Evaluation of Potential Major Malformations
Major Malformations

- Defined as structural abnormalities that meet the following criteria:
  - Have surgical, medical, or cosmetic importance
  - Ascertained up to one year of age

- NOT considered as major malformations:
  - All birth marks
  - All minor physical features
  - Deformities that represent normal response of fetal tissue to mechanical forces
Minor Malformations
Deformities
Major Malformations
Documentation of Anomalies

1. Conduct Infant Physical Exam

2. Complete Source documents/Infant Physical Exam CRF(IPE-1)

   If NO abnormalities noted on the exam ⇒ STOP

3. If abnormalities noted on exam:
   Complete Major Malformation Assessment Worksheet (MMAW)

   Per MMAW, does NOT meet inclusion criteria as possible Major Malformation Endpoint ⇒ STOP

4. Per Major Malformation Assessment Worksheet, the abnormalities DO meet inclusion criteria as possible Major Malformation Endpoint

   Confirm Permission to take photos was obtained during Informed Consent process

5. Complete Major Malformation Assessment Form

   Permission confirmed:
   Collect Photo images
   Upload Photos to Atlas

   Permission not documented on the IC ⇒ STOP

6. Upload Major Malformation Assessment Form to Atlas
1. Is there an 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. 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 there the abnormality/abnormalities identified during the physical exam any of the following:
   a. Birthmark?
      - 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” | proceed with evaluation as a potential major malformation endpoint as described in 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 section 10.7.3. |
| If there are 2 or more minor physical features identified for item 3c | 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 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.
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. 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:
Completed by:

Physical Exam Date (dd-MMM-yy):
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.
Photographing Infant

- Head/Neck/Torso – 4 Views
Photographing Infant

- Palm view of hands
- Top view of hands
- Top view of feet
Tips for taking the photos

- 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
- Write the infant PTID on a piece of paper and position near the infant in the photo
- Take extra views and select the best for uploading!
Uploading to ATLAS

- Sites should schedule a practice submission to confirm that:
  - On-site camera is adequate
  - Bandwidth is sufficient
  - Uploading is possible from your clinic computer
Major Malformation Scenario

Alfonso is a 3 day old with a very large discoloration on his forehead.
Major Malformation Scenario

- Is this a simple birthmark?
  - If yes, not a major malformation.
  - If this is more than a birthmark, refer to Pediatrician
  - Complete the MMA Worksheet to confirm, and then...

- Complete the MM Assessment Form
- Review IC to confirm permission granted to photograph infant.
- Take photographs per site SOPs and upload to ATLAS.
Thomas is born with albinism.

- Is this a major malformation?
Scenario Answer

- Albinoism is to be documented as a major malformation for this protocol.