01. Protocol Deviation Trends

KRIs:

- % key protocol deviation by study and site
- # of deviations by key deviation type by study and site

QTLs:

- Threshold: ≥ X% key protocol deviations
  - Threshold determined in conjunction with the Biostatistician based on study requirements (note: thresholds for study and site may be different)
  - If met
    - → Evaluate if site re-training is warranted
    - → Evaluate potential impact to analysis
- Threshold: > X deviations per key deviation type
  - Threshold determined in conjunction with the Biostatistician (and Medical Monitor if applicable) based on study requirements (threshold may vary based on each deviation type and may be different for study and site)
  - If met
    - → Evaluate potential impact to patient safety if applicable
    - → Evaluate if site re-training is warranted
    - → Evaluate potential impact to analysis

02. Safety Signals in Lab or Adverse Event Data

KRIs:

- **Frequency of serious adverse events (SAEs)**
- **% of subjects with clinically significant lab abnormalities or grade 3/4 lab abnormalities if CTCAE grading**
- **Unexpected trends in lab values (e.g., ALT, creatinine, etc.)**

QTLs:

- **Threshold: > than expected SAE rate per subject**
  - Based on initial study assumptions
  - If met
    - → Evaluate potential impact to patient safety
- **Threshold: ≥X% of subjects with lab abnormalities**
  - Threshold determined in conjunction with the Medical Monitor based on study requirements
  - If met
    - → Evaluate potential impact to patient safety
    - → Ensure accurate AE reporting is occurring
    - → Evaluate if there is a potential site procedure impact
- **Threshold: ≥X subjects with same unexpected lab signal**
  - Threshold determined in conjunction with the Medical Monitor based on study requirements
  - If met
    - → Evaluate potential impact to patient safety
    - → Ensure accurate AE reporting is occurring

03. Device Data Anomalies (e.g., Wearables, ePRO, etc.)

KRIs:

- **% of missing or corrupted device data entries by assessment**
- **# of deviations by key deviation type by% of device non-compliance instances per subject (e.g., not wearing, not completing assessments, etc.) study and site**
- **Frequency of outlier readings (e.g., HR > 180 bpm)**

QTLs:

- **Threshold: ≥X% missing or corrupted device data entries by assessment**
  - Threshold determined in conjunction with key study stakeholders (e.g. device vendor, Biostatistician, Clinical Operations, etc.) based on study requirements
  - If met
    - → Evaluate potential issue(s) with devices or transmission
    - → Evaluate potential impact to analysis if applicable
- **Alert: ≥X% missing assessments per subject**
  - If met
    - → Evaluate potential issue(s) with device or transmission
    - → Evaluate if subject retraining is warranted
- **Threshold: ≥X subjects with same or similar unexpected outlier readings**
  - Threshold determined in conjunction with the Medical Monitor based on study requirements
  - If met
    - → Evaluate potential impact to patient safety if applicable
    - → Ensure accurate AE reporting is occurring if applicable
    - → Evaluate potential issue(s) with devices

04. Investigational Product Dosing Compliance

KRIs:

- **% of missed doses by study and site**
- **% of incorrect doses/dosing errors by study and site**
  - May also consider KRI related to dose interruptions if applicable
- **% of subjects with dosing outside protocol-defined windows**

QTLs:

- **Threshold: ≥X% of total doses missed**
  - Threshold determined in conjunction with the Medical Monitor and Biostatistician based on study requirements (note: thresholds for study and site may be different)
  - If met
    - → Evaluate potential impact to patient safety
    - → Evaluate if site (or subject) re-training is warranted
    - → Evaluate potential impact to analysis
- **Threshold: ≥X% of total incorrect doses/dosing errors**
  - Threshold determined in conjunction with the Medical Monitor and Biostatistician based on study requirements (note: thresholds for study and site may be different)
  - If met
    - → Evaluate potential impact to patient safety
    - → Evaluate if site (or subject) re-training is warranted
    - → Evaluate potential impact to analysis
- **Threshold: ≥X% window dosing non-compliance**
  - Threshold determined in conjunction with the Medical Monitor and Biostatistician based on study requirements (note: thresholds for study and site may be different)
  - If met
    - → Evaluate potential impact to patient safety
    - → Evaluate if site (or subject) re-training is warranted
    - → Evaluate potential impact to analysis

05. Visit Window Adherence

KRIs:

- **% of visits outside protocol-defined windows by study and site**
- **Average (or median) deviation (in days) outside of scheduled visit window**

QTLs:

- **Threshold: ≥X% of visits outside window**
  - Threshold determined in conjunction with key study stakeholders (e.g. Medical Monitor, Biostatistician, Clinical Operations, etc.) based on study requirements (note: thresholds for study and site may be different, take into account dosing regime and critical data)
    - → Evaluate potential impact to patient safety
    - → Evaluate if site re-training is warranted
    - → Evaluate potential impact to analysis
- **Threshold: ≥X average (or median) days outside of scheduled visit window**
  - Threshold determined in conjunction with key study stakeholders (e.g. Medical Monitor, Biostatistician, Clinical Operations, etc.) based on study requirements (note: thresholds for study and site may be different, take into account dosing regime and critical data)
    - → Evaluate potential impact to patient safety
    - → Evaluate if site re-training is warranted
    - → Evaluate potential impact to analysis

06. Missing Data Trends

KRIs:

- **% of missing critical data assessments (risk-based) by study and site**

QTLs:

- **Threshold: ≥X% missing critical data assessments**
  - Threshold determined in conjunction with key study stakeholders (e.g. Medical Monitor, Biostatistician, Clinical Operations, etc.) based on study requirements (note: thresholds for study and site may be different)
    - → Evaluate potential impact to patient safety
    - → Evaluate if site re-training is warranted
    - → Evaluate potential impact to analysis

07. Data entry or issue resolution delay

KRIs:

- % of visits entered outside of target data entry window (e.g. all visit data to be entered within 10 business days) by site
- Average (or median) deviation (in days) outside of target data entry window by site
- % of open site queries after 30 days by site
- % of answered queries after 60 days by service line

QTLs:

- Threshold: ≥X% visits entered outside of target data entry window
  - Threshold determined in conjunction with Clinical Operations based on study requirements
    - → Evaluate if site re-training is warranted
- Threshold: ≥X% average (or median) days outside of target data entry window
  - Threshold determined in conjunction with Clinical Operations based on study requirements
    - → Evaluate if site re-training is warranted
- Threshold: ≥X% open site queries after 30 days
  - Threshold determined in conjunction with Clinical Operations based on study requirements
    - → Evaluate if site re-training is warranted
- Threshold: ≥X% answered site queries after 60 days
  - Threshold determined in conjunction with key study stakeholders (e.g. service lines, etc.) based on study requirements (note: take into account monitoring visit frequency)
    - → Evaluate root cause and if intervention is warranted