MTN-042 Study-Specific Procedures Manual
Overview and Control Document – Version History and Notice of Changes

Section Number	Section Title	Version Number(s)*	Version Date(s)*	Notice of Changes*
1	Introduction	1.0 1.1 1.2 1.3 2.0 2.1 2.2	19DEC2019 9APR2020 30JUN2020 17MAY2021 24AUG2021 15NOV2021 10MAY2022	• Added Clarification Memo #01 (dated 29APR2022) to section 1.1.
2	Documentation Requirements	1.0 1.1 2.0	19DEC2019 17MAY2021 24AUG2021	
3	Accrual and Retention	1.0 1.1 1.2 1.3 2.0 2.1	19DEC2019 9APR2020 30JUN2020 17MAY2021 24AUG2021 10MAY2022	• Added guidance on prescreening and screening activities permitted during the IRP pause • Updated sections 3.2.1 and 3.2.2 with cohort 3 specific accrual plan details, including site-specific accrual targets (table 3-1), minimum recruitment targets for 'early' gestational age cohort, and latest allowable EDD. • Noted that accrual SOPs may require updates to outline strategies for recruitment of the early gestational age cohort or plans for prescreening/screening during the IRP pause in section 3.2.4 • Added a new section 3.3.8 to outline procedures for transfer participants
4	Informed Consent	1.0 1.1 2.0	19DEC2019 17MAY2021 24AUG2021	
5	Study Procedures	1.0 1.1 1.2 1.3 2.0	19DEC2019 9APR2020 30JUN2020 17MAY2021 24AUG2021	• Updated section 5.3.1 to include Cohort 3 specific gestational age limits of 12 0/7 weeks – 29 6/7 weeks and to remove cohort 2-specific requirements for ultrasounds being done no later than the 28th week

		2.1 2.2	15NOV2021 10MAY2022	• Updated section 5.5 and Figure 1 to outline the Cohort 3 follow-up visit schedule and incorporate the clarifications about the visit schedule added with CM#01 to V2.0 • Specified that Cohort 3 IDIs will take place around a participant's 36th week gestation and after at least 4 weeks of product use is confirmed in section 5.5.3 • Fixed the section numbering from 5.10 to the end of section
6	Study Product Considerations for Non-Pharmacy Staff	1.0 1.1 2.0	19DEC2019 9APR2020 24AUG2021	
7	Clinical Considerations	1.0 1.1 1.2 2.0 2.1 2.2	19DEC2019 9APR2020 17MAY2021 24AUG2021 15NOV2021 10MAY2022	• Simplified and reorganized section 7.7 on ultrasound results to reflect Cohort 3 requirements • Updated section 7.9 to specify that the EPDS will be administered at enrollment, the 4-week visit corresponding with or following 30 weeks gestation, and the 6-week PPO visit for Cohort 3. • Specified that participants with EPDS scores ≥10 may be selected for a special case IDI. • Added that intergrowth weight-for-age percentile and severity grade are required on the PO CRF in section 7.10.2 • Updated Table 7-6 to indicate that the Intergrowth chart for preterm babies should be utilized for very preterm infants (<33 week), and added a new row specifying charts to use for preterm infants >33 weeks but <37 weeks. • Noted in 7.19.7 that interim visits to monitor infant growth may need to be considered between the 6- and 12-months visits

8	Adverse Event Reporting and Safety Monitoring	1.0 1.1 1.2 1.3 2.0 2.1 2.2	19DEC2019 9APR2020 30JUN2020 17MAY2021 24AUG2021 15NOV2021 10MAY2022	• AE term guidance updated throughout section to align with AE Text Guidance Document, v1.1 resource. • Section 8.5 updated to remove proteinuria from definition of preeclampsia WITH severe features • New section 8.12.2 added to provide reporting guidance for preterm delivery. • Clarified in section 8.17 that conditions outlined in the EUROCAT guidelines Chapter 3.3 are reportable to DAIDS as SAE/EAEs, unless the DAIDS EAE manual specifies the condition should not be reported (e.g., polydactyly). • Added guidance to section 8.21 about how to document AEs that are improving in grade but not yet back to baseline.
9	Counseling Considerations	1.0 1.1 2.0 2.1	19DEC2019 9APR2020 24AUG2021 10MAY2022	• Updated the name of the adherence counseling manual to remove reference to MTN-043.
10	Laboratory Considerations	1.0 1.1 1.2 1.3 2.0 2.1 2.2	19DEC2019 9APR2020 30JUN2020 01FEB2021 24AUG2021 15NOV2021 10MAY2022	• Appendix 10-2 (LDMS Specimen Management Guide to Logging in MTN-042 Specimens) updated to specify the aliquot volume as 1mL for maternal plasma samples and to include a new row for plasma for DPV Infant samples.
11	Data Collection	1.0 1.1 1.2 1.3 2.0 2.1	19DEC2019 9APR2020 30JUN2020 17MAY2021 24AUG2021 10MAY2022	• SDMC staffing updates made within the Introduction section. • Table 11-1 updated to reflect Cohort 3 Visit timing requirements. • Table 11-3 updated to reflect the Cohort 3 Visit code assignments. • Table 11-6 updated to include Participant Transfer and Receipt CRFs

12	Data Communiques	1.0 2.0	19DEC2019 24AUG2021	
13	Reporting Plan	1.0 1.1 2.0 2.1	19DEC2019 17MAY2021 24AUG2021 10MAY2022	• SDMC staffing updates made within the Introduction section.
14	DELIVER Qualitative Component	1.0 1.1 1.2 2.0 2.1 2.2	19DEC2019 9APR2020 1JUN2021 24AUG2021 15NOV2021 10MAY2022	• Table 14-1 updated to reflect updated targets for Cohort 3 qualitative accrual. • Eligibility Criteria section moved earlier, now section 14.3.1; associated section number updates made throughout. • New section 14.3.3 added to outline the Cohort 3 qualitative accrual plan and the site-specific accrual targets. • Table 14-4 updated to include the Cohort 3 Sample Qualitative Participant Log. • New section 14.5 added to provide guidance on qualitative considerations for participants transfers. • New section 14.10.3 added to provide guidance on use of the Timeline Tool for Cohort 3; reference to the timeline tool also added to Appendix 14-1 (SFTP Instructions) and new section 14-3 (Example of a Timeline Tool) • Section 14.10.6 updated to reflect file naming conventions for Cohort 3.

***Highest version number/date listed is current and supersedes all previous listed version(s). Notice of Changes summarizes any significant changes that have been made during the current review period.**

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Review Period: 17MAR2022-09MAY2022

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**Applicable section version numbers and dates as listed in Overview and Control Document table, Version 2.2, dated 10MAY2022*

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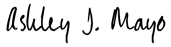
Ashley J. Mayo amayo@fhi360.org Family Health International Inc - Part 11 Security Level: Email, Account Authentication (Required) **Electronic Record and Signature Disclosure:** Accepted: 11/6/2019 1:40:28 PM ID: 65b116f5-2a06-4080-8a0e-fe9e97084303	 Signature Adoption: Pre-selected Style Signed by link sent to amayo@fhi360.org Signature ID: E35C3483-DC33-4F63-9685-A017DB5F043C Using IP Address: 73.36.165.195 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/11/2022 4:17:24 PM Viewed: 5/11/2022 4:18:14 PM Signed: 5/11/2022 4:18:47 PM

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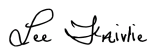
Lee Fairlie LFairlie@wrhi.ac.za Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signed by link sent to LFairlie@wrhi.ac.za Signature ID: 5532C86B-99CA-4262-B4DE-BCAE10D33C14 Using IP Address: 155.93.130.21 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/11/2022 4:17:26 PM Viewed: 5/13/2022 1:32:35 AM Signed: 5/13/2022 1:33:19 AM
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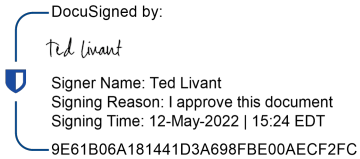
Ted Livant elivant@mwri.magee.edu Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signed by link sent to elivant@mwri.magee.edu Signature ID: 9E61B06A-1814-41D3-A698-FBE00AECF2FC Using IP Address: 72.77.16.120 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/11/2022 4:17:26 PM Viewed: 5/12/2022 3:24:06 PM Signed: 5/12/2022 3:24:41 PM
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