental toxins, cleaning agents, etc., should be pursued. Information should be updated at each follow-up visit. The purpose for obtaining this information during screening and enrollment is to:

- Assess and document participant eligibility for the study
- Assess and document the participant's baseline medical conditions and symptoms, for comparison with signs, symptoms, and conditions that may be identified or reported during follow-up
- Assess and document risk factors other than possible *in utero* exposures to study products that could contribute to fetal demise, other adverse pregnancy outcomes or congenital malformations.

10.1.1 Focused Baseline Medical History

The site is encouraged to collect pertinent baseline medical history data in their source documentation. For enrolled participants, all baseline conditions identified as ongoing at the time of the Screening and Enrollment Visit are documented on the Medical History form (non-DataFax), Pregnancy Report and History form (DataFax) and Genetic Screening History form (DataFax). Recurring and/or chronic conditions are considered ongoing whether or not they are present/active at baseline.

When obtaining a focused baseline medical history for MTN-016, it is not necessary to document the participant's lifetime medical history. Rather, focus on conditions that have occurred and symptoms that were experienced since the participant became pregnant and probe for the most accurate information available on the participant's current health and pregnancy vis-à-vis the reported history. Several additional guidelines are presented below:

- Review the participant's prenatal record, ultrasound reports and, if indicated, her inpatient chart.
- Record symptoms, illnesses, allergies, and surgeries.
- Document existence and extent of recreational drug, tobacco and/or alcohol use.

- Document recent past and current exposures to toxic chemicals, substances, or materials such as work pollutants, contaminated water, pesticides, fertilizers, environmental toxins, cleaning agents, etc.
- Record maternal and paternal family history of:
    - Cleft lip or palate
    - Heart defects
    - Spina bifida (open spine)
    - Muscle disease/muscular dystrophy
    - Mental retardation
    - Down syndrome
    - Cystic fibrosis
    - Kidney disease
    - Sickle cell anemia
    - Haemophilia
    - Thalessemia
- Record both chronic and acute conditions, as well as both ongoing and resolved conditions.
- Record the number and outcome of each of the participant's prior pregnancies (for examples: live births, fetal death and/or still births, abortions, ectopic pregnancies), as well as any gynecologic and obstetrical procedures/surgeries.
- Document medications taken during pregnancy on the Woman Concomitant Medications Log form, as described in Section 10.1.2.

Site clinicians are encouraged to use their clinical experience and judgment to determine the best phrasing to elicit complete and accurate history information from study participants. Medical history obtained from participants via the parent protocol should be confirmed and updated for MTN-016. Sites should determine how to best capture source data in conjunction with FHI and establish source documentation SOPs for site staff to follow.

10.1.2 Initial Ascertainment of Concomitant Medications

The MTN-016 protocol requires documentation of all medications taken by study participants during pregnancy and throughout the course of the study.

For purposes of this study, medications include all of the following, regardless of route of administration:

- Prescription and "over-the counter" medications and preparations
- Vitamins and other nutritional supplements
- Herbal, naturopathic, and traditional preparations
- Recreational drugs

Other routes of administration, including intravenous, intravaginal and rectal medications/preparations and topical medications/preparations applied to the external genitalia are of particular interest for this study, as are douches and vaginal cleansers. Be sure to record all such medications/preparations.

The Woman Concomitant Medications Log form is the recommended source document for collecting information on participants' use of medications. It is recommended that study clinicians ascertain participants' baseline medication information in the context of conducting the baseline medical history. In addition to asking open-ended questions to elicit participant report of current medications, use the information obtained in the medical history to probe for additional medications that the participant may forget to report. For example, if the participant reports recurrent headaches as part of her medical history, but does not spontaneously list any medications taken for headaches, ask her if she takes any medications for the headaches. Similarly, if a participant reports taking a medication for a condition that she inadvertently did not report when providing medical history information, add the condition to the participant's baseline medical history information as appropriate.

10.2 Quarterly Visits: Woman

For enrolled participants, an interval medical history and update of concomitant medications are obtained at the quarterly visit(s).

10.2.1 Interval Medical History

When completing the interval history, it is not necessary to actively review/inquire about every body system; it is acceptable to actively inquire about the current status of conditions recorded as ongoing at the time of the prior visit, and then to ask the participant an open-ended question such as "Have you had any other symptoms or health problems since your last visit?" to complete the history.

Site clinicians are encouraged to use their clinical experience and judgment to determine the best phrasing to elicit complete and accurate follow-up information from study participants. Also be mindful that, if the participant is still being followed through the parent protocol, there may be overlap in collection and reporting of this history. Please refer to your site SOP for guidance on appropriate source documentation.

10.2.2 Updating of Concomitant Medications Information

At each visit in which concomitant medications information is obtained, retrieve the participant's Woman Concomitant Medications Log form, record any new medications taken by the participant, and actively inquire as to whether the participant is still taking medications listed previously, at the same dose and frequency. Also actively inquire as to whether the participant has begun taking any new medications since her last visit, including medications obtained outside the study (not provided by the study staff). To further probe for updates, if the participant reports any illnesses, symptoms, etc., since her last visit, inquire as to whether she took any medications for these. Add all new information to the form, using additional form pages as needed. Similarly, if a participant reports taking a new medication for a condition that she inadvertently did not report when providing interval medical history information, add the condition to her source documentation. As with the medical history, if the participant remains enrolled in the parent study, ensure all appropriate source documents are completed appropriately per your site's SOP.

10.3 Ultrasound Assessment

Either at the Screening and Enrollment Visit or at a subsequent Quarterly Visit, if the woman is still pregnant, a minimum of one ultrasound exam should be performed. In cases where the study site already has a copy of results for an ultrasound meeting gestational age and

measurement criteria recommended by the protocol, and allowing for complete documentation of the Ultrasound Results form, the protocol defined ultrasound may be omitted. When possible, site staff should attempt to conduct one ultrasound during the time period between 20 and 28 weeks (inclusive).gestation, but earlier ultrasound exam results should also be documented if available.

The primary purpose of the ultrasound is to establish gestational age. However, anatomical survey data are to be reported if available. Special note should be made of abnormal findings and care should be taken to follow up on these in the event of a live birth. Work up of suspected or confirmed anomalies is to be done on infants as per section 10.7 of the SSP. History of abnormal ultrasound would be relevant to that work up.

For each ultrasound exam:

- Perform or refer for performance of obstetrical ultrasound
- Complete Ultrasound Results form, including dating and anatomical survey data (as appropriate by gestational age).

Ultrasound exams should include, at a minimum, the following measurements:

- If estimated gestational age is <14 0/7 weeks, a crown-rump length
- If estimated gestational age is 14 0/7 weeks or greater, a biparietal diameter (a femur length is useful but not required)

If the woman has had more than one ultrasound during the pregnancy, it is requested that all of the results be reported on the appropriate CRF. And, if the woman is enrolled after delivery, it is requested that sites collect and report all available ultrasound data collected during the pregnancy.

10.4 Pregnancy Outcome

The Pregnancy Outcome will always be reported as part of another visit: screening and enrollment, quarterly or interim visit. Complete all of the requested activities of the primary visit. Sites are encouraged to collect pregnancy outcome data at or close to the time of labor and delivery to ensure complete and accurate data. Because pregnancy outcome data are also to be collected for the parent protocol, please ensure that source documents are collected and stored appropriately as per site-specific SOPs.

If the woman is already enrolled at the time that the Pregnancy Outcome is reported, update the interval medical and concomitant medication history. In addition, update the pregnancy history including but not limited to pregnancy-related morbidities such as:

- hypertensive disorders of pregnancy
- antenatal hemorrhage
- abnormal placentation (e.g., placenta previa, placenta accreta)

Finally, obtain information on the outcome of the pregnancy:

- Type and number of pregnancy outcome(s)
- If delivery, type of delivery (e.g., caesarian section, standard vaginal, or operative vaginal (includes delivery with forceps and/or vacuum)
- Pregnancy outcome (live birth, stillbirth/intrauterine fetal demise, abortion)
- Complications related to pregnancy outcome
    - Delivery-related complications (e.g., intrapartum and/or postpartum hemorrhage, non-reassuring fetal status/fetal distress, chorioamnionitis)
    - Non-delivery-related complications
- Fetal/infant congenital anomalies

Note that complications related to pregnancy outcome and congenital anomalies may be reportable as adverse events under the parent protocol; please see section 11 of the MTN-016 SSP as well as the safety and reporting guidelines of the parent protocol for more information.

10.4.1 Pregnancy Outcome: Collecting Baseline Infant Information

The MTN-016 informed consent includes permission to obtain baseline infant information from the woman's medical record. Some or all of the following data will be recorded in the labor and delivery records and may be captured at this visit:

- Gender
- Weight
- Length
- Head circumference
- Abdominal circumference
- Gestational age
- Apgar scores

10.5 Initial Newborn/Infant Assessment

If the pregnancy results or resulted in a live-born infant, an assessment of the infant should take place within 10 days of life, if reasonably possible. If necessary, the evaluation may take place off site. Sites should discuss delivery plans with each participant and establish a realistic plan for obtaining labor and delivery data as well as being able to conduct the initial infant exam. Birth/medical history as well as record of any medication taken or being administered should be obtained. While parent/guardian report is acceptable, clinicians are encouraged to seek out primary medical records whenever possible.

10.5.1 Newborn/Infant Medical History

Sites should record the medical history of the newborn/infant – from the time of birth through the time of this visit -- on the Infant Medical History Log. Note that this is a non-datafax form.

10.5.2 Concomitant Medications

Any medications dispensed to the infant from the time of birth through the time of this enrollment visit should be documented on the Infant Concomitant Medication Log. Please note the start and stop dates of these medications as well as the indication, frequency, dose and route.

10.5.3 Newborn/Infant Physical Exam

A complete physical exam should be performed as described in the protocol (Appendix III of the protocol). Elements to be documented include:

- Gestational age based on Ballard assessment
- Weight and length, as well as an assessment of proportionality/symmetry (weight for length)
- Head circumference
  - Position the tape at whatever points on the forehead and occiput give maximal circumference
- Abdominal circumference (ideally within the 10 day window; not to be collected/recorded if infant is >1 month of age)
  - Measurement is made in the plane of the umbilicus when the infant is recumbent.
- Confirmed or suspected anomalies: please see section 10.7.

10.6 Months 1, 6, and 12: Infant

10.6.1 Infant Interim History

An interim medical history should be obtained at each study visit. Document any conditions that arose since the last visit on the Infant Medical History Log. Follow up on any medical conditions noted on the Infant Medical History Log and note the resolution date as appropriate.

10.6.2 Concomitant Medications

Any medications that the infant may have taken since the last study visit should be recorded on the Infant Concomitant Medications Form. Please note the start and stop dates of these medications as well as the indication, frequency, dose and route.

10.6.3 Physical Exam

A complete physical exam should be performed as described in Appendix III of the protocol. Growth trajectory should be assessed by plotting serial weights and lengths.

10.6.4 Developmental Screening Exam

A Denver II Developmental Screening Exam should be done at Month 6 and Month 12 .. Confirmed or suspected anomalies should be documented as per section 10.7.

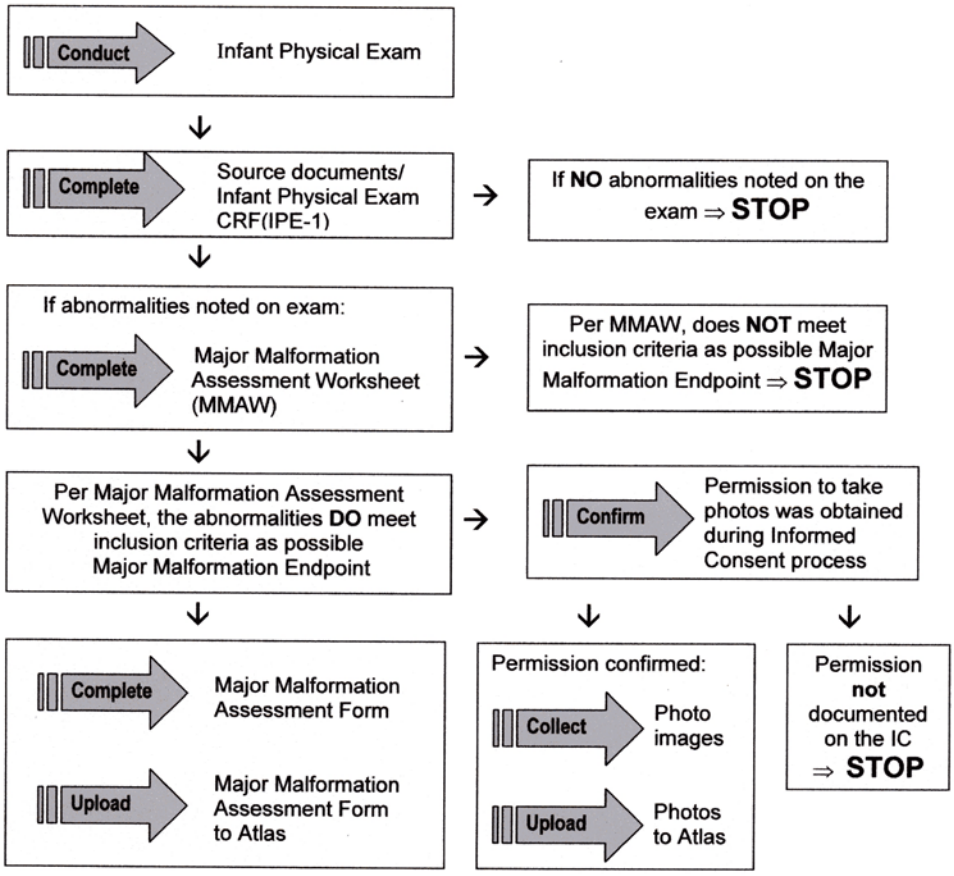
All sites have been provided with the Denver II training manual, video(s) and kit. For information on obtaining these materials, please contact the MTN CORE at mtn016mgmt@mtnstopshiv.org.

Because the initial training of site personnel may precede – by many months -- the actual examination of any infant enrolled in MTN-016, refresher trainings may need to be arranged to ensure that competence and standardization across all sites are maintained.

If there is a change in the clinician designated to conduct this exam at the site, please contact the MTN CORE (mtn016mgmt@mtnstopshiv.org) immediately to arrange for appropriate training of new staff.

10.7 Documentation of Suspected or Confirmed Anomalies

If the infant has any suspected or confirmed anomalies, the clinician should document the anomalies in as much detail as possible on the source documents and/or the Infant Physical Exam form, as well as complete the Major Malformation Assessment Worksheet (MMAW) (Section 10.7.1; Appendix 10-1). Congenital anomalies may be reportable under the parent protocol; refer to MTN-016 SSP section 11 and to the parent protocol SSP for documentation guidance for adverse event reporting. Evaluation of the suspected or confirmed anomalies will be according to the schema below. Details are in the sections that follow.



10.7.1 Major Malformation Assessment Worksheet

The Major Malformation Assessment Worksheet can be found in Appendix 10-1 and will help determine if any malformation(s) noted on the Infant Physical Exam form meet the criteria for consideration as an MTN-016 primary endpoint. The MMAW should be completed by the clinician who conducted the physical exam and should be completed while the infant is still in the clinic.

Note: Presence or absence of a major malformation does not affect study eligibility.

Major malformations are structural abnormalities that meet the following criteria (Protocol section 4.2):

1. Having surgical, medical, or cosmetic importance
2. Ascertained up to one year of age

The following will not be considered as major malformations:

1. All birth marks
2. All minor physical features
3. Deformities that represent the normal response of fetal tissue to mechanical forces (i.e., atypical body part growth and/or appearance attributable to fetal position and/or pressure of surrounding maternal tissue(s). For example, molding of the skull, also known as positional plagiocephaly, would not be considered a major malformation.

Approximately 4% of newborn infants have a single minor anomaly or physical difference on physical examination. Although these "physical differences" may not have clinical significance, it is important to recognize that they may be associated with major occult malformations or genetic syndromes. For the purposes of MTN-016, the presence of a single minor anomaly will not be considered a major malformation but the presence of two or more may raise the index of suspicion.

Examples of minor anomalies that would not be considered major malformations include (this list is not inclusive):

- microcephaly
- pilonidal cyst
- syndactyl
- paraphymosis
- clinodactyly
- supernumerary nipples
- preauricular pits
- sacral dimples

Examples physical findings that may be the normal response of fetal tissue to mechanical forces (and so not reportable as potential major malformations) include:

- talipes (however, this may be malformation; physical exam and ultrasound may be helpful to determine primary cause of this physical difference)
- inguinal hernia
- hip dysplasia

Examples of anomalies that may be common at participating MTN-016 sites and that would need to be evaluated as possible major malformations are (this list is not inclusive):

- cleft palate
- imperforate anus
- neonatal teeth
- talipes (if not attributable to fetal position and/or pressure of surrounding maternal tissue)
- undescended testes
- polydactyly
- spina bifida
- hypospadias

If the Major Malformation Assessment Worksheet indicates that the abnormality noted on the Infant Physical Exam form may be eligible as a major malformation endpoint, proceed with:

- completing the Major Malformation Assessment form (Section 10.7.2; Appendix 10-2)
- uploading the Major Malformation Assessment form to the MTN Atlas web page (section 10.7.4)

and, if consent has been obtained and documented:

- completing a photo survey of the infant (see section 10.7.3)
- uploading photographs to the MTN-016 Atlas web page (section 10.7.4)

Depending on the nature of the malformation(s), the infant should be referred for appropriate clinical care as is deemed necessary by the site MTN-016 Investigator of Record or designee.

The MMAW should be filed with the infant's MTN-016 study records.

10.7.2 Major Malformation Assessment form

The Major Malformation Assessment form (MMA) can be found in Appendix 10-2 and is only to be completed if the results of the MMAW indicate that the abnormality noted on the physical exam may be eligible as a major malformation endpoint. The MMA should be completed by the clinician who conducted the physical exam and should be completed while the infant is still in the clinic.

All completed MMA forms will be submitted to the MTN-016 Atlas web page https://atlas.scharp.org/cpas/project/MTN/016/begin.view (See section 10.7.4 for uploading instructions). The MTN-016 MMA form (available in the Study Implementation Materials section of the MTN-016 webpage) – in conjunction with the Infant Physical Exam, Woman Concomitant Medications Log, Genetic Screening History, Pregnancy Report and History, and any photographs -- will be reviewed by the MTN-016 geneticists. Site staff will submit completed forms and CRFs within two business days of the physical exam.

Note: The scope of the review by the MTN-016 geneticists is to determine whether the abnormality meets criteria as a major malformation endpoint for MTN-016. This review is not intended to be a consult and should not delay or take the place of appropriate local referrals.

The completed MMA form must be filed with the infant's MTN-016 study records.

10.7.3 Photographing Abnormalities

It is important to recognize that the abnormalities detected on physical exam may have no clinical significance. Even so, these abnormalities may be associated with malformations and genetic diseases. For this reason, it is requested that, in addition to taking specific photos of the abnormality (or abnormalities) identified on the physical exam, the site is asked to do a complete photo survey of the infant (details below). This will enable the geneticists working with MTN-016 to determine if there are other subtle findings on the physical exam that may not be apparent to the clinicians at the sites. Having the same geneticists review all cases from each of the participating MTN-016 sites will also provide the team with standardization in the assessing whether any given abnormality meets criteria as a major malformation endpoint for MTN-016. As noted above, this review by the MTN-016 geneticists is not intended to be a consult; sites should pursue appropriate follow up as clinically indicated.

If the MMAW indicates that a photo survey should be collected, the site Investigator of Record or designee should determine whether the photo survey will contribute to assessing the abnormality (or constellation of abnormalities). If the IoR or designee is uncertain of the utility of the photos, it's requested that the survey be pursued for the reasons listed above. There may be rare cases in which a photo survey would be non-contributory.

If the parent/guardian had agreed during the Informed Consent process to have photographs taken of the child – and such consent has been confirmed by checking the signature page of the Informed Consent – the clinician should arrange for photographs to be taken as the ideal method of documentation.

For any and all suspected abnormal findings, please include close up images of the abnormality from as many perspectives as are possible(front, rear, left and right lateral, as appropriate). Note that the area of interest should comprise about 75% of the screen, or as much as possible without losing focus. These additional views are requested for all abnormalities noted on the physical exam and are requested even if the abnormality appears in one of the required views.

Any photographs obtained must be stored and managed as part of the infant's medical record as source documents.

Tips for taking photographs:

- Mother should be present
- Keep the baby warm
- Easiest when baby is fed and calm
- Don't force any positions
- Extra lighting may be needed; do use a flash if available
- Solid background is preferred
- Take extra views and select the best for uploading

10.7.4 Uploading the Major Malformation Assessment form and Photographic Documentation

Each study site is asked to upload all completed MMA forms and all images of suspected or confirmed malformations collected to the Atlas web page.

Note: informed consent must have been obtained/confirmed prior to taking or submitting any photographs. A woman may change her mind about having photographs taken of her infant. If the woman had previously agreed to the photos, the source documentation must be clear that she is no longer willing to have the photos taken. If she had previously declined but now agrees, she must be re-consented. Making a note in the source records is not adequate documentation in that case. Finally, if a woman has granted permission on the informed consent but is not keen to have all views taken, please obtain whatever images are allowed and document the participant's restrictions in the source records.

Sites should upload all images collected for each infant participant, starting with images from the Newborn/Initial Visit (Visit Code 1.0). All MMA forms and images should be uploaded within 2 business days of the visit. When you are ready to upload the MMA form and image files, please follow the instructions below:

1. To prepare the **MMA form** for uploading, you will need:
    a. to save the Word document file on the computer used to access the Atlas web page,
    b. to convert the file to an Adobe PDF file,
    c. to know the location of the saved file on the computer and to already have named the file you plan to upload using the following naming convention:

        MMAform_Site_PTID_examdate.pdf

    To continue with instructions for uploading the MMA form, please proceed to Step 3.

2. To upload abnormality **image files**, you will need:
    a. the save image files on the computer used to access the Atlas web page,
    b. the PTID, Visit Code, and Exam Date for each set of participant image files you wish to upload, and

c. to know the location of the saved image files on the computer and to already have renamed each image file you plan to upload using the following naming conventions (sites and anatomical locations):

Site_PTID_datecollected_anatomiclocation_#

For example, a photograph of the front view of the whole body taken at the Pittsburgh site collected for PTID 302-1234-5-1 on 17-Nov-2009 will be named "Pitt_302123451_17nov09_fullbodyfront_1". If a second image was taken on this same day for the same PTID and anatomical location, the file will be named "Pitt_302123451_17nov09_fullbodyfront_2". Please use the tables below for site names and anatomical locations used in naming the image files.

Site Name		**Name used for image file naming convention**
Pittsburgh: Magee Women's Hospital of the University of Pittsburgh Medical Center	→	Pitt
Zimbabwe, Harare: Spilhaus	→	Spilhaus
Zimbabwe, Chitungwiza: Seke South	→	Seke
Zimbabwe, Chitungwiza: Zengeza	→	Zeng
Malawi, Blantyre: Queen Elizabeth Hospital	→	Blantyre
Malawi: Lilongwe: Lilongwe Central Hospital	→	Lilongwe
Zambia, Lusaka: Kamwala Clinic	→	Kamwala
South Africa, Durban: RK Khan Hospital	→	RKKhan
South Africa, Durban: Valley Trust/Botha's Hill	→	Bothas
South Africa, Klerksdorp: Aurum	→	Aurum
South Africa, Durban: Isipingo	→	Isipingo
South Africa, Durban: Overport	→	Overport
South Africa, Johannesburg: RHRU Tshireletso Clinic	→	RHRU
South Africa, Durban: Tongaat	→	Tongaat
South Africa, Durban: Verulam	→	Verulam
Uganda, Kampala: Makere University/Johns Hopkins University	→	Kampala
South Africa, Durban: eThekwini	→	eThekwini

Note: Files for upload must not exceed 250 MB and ALL files must be named uniquely.

The anatomical locations to be targeted for every infant on whom an eligible abnormality is/are identified are:

Anatomical Location		**Suggested Atlas Term**
Front view of face/neck and upper torso	→	face.neck.torso
Rear view of head/neck and upper back	→	head.neck.back
Left lateral view of face/head/neck	→	leftface.neck
Right lateral view of face/head/neck	→	rightface.neck
Front view of infant (full body; unclothed)	→	fullbodyfront
Rear view of infant (full body; unclothed)	→	fullbodyrear
Dorsal view of hands	→	dorsalhands
Palmar view of hands		palmhands
Dorsal (top) view of feet	→	dorsalfeet
Front view of any suspected abnormal finding(s)*	→	front[*sites to specify location]*
Rear view of any suspected abnormal finding(s)*	→	rear[*sites to specify location]*
Left lateral image of any suspected abnormal finding(s)*	→	left *[sites to specify location]*
Right lateral image of any suspected abnormal finding(s)*	→	right[*sites to specify location]*

*Even if the abnormality is captured in one of the required images, close-up front, rear, and left and right lateral images of the abnormalities are requested to provide necessary detail.

3. For uploading MMA forms and image files, go to the MTN-016 Atlas web page (by accessing this link: https://atlas.scharp.org/cpas/project/MTN/016/begin.view) or, in your web browser, type in "atlas.scharp.org", click on the "MTN" button, and then click on "MTN 016."

4. Make sure you are signed into Atlas – in the upper right-hand corner of the screen, click on "Sign in." Enter your full email address along with your Atlas password. If you have any problems signing in, email atlas@scharp.org.

5. On the left side of the MTN-016 Atlas web page, in the Project Folders window, under the 016 link, click on the "Photographic Documentation" link.

6. You should now be on the page titled "Photographic Documentation." Complete the "Participant Information" fields - Participant ID (PTID), Visit Code and Exam Date. If you are not sure how to complete these items, see the examples listed immediately below each data field. Click the "Next" button to go to the next step.

7. Upload as many images files as needed for a given PTID and given visit code using the "Browse" button to search for files on your computer. If you do not have any image files to upload, click the "Next" button to go to the next step.

8. Once you have browsed and selected all the image files you wish to upload for the participant and the visit, click the "Next" button to go to the next step.

9. Next you will select the Major Malformation Assessment form you wish to upload using the "Browse" button to search for the file on your computer. Note: a Major Malformation Assessment form must be selected for uploading. Once you have selected the MMA form, click the "Next" button to go to the next step.

10. If you would like to add any comments they can be entered here. This is optional.

11. When you are ready to have all the selected files (images and MMA form) uploaded, click the "Submit" button at the bottom of the page. Remember that files will not be uploaded until you have submitted the form by clicking the "Submit" button.

12. Once you have submitted your files, you will immediately receive a Confirmation of Submission message on Atlas. If you do not receive this confirmation message contact atlas@scharp.org.

13. If needed, you will be able to upload additional Major Malformation Assessment forms and image files for other PTIDs and/or visit codes Confirmation of Submission page you will be.

Note: SCHARP will ensure that all relevant DataFax CRFs (once received from the study site) will be available for review by the MTN-016 geneticists in conjunction with the MMA form and images submitted for any given participant.

10. 8 Infant Laboratory Assessment

The parent/guardian of an enrolled infant born to an HIV-infected woman who was known to be infected at the time of the pregnancy may request that the infant be tested for HIV through MTN-016 or through a local HIV Care and Treatment program.

These labs include HIV-1 testing (RNA and DNA PCR) and, for those infants identified as HIV infected, HIV resistance testing. Details about specimen collection and processing may be found in SSP section 12.5.

Appendix 10-1

MTN-016 Major Malformation Assessment Worksheet

1. Is/are the abnormality/abnormalities identified during the physical exam a structural abnormality with surgical, medical or cosmetic importance?
   - □ Yes
   - □ Unsure
   - □ No → If no, abnormality identified during the physical exam does NOT meet the inclusion criteria as a major malformation endpoint for MTN-016. The Major Malformation Assessment of these findings is complete. **STOP, end of worksheet.**

2. Was/were the abnormality/abnormalities ascertained prior to one year of age?
   - □ Yes
   - □ Unsure
   - □ No → If no, the abnormality identified during the physical exam does NOT meet the inclusion criteria as a major malformation endpoint for MTN-016. The Major Malformation Assessment of these findings is complete. **STOP, end of worksheet.**

3. Is/are the abnormality/abnormalities identified during the physical exam any of the following:
   a. Birth mark?
      - □ Yes
      - □ Unsure
      - □ No
   b. A deformity or deformities that represent the normal response of fetal tissue to mechanical forces? That is, an atypical body part growth and/or appearance attributable to fetal position and/or pressure of surrounding maternal tissue(s). For example, molding of the skull, also known as positional plagiocephaly, would not be considered a major malformation.
      - □ Yes
      - □ Unsure
      - □ No
   c. Minor physical feature(s)?
      - □ Yes. Were 2 or more minor physical features identified on this exam?
        - □ Yes
        - □ No
      - □ Unsure
      - □ No

Presuming that questions 1 and 2 are answered either “yes” or “unsure”:

If the responses to items 3a, 3b, **or** 3c are “no” or “unsure” If there are 2 or more minor physical features identified for item 3c	→	**proceed with evaluation** as a potential major malformation endpoint as described in SSP section 10.7. Complete the MTN-016 Major Malformation Assessment form and, if consent has been obtained and documented, obtain photographic documentation as outlined in SSP section 10.7.3.
For all other responses to items 3a, 3b, and 3c	→	the malformation(s) identified does NOT meet the inclusion criteria as a major malformation endpoint for MTN-016. The Major Malformation Assessment is complete. **STOP and do not complete the Major Malformation Assessment form.**

Note: Do not submit this worksheet to Atlas. Store it with participant MTN-016 study records.

Appendix 10-2

MTN-016 Major Malformation Assessment Form

Instructions: This form is completed if indicated per the instructions on the Major Malformation Assessment Worksheet. Submit this completed form to Atlas within 2 business days of completion of the physical exam. *Note: Do not submit the worksheet to Atlas, but store it with participant MTN-016 study records.*

IMPORTANT: Complete all required fields so the clinical reviewers have all information required to follow-up as needed.

Site Name: **Physical Exam Date (dd-MMM-yy):**
Completed by: **Email Address:**

Infant PTID: **Infant Birth Date (dd-MMM-yy):**

History:
All relevant data submitted via DataFax will be made available to the MTN-016 clinical reviewers and do not need to be resubmitted. However, information collected on non-DataFax forms (such as the Woman Medical History Log form and the Infant Medical History Log form) will not be in the MTN-016 database. Therefore, pertinent information from those forms or other source documents must be provided here. It is important that all records are consistent.

Description of malformation(s)
The Infant Physical Exam form, Woman Concomitant Medications Log form, Genetic Screening History form and Pregnancy Report and History form will be available to the MTN-016 Clinical Team, so there is no need to repeat findings already submitted. However, additional details can be provided here. Particularly if you were unable to collect and send photographs, a detailed description and/or sketch of the physical findings should be included.

Assessment (What is your assessment of malformation(s) described?)

Plan (What is your plan for referral or follow up of these malformations?)

Note: Store this completed MTN Major Malformation Assessment form with participant MTN-016 study records.