MTN-020
Data Communiqué #13

November 18, 2014

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AE Outcome Date when treatment is indicated

- For AEs requiring treatment, the outcome date should reflect when all associated symptoms have resolved (or returned to baseline severity) or the date when treatment is completed, whichever is later.
- An AE is not considered resolved until both symptoms **and** treatment have been completed.

Example: A participant presents with Grade 2 vaginal discharge on 23May14 and is prescribed doxycycline. Her symptoms resolve on 27May14 and completes her antibiotic regimen on 06Jun14. The AE outcome date recorded in Item 6 should be **06Jun14**.

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Assignment of Severity Grade- Genitourinary infections & symptoms

- If an AE is graded using the general infection row of the main DAIDS Tox Table and treated with antimicrobial therapy, the infection must be graded automatically at Grade 2 or higher (see SSP section 11.4).

PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
INFECTION				
Infection (any other than HIV infection)	Localized, no systemic antimicrobial treatment indicated AND Symptoms causing no or minimal interference with usual social & functional activities	Systemic antimicrobial treatment indicated OR Symptoms causing greater than minimal interference with usual social & functional activities	Systemic antimicrobial treatment indicated AND Symptoms causing inability to perform usual social & functional activities OR Operative intervention (other than simple incision and drainage) indicated	Life-threatening consequences (e.g., septic shock)

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Assignment of Severity Grade- Genitourinary infections & symptoms

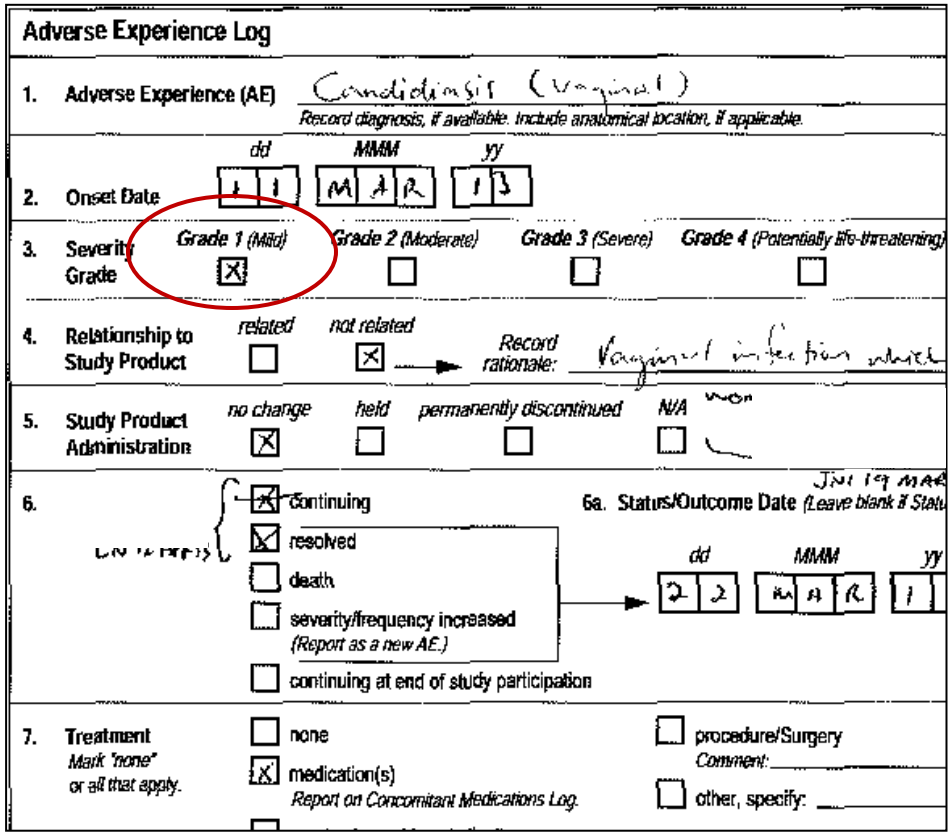
- However, if a genitourinary AE is treated with systemic antimicrobials, the severity grade will depend of whether the FGGT or the main DAIDS Tox Table is used to grade the AE.
    - When grading an AE according to the main DAIDS Tox Table, treatment with systemic antimicrobials warrants a severity grade of 2 or higher.
    - When grading an AE according to the FGGT, treatment with systemic antimicrobials may still be covered under severity grade 1. Grading depends on criteria defined in given row.

Assignment of Severity Grade- Genitourinary infections & symptoms

Example #1:

A participant presents with mild vaginal discharge and itching and wet mount results are positive for candida. She is given a dose of fluconazole for treatment.

- This infection should be assigned as Grade 1 per the criteria in the Candida row of the FGGT regardless of whether an antimicrobial was prescribed.



Adverse Experience Log

1. **Adverse Experience (AE)** — Candidiasis (vaginal)
   Record diagnosis, if available. Include anatomical location, if applicable.
2. **Onset Date** — dd: 11 MMM: MAR yy: 13
3. **Severity Grade** — Grade 1 (Mild): X; Grade 2 (Moderate): ☐; Grade 3 (Severe): ☐; Grade 4 (Potentially life-threatening): ☐
4. **Relationship to Study Product** — related: ☐; not related: X → Record rationale: Vaginal infection which
5. **Study Product Administration** — no change: X; held: ☐; permanently discontinued: ☐; N/A: ☐ non
6. — Continuing: X; resolved: X; death: ☐; severity/frequency increased *(Report as a new AE.)*: ☐; continuing at end of study participation: ☐
   6a. **Status/Outcome Date** *(Leave blank if Statu* — dd: 22 MMM: MAR yy: 1
7. **Treatment** *Mark "none" or all that apply.* — none: ☐; medication(s): X *Report on Concomitant Medications Log.*; procedure/Surgery: ☐ *Comment:*; other, specify: ☐

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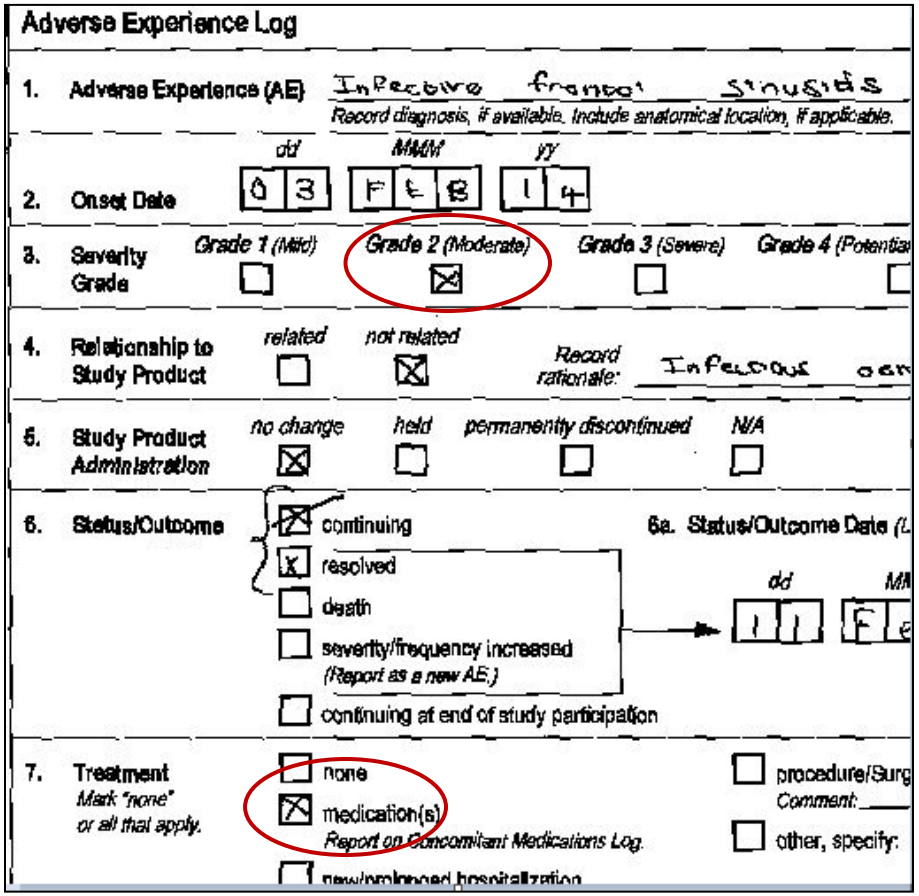
Assignment of Severity Grade- Genitourinary infections & symptoms

Example #2:

A participant presents with mild nasal congestion, fever, and headache consistent with infective frontal sinusitis and is prescribed Augmentin.

- ❑ This infection should be assigned as at least Grade 2 per the criteria in infection row of the DAIDS General Tox table as systemic antimicrobial treatment was indicated.



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Documentation of Missed Menses Events – During Follow up

- Missed menses AEs that extend >3 months should be documented by updating the completed AE log CRF for 'missed menses':
  - ✓ Update Item 1 with a new AE term of either:
    - ➢ "Oligomenorrhea" for missed menses 4-5 months in duration
    - ➢ Or, "Amenorrhea" for missed menses >6 months in duration
  - ✓ Update Item 3 with a new severity grade
- A new AE log CRF should not be completed to document increased duration of the same infrequent bleeding event.

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Documentation of Missed Menses Events – During Follow up

The updated AE term and severity grade should be assessed per the FGGT row for 'unexplained infrequent bleeding". Note: This row excludes missed menses due to hormonal contraception, pregnancy, or post-partum.

UTERINE BLEEDING AND PREGNANCY COMPLICATIONS					
PARAMETER	**GRADE 0 NORMAL**	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
ABNORMAL UTERINE BLEEDING UNRELATED TO PREGNANCY					
Unexplained infrequent bleeding (excludes expected absence of menses due to hormonal contraception or pregnancy/postpartum)	Participant report of normal or expected bleeding frequency	No menses for 1-3 months (missed menses)	No menses for > 3 months (oligomenorrhea/ amenorrhea)	NA	NA

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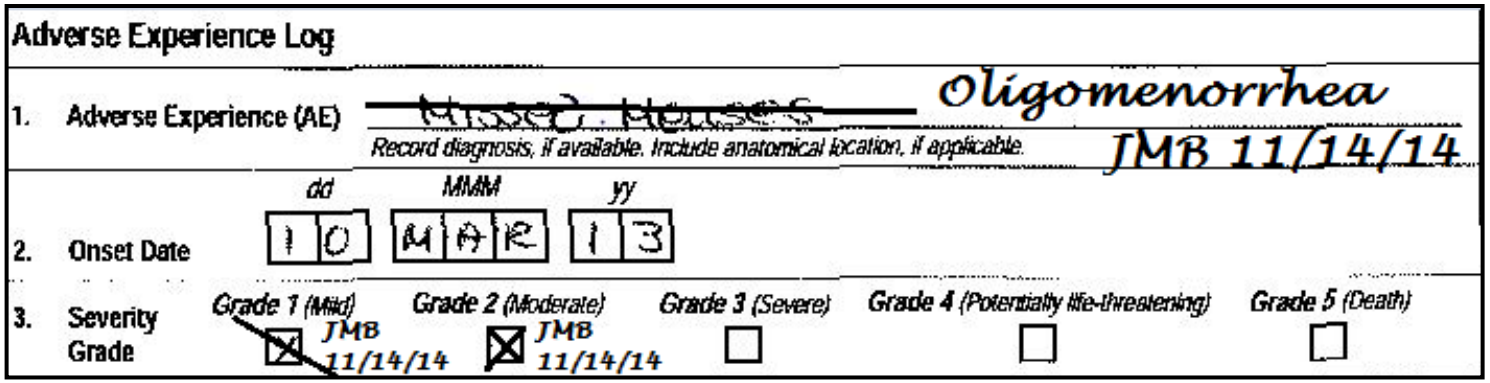
Documentation of Missed Menses Events – During Follow up

Example:

A participant experiences unexplained infrequent bleeding for 2 months and an AE log CRF is completed for Grade 1 'missed menses'. She continues to miss her menses for 2 subsequent months. One the same AE log CRF:

- ✓ Item 1 should be updated to "Oligomenorrhea"
- ✓ Item 3 should be updated to a severity grade of "2"



Adverse Experience Log

1. Adverse Experience (AE): ~~Missed Menses~~ Oligomenorrhea JMB 11/14/14
   Record diagnosis, if available. Include anatomical location, if applicable.
2. Onset Date: dd 10 MMM MAR yy 13
3. Severity Grade: Grade 1 (Mild) ☒ JMB 11/14/14 (~~Missed Menses~~) Grade 2 (Moderate) ☒ JMB 11/14/14 Grade 3 (Severe) ☐ Grade 4 (Potentially life-threatening) ☐ Grade 5 (Death) ☐

If the participant continues to experience missed menses for 6 or more months, in total, the AE log CRF should be updated once again to reflect the new AE term of "amenorrhea" in Item 1.

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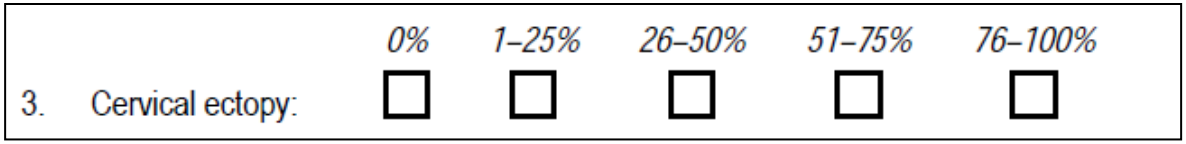
Cervical Ectopy Assessment

- Cervical ectopy is a required assessment in ASPIRE, but is considered neither a normal nor abnormal finding.

- Cervical ectopy assessment is required in Item 3 on the Pelvic Exam CRF.



However, the 'no normal variants or abnormal findings' box on the Pelvic Exam Diagrams non-DataFax form may be marked if only ectopy is observed. The presence of cervical ectopy is common and should not factored into questions on the diagram form.

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CRF Tracking System (CTS) Reminder

- CTS provides two types of emailed reports to track the number of CRFs received and validated at SCHARP:

Reception Report:

List of transmissions received from a site and includes date/time of transmission, # pages received, unique "Fax Raster" ID"

Validation Report:

List of Study number, PTID, Fax ID page number, CRF plate number, visit code, and validation date for each CRF received and validated at SCHARP

To manage the frequency of these reports and the staff who should receive these reports, email **support@scharp.org** to complete a CRF Tracking System Registration Form.

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Questions?

- Please contact Jen Berthiaume and Karen Patterson with any questions you have about this slide presentation or the Data Communiqué.

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