PSRT Queries and Study Product Relatedness

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Queries

- Twenty-four, as of February 8, 2013
- Turn-around time for query responses initially an issue but now is 24 hours or less most of the time
- Some lost queries
  - Contact management team
  - Re-send as soon as possible

Query Topics

- Study/Protocol Guided
  - Product holds: 5
  - (Product return: 2)
  - (Resume product: 3)
  - Eligibility: 1
- SSP Directed
  - HIV testing: 4
- Clinical/Other
  - Genitourinary infection: 2
  - Genital bleeding: 4
  - Other: 3

Product Hold Examples

- IoR discretion
  - Recurrent cervicitis
  - Rash
- Participant initiated
  - Partner wanted participant to remove the ring

Product Return

- SSP Section 9.7
  - If the vaginal ring **cannot be retrieved** (i.e., participant disposed of it or product was lost after removal) this must be documented on the CRF and the related details and counseling around the need to ensure return of product to site should be detailed in the participants chart notes.

Resume Product

- Usually follow product holds
  - Informational queries that provide some clinical follow-up
    - Cervicitis resolved
    - Rash resolved/resolving…

HIV Testing – SSP 6.5.3

Participants With a Positive Rapid HIV Test Who Are Confirmed as HIV-uninfected

- For participants who have a positive rapid HIV test result and are later confirmed HIV-uninfected per the algorithm in protocol Appendix III, product use should continue to be held and the IoR or designee should immediately consult with the PSRT for further guidance.
- REVISED NOW

Clinical/Other

- Genitourinary infections
  - Cervicitis
- Other
  - Laboratory abnormalities
  - Participant who drops out of study participation

Genital Bleeding

- Infrequent bleeding/Missed menses
- Menorrhagia/metrorrhagia
- Menses and ring use
  - Participant removing ring believing that the ring “hampers” blood flow

Questions regarding the PSRT Query Process?

Suggestions/Input?

Relationship to Study Product

Relationship to Study Product

Relationship to Study Agent

- The site investigator is responsible for assessing the relationship between the AE and the study agent(s)
- Site investigators must determine whether there is a **reasonable possibility** that the study agent(s) caused or contributed to an AE

Relationship Relies on:

- A temporal relationship between the event and administration of the study agent(s),
- A plausible biological mechanism for the agent to cause the AE,
- Another possible etiology for the AE,
- Previous reports of similar AEs associated with the study agent or other agents in the same class, and
- Recurrence of the AE after re-challenge or resolution after de-challenge, if applicable.

Terms Used:

- **Related** – There is a reasonable possibility that the AE may be related to the study agent(s).

- **Not Related** – There is not a reasonable possibility that the AE is related to the study agent(s).

When Deemed NOT Related:

- An alternative etiology, diagnosis, or explanation for the SAE/AE should be provided.
  - If new information becomes available, the relationship assessment of any AE should be reviewed again and updated, as required.

Mode: Number pages sequentially (001, 002, 003) for each participant. Page 002

MTN-020 ASPIRE (192) AE-1 (460)

Participant ID
Site Number Participant Number Clinic

Date Reported to Site: 24 (dd) DEC (MMM) 12 (yy)

Adverse Experience Log

1. Adverse Experience (AE): Intermittent urticarial rash on arms, thighs, abdomen and back
Record diagnosis, if available. Include anatomical location, if applicable.

2. Onset Date: 20 (dd) DEC (MMM) 12 (yy)

3. Severity Grade: Grade 1 (Mild) ☐ Grade 2 (Moderate) ☒ Grade 3 (Severe) ☐ Grade 4 (Potentially life-threatening) ☐ Grade 5 (Death) ☐

4. Relationship to Study Product: related ☒ not related ☒ → Record rationale: Not related is correct. ~~No other cause (end of allergen season)~~ Rash did resolve with ring re-inserted ∴ not related.

5. Study Product Administration: no change ☐ held ☒ permanently discontinued ☐ N/A ☐

6. Status/Outcome: continuing ☒ resolved ☐ death ☐

6a. Status/Outcome Date (Leave blank if Status/Outcome is "continuing."): 14 (dd) JAN (MMM) 13 (yy)

☐ severity/frequency increased
(Report as a new AE.)

☐ continuing at end of study participation

7. **Treatment**
Mark "none" or all that apply.

☐ none
☒ medication(s)
Report on Concomitant Medications Log.
☐ new/prolonged hospitalization
Comment: _____

☐ procedure/Surgery
Comment: _____
☒ other, specify: Prescription given for chlorpheniramine

8. Is this an SAE according to ICH guidelines? ☐ yes ☒ no

9. Has/will this AE be reported as an EAE? ☐ yes ☒ no

10. At which visit month was this AE first reported? 0 3 . 1 *Visit month required (regular or interim)*

11. Was this AE a worsening of a pre-existing condition? ☒ yes ☐ no

EXACT COPY From SC

Comments: Intermittent urticarial rash lasts about 1-2 hours and appears on daily basis from 19Dec12 and ongoing. No aetiology from history as to possible allergen. Vaginal ring removed and participant to be followed up in few days for possible reinsertion. Rash did not resolve with ring re-inserted ∴ not related

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Staff Initials / Date

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When Deemed Related…?

primary: arrival: Mon Jan 14 23:41:55 2013

[redacted]

Note: Number pages sequentially (001, 002, 003) for each participant. Page 001

MTN-020 ASPIRE (192) AE-1 (460)

Participant ID	Date Reported to Site
Site Number / Participant Number / Chk	08 JAN 13 (dd / MMM / yy)

Adverse Experience Log

1. **Adverse Experience (AE)**: Headaches
   Record diagnosis, if available. Include anatomical location, if applicable.

2. **Onset Date** (dd / MMM / yy): 02 JAN 13

3. **Severity Grade**: ☐ Grade 1 (Mild) ☒ Grade 2 (Moderate) ☐ Grade 3 (Severe) ☐ Grade 4 (Potentially life-threatening) ☐ Grade 5 (Death)

4. **Relationship to Study Product**: ☒ related ☐ not related → Record rationale: _____

5. **Study Product Administration**: ☒ no change ☐ held ☐ permanently discontinued ☐ N/A

6. **Status/Outcome**: ☒ continuing — 6a. **Status/Outcome Date** *(Leave blank if Status/Outcome is "continuing.")*

☒ resolved
☐ death
☐ severity/frequency increased
(Report as a new AE.)
☐ continuing at end of study participation

→ dd: 09 MMM: JAN yy: 13

7. **Treatment** *Mark "none" or all that apply.*	☐ none ☒ medication(s) *Report on Concomitant Medications Log.* ☐ new/prolonged hospitalization *Comment:*	☐ procedure/Surgery *Comment:* ☐ other, specify:	
8. Is this an SAE according to ICH guidelines?	☐ yes	☒ no	
9. Has/will this AE be reported as an EAE?	☐ yes	☒ no	
10. At which visit month was this AE first reported?	01.0 *Visit month required (regular or interim)*		
11. Was this AE a worsening of a pre-existing condition?	☐ yes	☒ no	

EXACT COPY From SC

Comments: Ppt has Grade 1 elevated blood pressure ~~BP~~ which may be related to these headaches but relationship to product is possible. Participant reports a similar event previously but has not experienced any headaches in the last 11 months

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primary: arrival: Wed Feb 6 01:39:13 2013

Page 003

MTN-020 ASPIRE (192) AE-1 (460)

Participant ID	Date Reported to Site
Site Number / Participant Number / Clinic	dd: 15 MMM: JAN yy: 13

Adverse Experience Log

1. Adverse Experience (AE): CERVICITIS
   Record diagnosis, if available. Include anatomical location, if applicable.

2. Onset Date: dd: 14 MMM: DEC yy: 12

3. Severity Grade: Grade 1 (Mild) ☐ Grade 2 (Moderate) ☒ Grade 3 (Severe) ☐ Grade 4 (Potentially life-threatening) ☐ Grade 5 (Death) ☐

4. Relationship to Study Product: related ☒ not related ☐ → Record rationale: _____

5. Study Product Administration: no change ☒ held ☐ permanently discontinued ☐ N/A ☐

☐ death

☐ severity/frequency increased
(Report as a new AE)

☐ continuing at end of study participation

→ [ ][ ] DEC [1][2]
DON'T KNOW

7. **Treatment**
Mark "none" or all that apply.

☐ none

☒ medication(s)
Report on Concomitant Medications Log.

☐ new/prolonged hospitalization
Comment: _____

☐ procedure/Surgery
Comment: _____

☐ other, specify: _____

8. Is this an SAE according to ICH guidelines? ☐ yes ☒ no

9. Has/will this AE be reported as an EAE? ☐ yes ☒ no

10. At which visit month was this AE first reported? [0][3].[0] *Visit month required (regular or interim)*

11. Was this AE a worsening of a pre-existing condition? ☐ yes ☒ no

EXACT COPY From SC

Comments: pt reported to nurse that after her visit (13 DEC 12 - month 02), she went to her local clinic on the 14 DEC 12 and was diagnosed with cervicitis, she had dyspareunia, vaginal discharge, was treated with syndromic management at clinic when she presented for month 03, symptoms had resolved, female pelvic exam was normal.

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Staff Initials / Date

Note: Number pages sequentially (001, 002, 003) for each participant. Page 002

MTN-020 ASPIRE (192) AE-1 (460)

Participant ID
Site Number | Participant Number | Chk

Date Reported to Site: 11 (dd) JAN (MMM) 13 (yy)

Adverse Experience Log

1. Adverse Experience (AE): Grade 2 WEIGHT LOSS -UNINTENTIONAL
   Record diagnosis, if available. Include anatomical location, if applicable.

2. Onset Date (dd MMM yy): 11 JAN 13

3. Severity Grade: Grade 1 (Mild) ☐ | Grade 2 (Moderate) ☒ | Grade 3 (Severe) ☐ | Grade 4 (Potentially life-threatening) ☐ | Grade 5 (Death) ☐

4. Relationship to Study Product: related ☒ | not related ☐ → Record rationale: _____

5. Study Product Administration: no change ☒ | held ☐ | permanently discontinued ☐ | N/A ☐

6. Status/Outcome: ☒ continuing ☐ resolved ☐ [illegible]

6a. Status/Outcome Date (Leave blank if Status/Outcome is 'continuing.') (dd MMM yy): _____

☐ continuing at end of study participation

7. **Treatment**
Mark "none" or all that apply.

☒ none
☐ medication(s)
Report on Concomitant Medications Log.
☐ new/prolonged hospitalization
Comment: _____
☐ procedure/Surgery
Comment: _____
☐ other, specify: _____

EXACT COPY From SC

8. Is this an SAE according to ICH guidelines? ☐ *yes* ☒ *no*

9. Has/will this AE be reported as an EAE? ☐ yes ☒ no

10. At which visit month was this AE first reported? 03.0 *Visit month required (regular or interim)*

11. Was this AE a worsening of a pre-existing condition? ☐ *yes* ☒ *no*

Comments: _____

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Staff Initials / Date

Participant ID

Site Number | Participant Number | Chk

Date Reported to Site: 10 (dd) JAN (MMM) 13 (yy)

Adverse Experience Log

1. **Adverse Experience (AE)**: Vulvovaginal Candidiasis
   Record diagnosis, if available. Include anatomical location, if applicable.

2. **Onset Date** (dd MMM yy): 08 JAN 13

3. **Severity Grade**: *Grade 1 (Mild)* ☐ | *Grade 2 (Moderate)* ☒ | *Grade 3 (Severe)* ☐ | *Grade 4 (Potentially life-threatening)* ☐ | *Grade 5 (Death)* ☐

4. **Relationship to Study Product**: *related* ☒ | *not related* ☐ → *Record rationale:* _____

5. **Study Product Administration**: *no change* ☒ | *held* ☐ | *permanently discontinued* ☐ | *N/A* ☐

6. **Status/Outcome**: ☒ continuing ☐ resolved

6a. **Status/Outcome Date** *(Leave blank if Status/Outcome is "continuing.")* (dd MMM yy)

☐ death

☐ severity/frequency increased
(Report as a new AE.)

☐ continuing at end of study participation

→ ☐☐ ☐☐☐ ☐☐

7. **Treatment**
Mark "none" or all that apply.

☐ none

☒ medication(s)
Report on Concomitant Medications Log.

☐ new/prolonged hospitalization
Comment: _____

☐ procedure/Surgery
Comment: _____

☐ other, specify: _____

8. Is this an SAE according to ICH guidelines? ☐ *yes* ☒ *no*

9. Has/will this AE be reported as an EAE? ☐ *yes* ☒ *no*

10. At which visit month was this AE first reported? 0 3 . 0 *Visit month required (regular or interim)*

11. Was this AE a worsening of a pre-existing condition? ☐ *yes* ☒ *no*

EXACT COPY From SC

Comments: Pt reported vaginal discharge.

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