



MTN-036 Clinical Management and Laboratory-Related CRFs

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MTN-036

Clinical Management CRFs



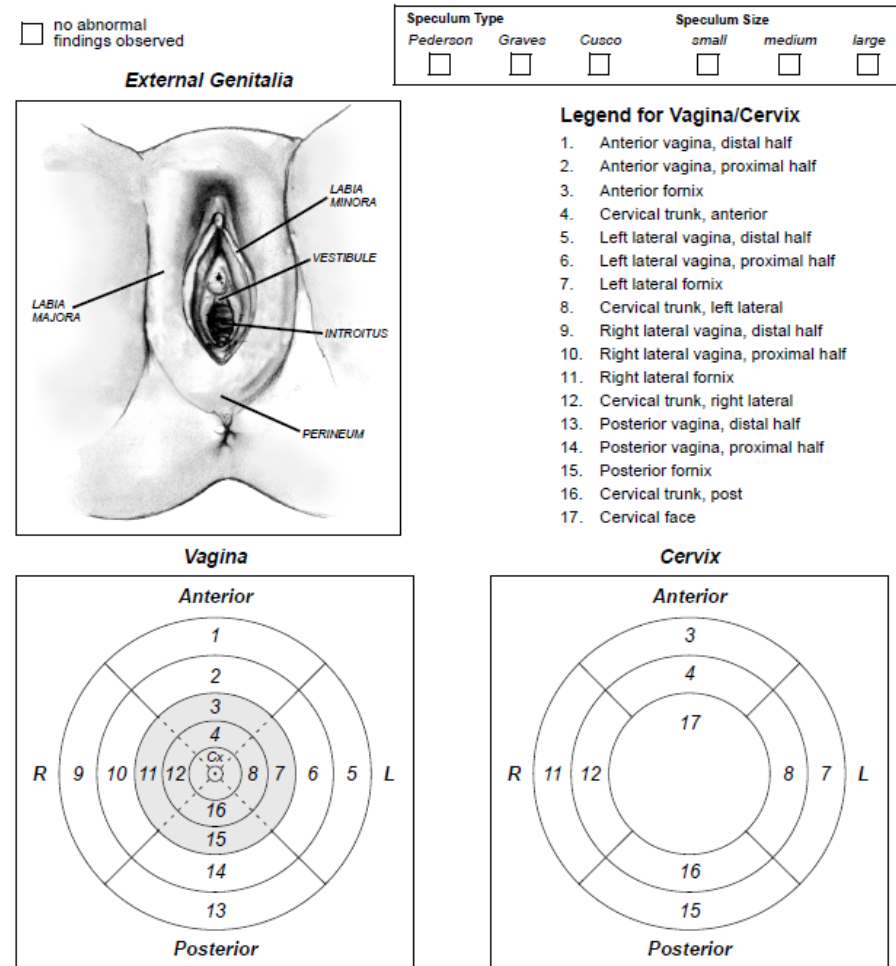
eCRFs for Clinical Management

- ✓ Vital Signs
- ✓ Physical Exam
- ✓ Pelvic Exam CRF & Diagrams
- ✓ Adverse Event Summary & Log
- ✓ Pregnancy Report
- ✓ Pregnancy History
- ✓ Pregnancy Outcome Log



Pelvic Exam Diagrams

- Pelvic Exam Diagrams will be available for download on MTN-036 ATLAS webpage
- Completed whenever a pelvic exam is conducted
- Used as the source document for all normal and abnormal pelvic exam findings
- Record all abnormal findings on the Pelvic Exam eCRF



AE CRF Reporting

All AEs in MTN036 are reportable on an AE Log CRF.

AE reporting period = randomization through date of study exit

Order of Forms

- Some forms have customized drop-down lists to link AEs.
- The Adverse Experience form needs to be filled out first in order to generate the drop-down lists and link the applicable AE on the following forms (if applicable):
 - Concomitant Medications
 - Pelvic Exam
 - Product Hold
 - Product Discontinuation
 - Study Discontinuation

Date Reported to Site

- Date clinic staff became aware of AE
- This could be:
 - Date of clinic visit/assessment
 - Date of phone call in which new AE reported
 - Date clinic staff became aware of abnormal lab result
 - Cannot be before Onset Date
- Complete date (day, month, year) is required

AE Text Description

- Report only one diagnosis, symptom or sign per page
 - Record unifying diagnosis whenever possible
- Avoid using abbreviations
- Review for correct spelling
 - Variations in spelling can lead to differences in AE coding, meaning similar AEs will appear differently in AE safety reports
- Do not report surgeries as AEs (these are treatments)

AE Text Description

- Include anatomical location if not already stated (e.g. vaginal ulcer, cervical erythema)
- For lab AEs, include direction of lab value (increased or decreased)
 - Exception: If STI Test Result is positive, report STI diagnosis (i.e. genitourinary gonorrhoea) rather than as “X test positive”
- Record as much detail as possible to accurately and completely describe AE
- Text is used for MedDRA coding
- Up to 200 characters allowed in text field

AE Text Description – Things to note for MTN-036

- If an STI test result is positive
 - report the STI diagnosis (i.e., genitourinary gonorrhea) rather than as “X test positive”
- “Genital ulcer disease” is not a codable event. Need to note a specific STI if possible; otherwise report “Ulcer” with anatomical location(s)
- Reporting of assault
 - Report each physical adverse event as an AE
 - In AE text, add “...due to assault”

AE Text MedDRA Coding – Things to Consider in MTN-036

- Specify in AE text description if the AE is related to a procedure (iatrogenic)
 - Affects MedDRA coding
 - If “related to procedure” is put in comments only, MedDRA coders will place clinical query
- If the AE is due to the act of study ring insertion or removal, include this information in the AE text description
 - Ex: “pelvic pain due to ring removal”
 - Text about the ring will cause AEs to be coded to device MedDRA terms rather than a term that describes the AE
- If the AE is NOT due to the act of study ring insertion/removal, do not include mention of the ring in AE text description
 - Ex: “pelvic pain ~~while ring is in place~~”

AE Text MedDRA Coding – Things to Consider in MTN-036

Reproductive/Genital Pain AE severity grading

- Use the pain row on the FGGT rather than the grading provided on the general tox table.
- Note: Per the pain row of the FGGT, if any type of non-narcotic medication is taken for the pelvic/reproductive pain AE, the AE must be at least a severity grade of 2

INDIVIDUAL SIGNS/SYMPTOMS					
PARAMETER	GRADE 0 NORMAL	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE- THREATENING
PAIN AND TENDERNESS (Specify Area: Vulvar/Perineum, Vagina, Cervix (including cervical motion tenderness), Uterus, Adnexae, Pelvic/Lower Abdominal, or Ovary)					
*Note – if both pain and tenderness are present, only report the one with the most severe grade					
Pain* ¹	None	Pain causing no or minimal interference with usual social & functional activities	Pain causing greater than minimal interference with usual social & functional activities or the need for non-narcotic medication	Pain causing inability to perform usual social & functional activities or the need for narcotic medication	Disabling pain causing inability to perform basic self-care functions OR hospitalization (other than emergency room visit) indicated

AE Text MedDRA Coding – Things to Consider in MTN-036

- If a participant reports ANY combination of vulvovaginal symptoms at a given visit (pain, itching, erythema, edema, rash, tenderness, discharge), before filing each as unique events, consider whether or not there is an overarching diagnosis OR if the term VULVUOVAGINITIS can be used
- Pregnancy outcomes should not be reported as AEs (i.e. spontaneous abortions) – only the resulting maternal complications (if any)
- “Genital ulcer disease” is not a codeable event. Need to note a specific STI OR they should just report “Ulcer” with the anatomical location(s)

Onset Date

- Date AE began at given severity/frequency
- This could be:
 - Date of clinic visit/assessment/exam
 - Date ppt-reported symptom started/worsened
 - Collection date of sample that yielded abnormal lab result
 - On or prior to Date Reported to Site
 - Record complete date whenever available (Month and Year required)

Is the AE still ongoing?

- Select 'Yes' if AE is continuing at time it is first reported
 - Outcome = 'Recovering/Resolving' or 'Not recovered/resolved'
- If 'No', complete Outcome Date

Outcome Date

- Record complete date whenever available (Month and Year required)
- Outcome = ‘recovered/resolved’, ‘resolved with sequelae’, or ‘fatal’
- Can be based on:
 - Date on which participant reports no longer experiencing AE or associated symptoms
 - Date of study visit or specimen collection at which it is first noted AE has resolved or returned to baseline status

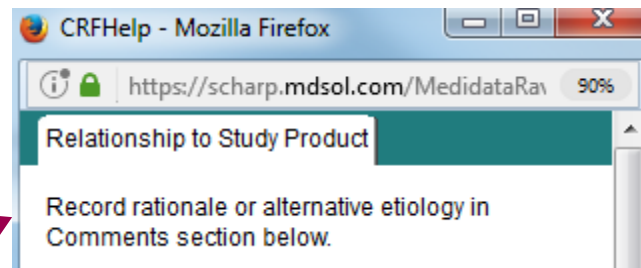
Severity Grade

- Select severity grade per FGGT or DAIDS Tox Table
 - If condition appears on both tables, use FGGT or to assess for severity

Severity Grade	...	○ / [] [] [] []
Relationship to Study Product?	Grade 1 (Mild)	○ / [] [] [] []
Action Taken with Study Product	Grade 2 (Moderate)	○ / [] [] [] []
Other action(s) taken	Grade 3 (Severe)	○ / [] [] [] []
.....	Grade 4 (Potentially life-threatening)	○ / [] [] [] []
	Grade 5 (Death)	○ / [] [] [] []

Relationship to Study Product

- Rationale (reason) of AE is required in the Comments section for each reported AE regardless of relationship of AE to study product



Relationship to Study Product

Related Not Related

Action Taken with Study Product

- Dose not changed: No change to participant's planned use of study product as a result of the AE (Should be selected if ppt is still in product use period and AE does not result in clinician-initiated permanent discontinuation of study product)
- Dose reduced: NA for MTN-036
- Dose increased: NA for MTN-036
- Drug withdrawn: Select if AE results in permanent discontinuation of study product
 - Select 'drug withdrawn' for each AE contributing to permanent discontinuation
- Drug interrupted: Select if AE results in hold of study product
- Not applicable: Select if AE onset date is on or after date the participant discontinues study product use
 - AE reported after Visit 11
 - AE = Grade 5 (death)
 - Study product already held or discontinued for different AE or reason

Other action(s) taken

- Record all action(s) taken, including any medications/treatments used and/or prescribed for AE
 - Participant self-report is fine
- Once confirmed meds/treatment used, record on Con Meds Log
 - Link each AE on Con Meds Log
- Use ‘Other’ for meds/actions indicated but not yet used
 - Update and resubmit eCRF once med or procedure has taken place
- If new/prolonged hospitalization, therapeutic procedure/surgery, or diagnostic procedure, specify details in Comments section

Outcome

- **Recovered/resolved:** AE is no longer present, has returned to baseline severity/frequency, or has increased in severity/frequency
 - Note: If ppt started taking medication to control AE, AE is not considered resolved while medication is still indicated
- **Recovering/resolving:** AE is continuing and has not yet resolved or returned to baseline severity/frequency
- **Resolved with sequelae:** Ppt recovered from AE, but with remaining effects or impairment.
 - Ppt recuperated but retained pathological conditions resulting from prior disease or injury
- **Not recovered/resolved:** AE continuing at time of participant study exit/termination from study
- **Fatal:** Should be selected only if severity grade for this AE is Grade 5.
 - Any other AEs continuing at time of death should be changed to ‘not recovered/resolved’

SAE and EAE

- **SAE item:** Select 'Yes' if AE meets SAE criteria
- **EAE item:** Select 'Yes' if AE has been or will be reported as an EAE
 - Specify 10 digit EAE number in text field provided on AE Log eCRF

For AEs Reported as EAEs

- Compare AE Log form and EAE form for consistency
- Note that some cases may involve 1 EAE report but several AE Log forms (e.g. motor vehicle accident)
- Discrepancies will result in clinical query
- If previously reported EAE is updated, update applicable AE Log entry
- Enter AE Log eCRF at same time as submitting EAE report
- Contact SCHARP CSA and CDM with any questions related to AE/EAE consistency

Baseline Medical Condition

- Review completed Baseline Medical History Log entries to see if AE is worsening of ongoing baseline medical condition
 - If AE is worsening of baseline condition, do not complete end date for this condition within applicable log line

Comments Field

- Comments field is a **required** field to capture rationale for relatedness of AE to study product
 - Tells ‘story’ for why AE is considered related (or not related)
- Use Comments field to record additional notes as needed, making sure any comments are consistent with AE text
 - Include details if “Other action(s) taken” = New/prolonged hospitalization, therapeutic procedure/surgery, or diagnostic procedure
- Up to 400 characters allowed

AE Log

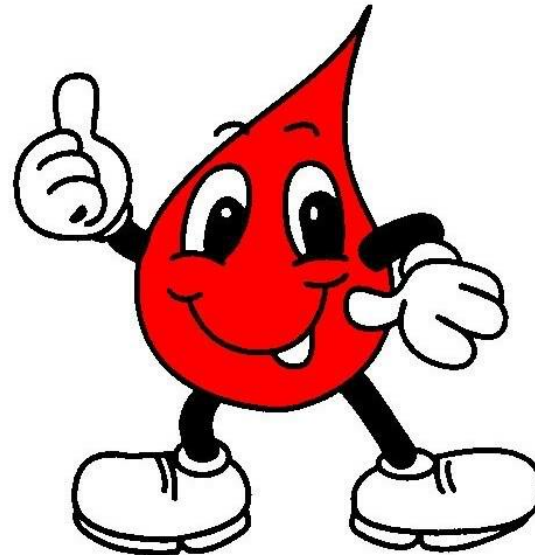
- Consider methods to identify AE Log entries for which the AE is still ongoing to help ensure these are reviewed and updated at each visit until Outcome is known
- Per MTN DM SOP, AE Log eCRFs should be completed within 1 day of site awareness

Questions?



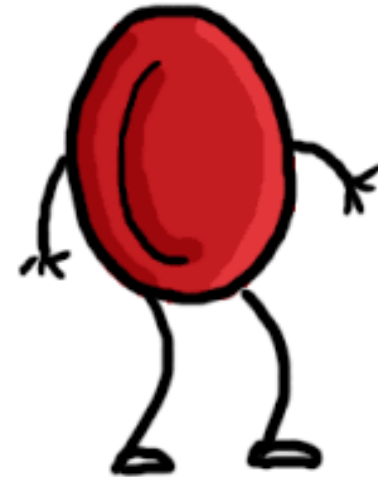
MTN-036

Laboratory Related CRFs



Laboratory Related CRFs

- ✓ Specimen Storage
- ✓ Cervical Specimen Storage
- ✓ Local Laboratory Results
- ✓ Hematology
- ✓ Pregnancy Test Results
- ✓ STI Test Results
- ✓ HIV Test Results
- ✓ HIV Confirmatory Test Results



Local Laboratory Results & Hematology eCRFs

- ❑ Rave will auto-populate the site lab at the top of the eCRFs
- ❑ Site lab normal ranges will auto populate for each of the analytes

Subject: 999425057
Page: Laboratory Results - V1 - Screening (1)

Lab: SCHARP [New Ranges](#)

HEMOGRAM

Hemogram not done/not collected

Hemogram collection date: 1 SEP 2014

Hemoglobin

	Data	Range Status	Unit	Range
Hemoglobin	13.4		g/dL	11.5 - 16.5
Hematocrit	40.1		%	36 - 47
MCV	86		fL	76 - 99
Platelets	262		10 ³ /mm ³	150 - 450
WBC	5.4		10 ³ /mm ³	4 - 12
Neutrophils	2440		cells/mm ³	2000 - 7500
Lymphocytes	2290		cells/mm ³	1000 - 4000
Monocytes	470			
Eosinophils	170			
Basophils	20			
AST(SGOT)	25		U/L	14 - 36
ALT(SGPT)	19		U/L	10 - 45
Creatinine	0.5		mg/dL	0.5 - 0.9

Hematology and Local Lab Analytes Conversion Tool

- Optional tool developed and maintained by FSTRF
- Enables sites to convert local lab values and enter them into Medidata Rave using the units reflected in DAIDS Tox Table
- Rounds converted lab values to three (3) digits after the decimal
- Available on ATLAS webpage

Laboratory Value Converter

This utility is a tool for converting Standard International (SI) Units to Conventional Units or Conventional Units to SI units. Enter a value, and then select the original and new units. The converted value will be displayed below rounded to three decimal places.

SCHARP provides this tool as a courtesy to site staff, for their optional and discretionary use, to convert study lab results into the appropriate units for entry into the study database. Users are responsible for ensuring that their conversion calculations are correct, and for entering the correct values into study CRFs as required. For questions regarding this tool, site staff may contact the SCHARP Clinical Data Manager for the given study.

All fields are required.

Value:


Original units:

New units:

Factor:

Converted value: 15.000 g / dL

Hematology and Local Lab Analytes Conversion Tool

	Data	Range Status	Unit	Range
Hemoglobin	13.2		g/dL	11.6 - 14.6
Hematocrit	40.2		%	34.1 - 43.3
MCV	84.7		fL	82.6 - 97.4
Platelets	223		10 ³ /μL	156 - 369
WBC	4.1		10 ³ /μL	3.8 - 10.6
Neutrophils	2.1		10 ³ /μL	2.24 - 7.68
Lymphocytes	1.5		10 ³ /μL	0.8 - 3.65
Monocytes	0.4		10 ³ /μL	0.3 - 0.9
Eosinophils	0.1		10 ³ /μL	0 - 0.4
Basophils	0.0		10 ³ /μL	0 - 0.06
	Data	Range Status	Unit	Range
AST (SGOT)	15		U/L	12 - 39
ALT (SGPT)	16		U/L	7 - 52

RAVE database will check severity grade provided on the ecRF against DAIDS tox table as part of real-time system queries.

Specimen & Cervical Specimen Storage CRFs

- Multiple plasma and CVF specimens for PK collected at Enrollment and Visit 10
- Enter new log line for each sample collected
 - Multiple log lines will be completed at Enrollment and Visit 10
 - Use the Time point fields to indicate the time point (e.g., 1 hour following ring insertion or 4 hours following ring removal) for each sample
 - One log line will be completed at all other visits
 - Choose “Not Applicable” in the Time point fields

Questions?



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