

Investigator Responsibilities

MTN-017 Meeting

MTN Annual Meeting

February 10, 2013



Objectives

- Review and discuss Investigator Responsibilities as per relevant regulations and guidelines
- Review and discuss the responsibility associated with signing the Form FDA 1572 and the 8 commitments of this form
- Assess the impact of protocol noncompliance
- Analyze site oversight and how it applies to the delegation of responsibilities
- Focus on the oversight responsibilities related to the informed consent process, drug accountability and safety

Investigator Responsibilities and the Regulations

Investigator Responsibilities

The Investigator is ultimately responsible for all study-related activities at his or her site, regardless of who has been delegated the various study responsibilities

What does this mean?

- DAIDS has a number of position levels in the CTU/CRS structure:
 - CTU PI, CRS Leader, Investigator of Record
- The FDA is concerned ONLY with the Investigator (per the 1572).
 - Others in the DAIDS structure/chain of command will not be important in time of audit; it is the IoR who is answerable for the execution of the protocol

Investigator Responsibilities

- Ensure that the clinical investigation is conducted according to the Form FDA 1572 / Investigator of Record Agreement as well as ICH-GCP and country guidelines.
- Protect the rights, safety and welfare of subjects under the Investigator's care.

Investigator Responsibilities: Regulations and Guidances

For all DAIDS studies

- ❑ ICH E6 (Section 4.0)
- ❑ Investigator of Record Agreement (not required for IND studies)
- ❑ Code of Federal Regulations

For IND Studies

- ❑ US Form FDA 1572
- ❑ US FDA Guidance – Investigator's Responsibilities, (October 2009)

ICH E6 – Section 4.0

Investigator Responsibilities

4.1

**Investigator Qualification
and Agreements**

4.2

Adequate Resources

4.3

Medical Care of Trial Subjects

4.4

Communications with IRB/EC

4.5

Compliance with Protocol

4.6

Investigational Product

4.7

Randomization and Unblinding

4.8

**Informed Consent of
Trial Subjects**

4.9

Records and Reports

4.10

Progress Reports

4.11

Safety Reporting

4.12

**Premature Termination or
Suspension of a Trial**

4.13

Final Report(s) by Investigator



Country specific requirements

- As mentioned, this presentation has reviewed the US federal requirements for the clinical Investigator
- All local and country-level requirements must be also be met

FDA Clarification of Investigator Responsibilities

- Supervision of the conduct of the clinical investigation
- Delegation of tasks to study staff
- Training of study staff
- Supervision of staff and ongoing conduct of study
- Reporting protocol deviations
- Supervision of third parties (if applicable)
- Protection of the rights, safety and welfare of participants in clinical trials
- Provide reasonable medical care
- Provide reasonable access to medical care

Review of Form FDA 1572

The Form FDA 1572

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		Form Approved: OMB No. 0910-0014 Expiration Date: August 31, 2011 See <i>OMB Statement on Reverse</i> .	
STATEMENT OF INVESTIGATOR <i>(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)</i> (See instructions on reverse side.)		NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).	
1. NAME AND ADDRESS OF INVESTIGATOR			
Name of Sponsor/Applicant/Submitter or Other			
Address 1		Address 2	
City	State	ZIP or Postal Code	
2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED (<i>Select one of the following.</i>)			
<input type="checkbox"/> Curriculum Vitae		<input type="checkbox"/> Other Statement of Qualifications	
3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED			CONTINUATION PAGE for Item 3
Name of Medical School, Hospital, or Other Research Facility			
Address 1		Address 2	

By signing the 1572...

- The Investigator is agreeing that he or she will
 - personally conduct or supervise the described investigations.
 - be intimately involved with the study
 - have a full understanding of the protocol as well as stay informed of all participant and site issues.

- The Investigator should ensure procedures are established to escalate issues quickly.

Compliance with the Protocol

ICH E6 Section 4.5

21 CFR 312.60

21 CFR 812.100

Protocol Compliance

- The Investigator should conduct the trial in compliance with the protocol (agreed to by sponsor and regulatory authority) and approved by the IRB/EC. Investigator signing of the protocol confirms this agreement.
- Deviations from the protocol should not be implemented without agreement from the sponsor and approval from the IRB of an amendment

Protocol Compliance

- The Investigator or designee should document and explain any deviation from the approved protocol
- The Investigator may implement a deviation from or change in the protocol to eliminate an immediate hazard to trial subjects without IRB approval



Potential Impact of Noncompliance

- Impact on risk to the participant
- Risk of bias
- Impact on data quality
- Impact on scientific integrity and credibility
- Rejection of data
- Rejection of trial
- Selection for FDA Inspection
- Disqualification of Investigator
- Suspension of site activities

Site Oversight

Delegation of Responsibility Log

Delegation of Responsibility Log/Signature List

Sponsor: DAIDS

Study: MTN-003

Investigator Name: Dominick Reagan, MD

Site Number: 25

Page Number: 1

Name and Title of Site Staff Use Block Capitals	Signature	Initials	Responsibilities* (See below)										Involved From	Involved To	PI Initials	
			A	B	C	D	E	F	G	H	I	J	DD-MMM-YY	DD-MMM-YY		
DOMINICK REAGAN, MD, INVESTIGATOR	<i>Dominick Reagan, MD</i>	<i>DR</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	30-Mar-10		<i>DR</i>
PHILLIP DOLE, MD- SUB-INV	<i>Phillip Dole, MD</i>	<i>PD</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	30-Mar-10		<i>DR</i>
OLIVIA SEAGULL, PHARM.D.	<i>Olivia Seagull</i>	<i>OS</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	30-Mar-10		<i>DR</i>
KEVIN JONES, COUNSELOR	<i>Kevin Jones</i>	<i>KJ</i>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	30-Mar-10		<i>DR</i>
CECILIA COOPER, RN-COORDINATOR	<i>Cecilia Cooper, RN</i>	<i>CC</i>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	30-Mar-10		<i>DR</i>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			

DELEGATION OF RESPONSIBILITIES CODES	NOTES FOR COMPLETING THIS FORM
<p>A. Obtaining consent B. CRF entries C. Dispensing Medication D. Physical Examination E. Phlebotomy F. Essential Documents</p> <p>G. IP Receipt/Return H. Query Resolution I. Blood Pressure Measurements & QC self blood pressure monitor J. Other <u>Lab Report Interpretations</u></p> <p>*Delete those which do not apply</p>	<ul style="list-style-type: none"> • Please PRINT CLEARLY when completing this form • Please enter all dates in the DD-MMM-YY format (e.g., 21-JAN-01) • Use 'Involved From' and 'Involved To' to record staff changes during the study • Enter a new line and applicable dates when responsibilities change • PI should initial each line as individuals are assigned responsibilities

Principal Investigator Signature (Close Out): _____

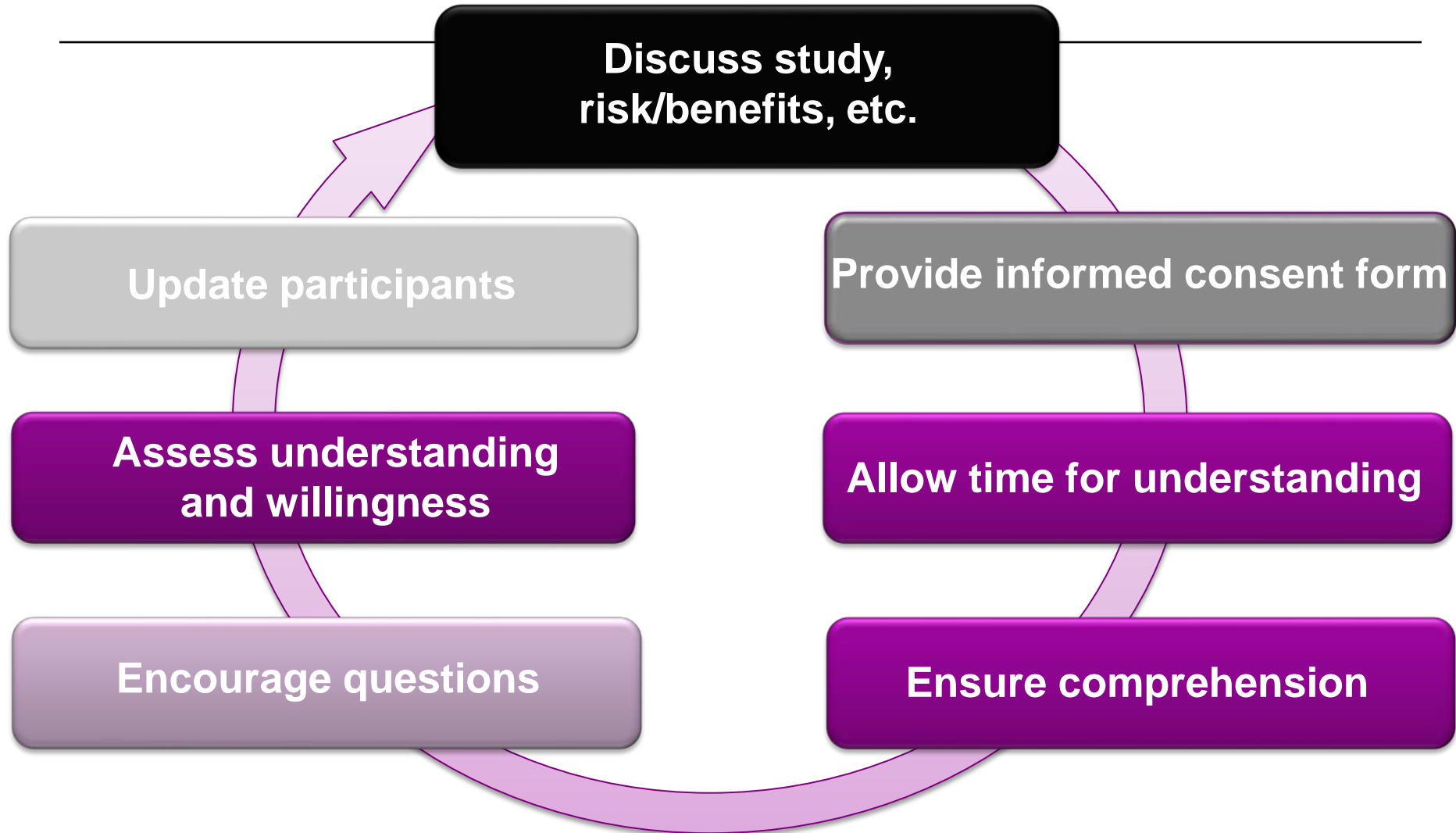
Date: _____

The role of the Investigator in ensuring informed consent

ICH E6 Section 4.8

21 CFR 50

The Consenting Process



Illiterate Participant

- Special considerations
 - Consider asking potential participant to read the informed consent form (ICF) out loud
 - Test writing skills
 - Read the informed consent form to the participant
 - Ask participant to “teach back”

- Requires a witness to the consent process

Investigational Study Product

ICH E6 Section 4.6

21 CFR 312.57(a)

21 CFR 312.62(a)

Investigational Study Product

- Responsibility for investigational product accountability lies with the Investigator/institution
- Some or all of these duties can be delegated to the pharmacist or other individual who is under supervision of the Investigator
- The product should be stored as specified by the sponsor and in accordance with regulatory requirements

Medical care of trial subjects and safety reporting

ICH E6 Sections 4.3 and 4.11

DAIDS Expedited Adverse Events Reporting Policy, DWD-POL-CL-013.03



Medical Care of Trial Subjects

- A qualified physician must be responsible for all trial-related medical decisions and ensuring medical care provided for any AEs while in the trial
- It is recommended that the Investigator inform the participant's primary physician about trial participation if the participant agrees
- The Investigator should attempt to find the reason for premature withdraw of participation from the trial when appropriate



Safety Reporting

- All SAEs should be reported to the sponsor per the EAE Reporting Manual (within 3 reporting days of site awareness). PTIDs (not names or other unique identifiers) should be used in these reports.
- AEs should be reported according to requirements per protocol
- Investigator should supply the IRB/EC and sponsor with any additional requested information



Thank You!

□ Questions/Discussion