

# Genital Bleeding in MTN 020

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Annual Meeting  
February 22, 2012





# Background

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- Genital Bleeding is common
  - Includes menses
  - Includes intermenstrual bleeding (IMB)
- Determining whether genital bleeding constitutes an “adverse event” will vary by protocol



# The VOICE Experience

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- **“Only unexpected bleeding is an AE”**
- Expected bleeding includes
  - Menses
  - Bleeding from missed oral contraceptive pill (ocp)
  - Spotting within one year of starting depo
  - Spotting within 3 months of ocp initiation
- Unexpected bleeding includes
  - Heavy or prolonged menses
  - Unexplained bleeding in between menses



# VOICE AEs

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- 11,500 Adverse Events
- Genital Bleeding Assessment Form
- 484 for bleeding events to date (4.2%)
  - Menorrhagia (137)
  - Metrorrhagia (276)
  - Menometrorrhagia (57)
  - Post coital bleeding (14)

# Your Feedback

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# The MTN 020 Response

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- Simplify

And

- Don't disregard bleeding presumed to be due to another cause



# Genital Bleeding in MTN 020

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- Is this bleeding event consistent with the participant's baseline bleeding pattern?
  - Yes = NO AE
  - No = AE



# Implications

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- Obtaining an accurate baseline bleeding history will be imperative
- The level of detail will be at the site's discretion
- Goal: A reasonable person reading the baseline history can determine whether a current bleeding event is consistent with baseline or not





# Scenario #1

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- 22 year old woman at screening describes regular moderate flow menstrual periods occurring every 24-32 days and lasting 3-6 days
  - She is started on depo-provera during the screening period
  - One month after enrollment she reports a 14 day bleeding episode occurring 30 days after her last menses
  - Has an AE occurred?

# Scenario #2

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- 22 year old woman describes regular moderate flow menstrual periods occurring every 24-32 days and lasting 3-6 days at screening
  - She is started on depo-provera during the screening period
  - One month after enrollment she reports 3 days of spotting 2 weeks after her last menstrual period
  - Has an AE occurred?



# Scenario #4

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- 22 year old woman describes unpredictable spotting on depo-provera at the screening visit. The spotting lasts 2-7 days, is light in flow, and can occur anywhere from 2 weeks to 3 months apart.
- 2 month after enrollment she reports 3 days of spotting 2 months after her last spotting episode
- Has an AE occurred?



# One BIG caveat

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- Multiple bleeding episodes deemed to be AEs may ultimately be captured as one open ended AE once a new pattern is identified

# Ongoing Metrorrhagia

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- 22 year old with monthly menses lasting 4-6 days at enrollment is enrolled into MTN 020
- In the screening period she has an implant placed for contraception
- At Month 1 she reports a 3 day period of light vaginal bleeding 2 weeks after her last menstrual period.
  - An AE for metrorrhagia is filed

# Ongoing Metrorrhagia

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- At month 2, the participant reports another episode of light bleeding this time lasting 5 days and occurring 2 weeks after the last episode
  - Pelvic exam is unremarkable
- Is this a new AE or a continuation of the previously filed AE?
- Clinician discretion
  - File a new AE and consider an open ended AE with her next event OR
  - Update the last AE to be ongoing



# Recurring Bleeding AEs in VOICE

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- 11,500 Adverse Events
- 484 for bleeding events
  - Menorrhagia (137 events in 120 ppts)
  - Metrorrhagia (276 events in 215 ppts)
  - Menometrorrhagia (57 in 49 ppts)
  - Post coital bleeding (14 in 14 ppts)
- 56 participants with 2 or more identical bleeding AEs
  - 19 of these with >2 AEs



# Amenorrhea

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- Unexplained amenorrhea should be recorded as a pre-existing condition
- Amenorrhea secondary to contraceptive use need not be recorded as pre-existing
- Amenorrhea in follow-up is an AE if it is different from baseline and NOT explained by contraception or pregnancy (as per the tox table)





# Evaluating Abnormal Bleeding

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- A new AE for genital bleeding should prompt a pelvic exam
- Whether bleeding in the context of an open AE should be evaluated is per clinician discretion



# Please Tell Us....

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- Is this clear? Logical?
- What challenges to this reporting method do you foresee?
- Will you miss the genital bleeding assessment form?
- How detailed should training at your site be regarding genital bleeding assessment, documentation and reporting?

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