DCP Safety Committee

Update and Review

January 19, 2017

Overview:

- FDA's IND Safety Final Rule
- DCP's Response
  - DCP Safety Committee
  - Harmonizing Medical Monitors' Process
- SAE Reporting
  - SAE Flow Chart Process
  - SAE Tracking and Signal Assessment
- Defined Regulatory Terms
  - Expectedness, Causality, Hospitalization

FDA's IND Safety Final Rule:

- 21 CFR §312.21
  - September 29, 2011
- Shifts from Strict Compliance to Interpretation and Medical Judgment
  - Reduce number of meaningless safety reports
  - Focus on SAEs that define a safety profile
  - Expedite FDA's review of critical safety data

DCP's Response:

- Establish DCP Safety Committee
  - October 27, 2014
- Multi-Disciplinary Team
  - Leslie Ford
  - Gary Della'Zanna
  - Margaret Wojtowicz
  - Chen Suen
  - Judy Smith
  - Vikrant Sahasrabuddhe
  - Don Johnsey
  - Linda Doody
  - Janet Rosecan

SAE Processing

- **Harmonize Medical Monitor Processing:**
  - **DCP's Electronic SAE Report Form**
    508 Compliant fillable PDF
  - **Electronic Signature** (mandatory)
  - **SAE Reporting and Data Base Monitoring**

DCP SAE Process Flow Chart

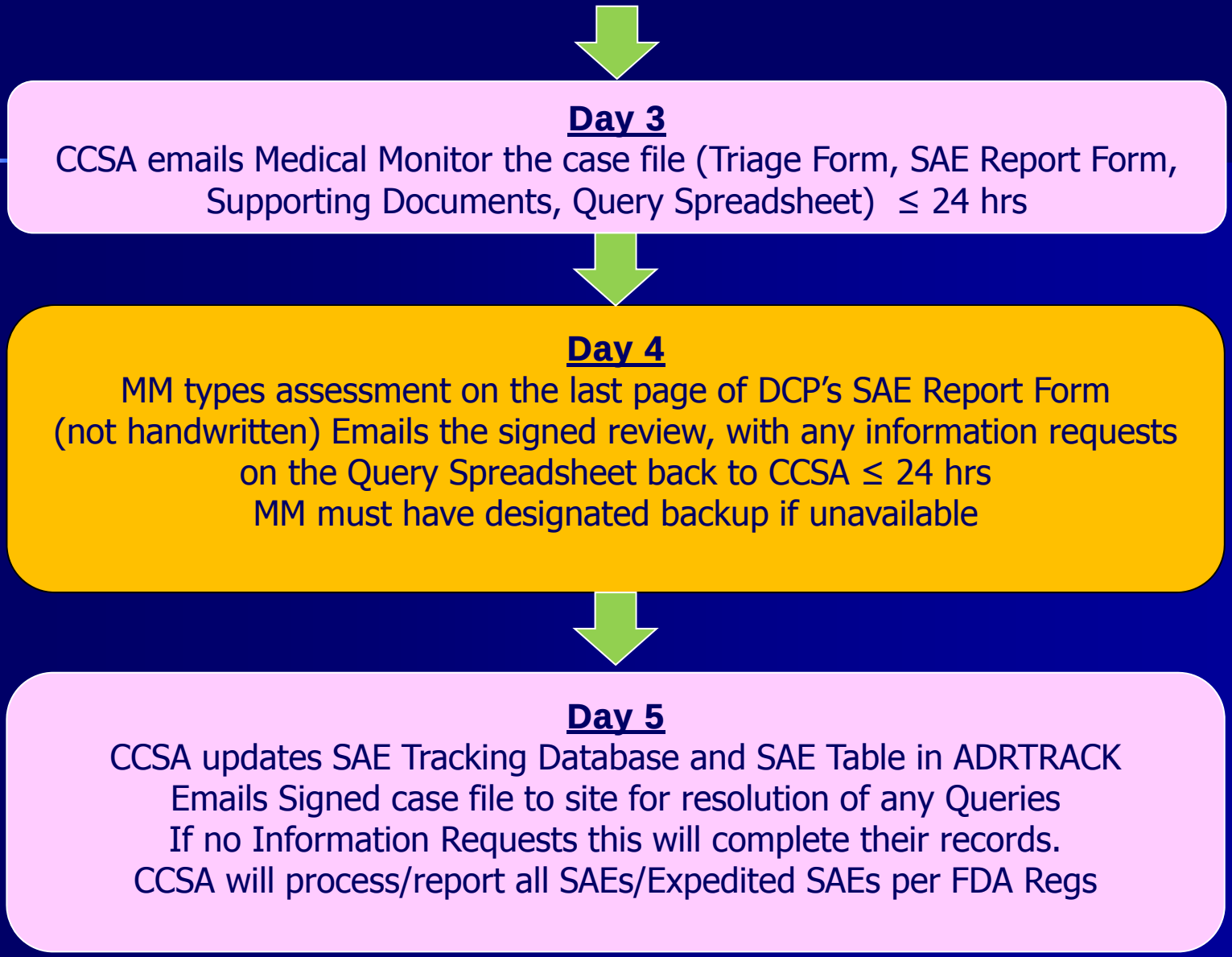
Day 0
Site notifies DCP & CCSA of SAE (telephone, email) ≤ 24 hrs of identification
Starts the FDA 15 day reporting clock (Day 0)

Day 1
Site submits by email a completed DCP SAE Report Form (one event/form)
to both DCP & CCSA ≤ 24 hrs

Day 2
CCSA assigns case number, date stamps report, performs initial assessment
for expedited reporting and preliminary MedDRA coding/mapping

Day 2
CCSA drafts the Narrative and Query Spreadsheet, Enters Report in
SAE Tracking Database (SAEDB1) and SAE Table (SAEDB2) in ADRTRACK

DCP SAE Process Flow Chart



DCP's SAE E-Form:

NCI Protocol/Grant No. _____
IRB Protocol No. _____ PID No. _____

NCI, DIVISION OF CANCER PREVENTION (DCP)
SERIOUS ADVERSE EVENT REPORT FORM

REQUIRED FIELDS ON ALL REPORTS

Today's Date:	Sponsor: NCI, DCP	Study (Indication):
Drug(s) under Investigation:	IND No.:	

A. Study Subject Information

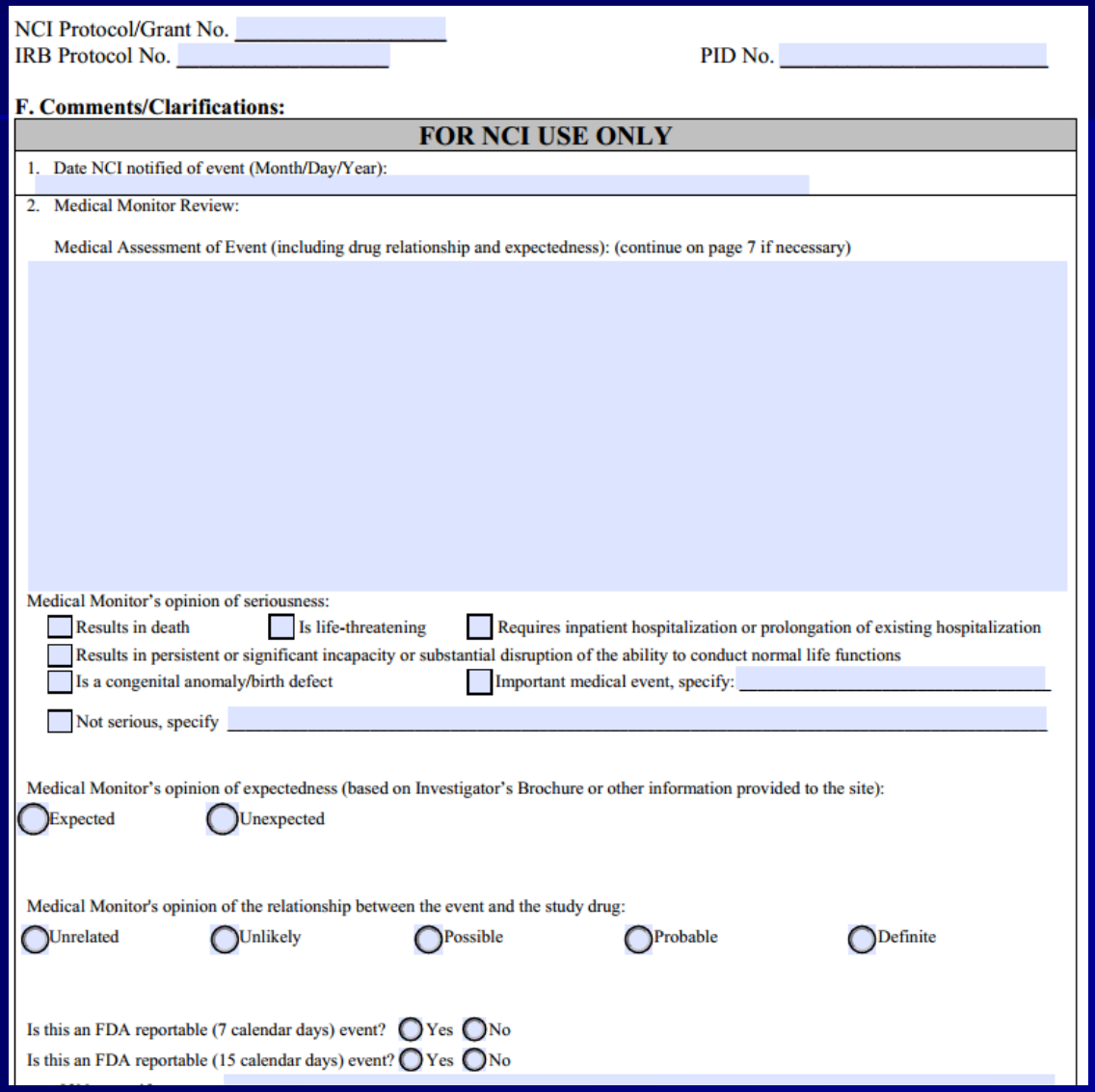
1. Study Participant # or PID #	2. Year of Birth:	3. Weight at Time of Event: ◯ kg ◯ lbs. ◯ not available	4. Height at Time of Event: ◯ cm ◯ in ◯ not available
Gender: (choose one) ◯ M ◯ F		Race:	Ethnicity:

B. Event Information

◯ Initial Event Report ◯ Follow-up Report _____

Event Onset Date: (Month/Day/Year)	Primary Event (diagnosis):
Event Approx. Time: (Indicate A.M./P.M.)	

DCP's SAE E-Form:



NCI Protocol/Grant No. _____
IRB Protocol No. _____ PID No. _____

F. Comments/Clarifications:

FOR NCI USE ONLY

1. Date NCI notified of event (Month/Day/Year):

2. Medical Monitor Review:

Medical Assessment of Event (including drug relationship and expectedness): (continue on page 7 if necessary)

Medical Monitor's opinion of seriousness:

☐ Results in death ☐ Is life-threatening ☐ Requires inpatient hospitalization or prolongation of existing hospitalization
☐ Results in persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
☐ Is a congenital anomaly/birth defect ☐ Important medical event, specify: _____
☐ Not serious, specify _____

Medical Monitor's opinion of expectedness (based on Investigator's Brochure or other information provided to the site):

◯ Expected ◯ Unexpected

Medical Monitor's opinion of the relationship between the event and the study drug:

◯ Unrelated ◯ Unlikely ◯ Possible ◯ Probable ◯ Definite

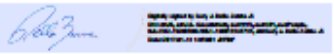
Is this an FDA reportable (7 calendar days) event? ◯ Yes ◯ No
Is this an FDA reportable (15 calendar days) event? ◯ Yes ◯ No

DCP's SAE E-Form:

Is this event to be communicated to other NCI contractors using this investigational drug? ◯ Yes ◯ No

>> If Yes, how? By telephone (attach a TC Form): ◯ Yes, attach TC Form ◯ No

Other (FAX, mail, e-mail, *etc.*): ◯ Yes, attach a copy of the correspondence ◯ No

Medical Monitor: Print name Gary Della'Zanna D.O. M.Sc. Signature  Date January 19, 2017

DCP Safety Committee :

- **Consortia Update Meeting:**
  - **Process Improvements based on “user” input**
  - **Communicate SAEs**
  - **Discuss any potential signal**
- **Education in evolving SAE “Definitions”**

Overview

Terms and Definitions

Serious Adverse Event (SAE):

- Death
- Life-threatening event
- Inpatient or prolongation of existing hospitalization
- Persistent or significant incapacity or disruption of the ability to perform ADLs
- Congenital anomaly or birth defect
- Important medical events that may not be immediately life-threatening- but require intervention to prevent one of the above.

Life-threatening event

- Allergic reaction resulting in angioedema of the larynx, allergic bronchospasm or anaphylaxis is considered life-threatening
- Allergic reaction resulting in only a rash on the face or generalized angioedema is not life-threatening.

Hospitalization

- DCP defines hospitalization as a hospital admission or stay equal to or greater than 24 hours.

- Exceptions:
  - hospitalization for procedures described in the protocol (e.g., surgery, colonoscopy or pharmacokinetic sampling)

Important Medical Event

- **FDA's examples:**
  - **Bronchospasm requiring intensive treatment**
  - **Convulsions/Seizures – regardless of whether or not it requires hospitalization.**
  - **Developing drug dependency or drug abuse.**

Attribution / Causality

- Definite
- Probable
- Possible
- Unlikely
- Unrelated.

Expectedness

- **Sponsor's Responsibility (DCP's MM)**
- **Unexpected is defined as:**
  - **Events not listed or not listed in the same specificity or severity in the Investigator's Brochure or other document providing risk information (e.g., package insert).**

Expedited Reporting

- **15-Day Reporting**
  - Serious
  - Unexpected
  - Any degree of attribution
- **7-Day Reporting**
  - Life Threating or Death

Baseline Assessments vs. AEs

- A sign, symptom or abnormal lab value present at the baseline should NOT be reported as an AE
- Any change in severity (worsening) or frequency since baseline assessment should be reported as an AE.
- Abnormal laboratory values determined to be of no clinical significance should not be reported as AEs.

Questions ???