

# UFHCC Data Integrity and Safety Committee Review

*“Why does my study need DISC review?”*

# What is the Data Integrity and Safety Committee (DISC)?

- ▶ The UFHCC DISC serves as the Data and Safety Monitoring Board (DSMB) for UFHCC investigator-initiated trials (IITs) and other qualifying clinical trials that do not have adequate external oversight, as determined by SRMC
- ▶ Mission Statement
  - ▶ “The mission of the DISC is to provide oversight and monitoring of trials conducted by the UFHCC, as assigned by the SRMC. The DISC is committed to safeguarding trial subjects and ensuring that the validity and integrity of trial data and operations are upheld.”

# DISC Review Purview

- ▶ DISC oversight includes review of the following:
  - ▶ Safety Data (i.e., Serious Adverse Events/Adverse Events)
  - ▶ Protocol Compliance
  - ▶ Efficacy Data
  - ▶ Dose Escalation
  - ▶ Interim Analyses and Stopping Rules
  - ▶ Data Quality and Trial Operations

# What is Risk Level?

- ▶ SRMC establishes the required level of monitoring for all studies under DISC oversight during the initial SRMC review.
- ▶ Risk level will be determined based upon the protocol phase, objectives, study intervention, level of risk to subjects, and overall complexity
  - ▶ NOTE: all phase III studies (regardless of the level of risk, such as minimal vs greater than minimal risk) *must* be overseen by a DSMB
- ▶ The assigned level of risk will be reported to the DISC and the study PI by the SRMC administrator (located in SRMC approval letter)
- ▶ Risk levels include the following:
  - ▶ Level 1 - Low Risk
  - ▶ Level 2 - Moderate Risk
  - ▶ Level 3 - High Risk
  - ▶ Level 4 - Very High Risk

# Risk Level Assessment Scores

- ▶ **Level 1 – Low-risk, investigator-initiated interventional trials. Examples include:**
  - ▶ Diagnostic or screening trials involving minimal risk procedures
  - ▶ Trials involving accepted doses of over-the-counter drug, or vitamins and supplements
  - ▶ Behavioral or health services research (HSR) trials
  - ▶ Trials involving diet or exercise involving minimal risk
- ▶ **Level 2 – Moderate-risk, investigator-initiated or externally sponsored interventional (such as drug, biologic or device) trials using FDA approved or commercially available compounds or interventions. Examples include:**
  - ▶ IND exempt phase II and III trials
  - ▶ Trials involving delivery of radiation therapy
  - ▶ Screening, diagnostic, behavioral, HSR, diet or exercise trials that involve invasive or greater than minimal risk procedures or interventions that ordinarily would be regarded as minimal or low risk but are being tested in a context where the risk might be perceived as higher

# Risk Level Assessment Scores

- ▶ **Level 3 – High-risk, investigator-initiated or externally sponsored interventional trials (such as investigator-sponsored INDs, phase I trials, studies requiring biosafety approval, or other areas that may be designated by NIH as high risk). Examples include: IND exempt phase II and III trials**
  - ▶ UF investigator as IND/IDE holder
  - ▶ Phase I drug, device, bone marrow transplant, cellular therapy, and surgical trials
  - ▶ Any trial that requires UF biosafety committee approval
  - ▶ UF multisite interventional trials
- ▶ **Level 4 – Complex trials involving very high risk to subjects and a high level of complexity such as first in human or gene transfer studies.**

# Study Monitoring Frequency by Risk Level

Risk Level	First DISC Meeting	DISC Monitoring Frequency
Level 1	No routine DISC monitoring is required for low-risk studies.	
Level 2	Within 6 months of the first subject accrual	Annual (12 months)
Level 3	Within 6 months of the first subject accrual	Semi-annual (6 months)
Level 4	Within 3 months of the first subject accrual	Quarterly (3 months)

# DISC Review Timeline

Weeks before DISC Meeting	Task
8	<b>DISC administrator</b> identifies studies up for audit, the <b>CTAT team</b> is notified.
6	<b>CTAT team</b> notifies the <b>study team</b> of audit with instructions and a deadline.
4	The audit is conducted by the <b>CTAT team</b> .
3	<b>DISC administrator</b> sends a DISC monitoring report to <b>the study team</b> for review and requests cumulative deviations and adverse events reports.  <b>CTAT team</b> sends <b>the study team</b> their audit findings and a deadline for response.
2	<b>Study team</b> sends a completed DISC monitoring report and cumulative deviations and adverse events reports to the <b>DISC administrator</b> .



# Clinical Trials Audit Team (CTAT)

- ▶ Approximately one month prior to the DISC meeting, studies will also undergo review from the Clinical Trials Audit Team (CTAT)
  - ▶ Study teams will receive a formal audit notification via email ~2 weeks prior to starting the audit
- ▶ The CTAT's review will include but is not limited to the following:
  - ▶ Regulatory Binder (e.g., IRB submissions, amendments, currently approved protocol, etc.)
  - ▶ Subject Charts (e.g., signed consent forms, screening, eligibility, treatment, data entry, disease response, follow-up etc.)
    - ▶ Access to REDCap and/or other E-Data capture must be granted to CTAT in advance
  - ▶ Delegation of Authority and Training Logs
  - ▶ Cumulative list of Adverse Events, SAEs, and Deviations
  - ▶ Prior audit findings

# Review Materials for the DISC Meeting

- ▶ DISC Audit Findings
  - ▶ After the CTAT team finishes their audit of the study, a formal letter with audit findings will be sent to the study team.
  - ▶ If a response is required, a deadline is given by the CTAT team.
- ▶ DISC Monitoring Report
  - ▶ Report pulled from OnCore to capture protocol information, past reviews, and accrual information. Study team is asked to review and confirm accuracy.
  - ▶ The DISC Monitoring Report includes the following:
    - ▶ General protocol details (e.g., study design, schema, etc.)
    - ▶ Current subject totals
    - ▶ Adverse Event Log
    - ▶ Deviation Log
    - ▶ Audit Findings
    - ▶ Template for Study presentation

# Review Materials for the DISC Meeting Contd.

- ▶ Cumulative Deviation Log and Adverse Events Log
  - ▶ The DISC admin can provide a template excel file
  - ▶ However, *we prefer this information be entered into OnCore or RedCap so that this information can be compiled cumulatively for all reviews now and in the future*
    - ▶ UFHCC OnCore Subject Registration document provides more information on how to enter this within OnCore: <https://cancercenter-a2.sites.medinfo.ufl.edu/wordpress/files/2022/02/Guidance-OnCore-Subject-Registration-and-Reporting-Process-V7-2022-01-27.pdf>

# Expectations for DISC Meetings

- ▶ The DISC typically meets every first Thursday of the month at 10 am
- ▶ On-agenda studies must have knowledgeable study staff in attendance to present/answer reviewer concerns
  - ▶ Preferred both PI AND Study Coordinator be in attendance to address questions from the DISC reviewers
  - ▶ A template to facilitate the study overview is included in the email from the DISC Administrator. It is highly recommended to utilize this template to present the study summary; the template captures what the DISC reviewer(s) are interested in hearing.

# DISC Meeting

- ▶ DISC meetings will have both an Open and Closed Session
- ▶ **OPEN Session**
  - ▶ Study team presents the summary of the protocol and current status
  - ▶ The CTAT present the audit findings
  - ▶ Reviewers discuss comments and concerns identified during their review
  - ▶ Study team responds to any comments
- ▶ **CLOSED Session**
  - ▶ The study team and conflicted DISC members are asked to leave or placed in a waiting room (if via Zoom)
  - ▶ Committee will vote on the study
    - ▶ **Study Continuation as Planned:** There are no Outstanding subject safety or data integrity issues
    - ▶ **Study Continuation with Stipulations and/or Modifications:** Questions regarding the study, subject safety or data integrity may require a written response or modification to the study protocol/materials
    - ▶ **Study suspension with stipulations and/or modifications:** There are concerns regarding subject safety or data integrity that require an expedited response from the PI; accrual must be suspended until concerns are resolved.
    - ▶ **Study Termination:** There are issues that warrant immediate suspension of further accrual with or without discontinuation of study interventions for current subjects.

**\*Note: While DISC has the independent authority to recommend the suspension or termination of a clinical trial, all actions of this nature will involve the PI and ultimately require IRB and/or SRMC review and approval.**

# DISC Meeting Contd.

- ▶ A DISC memo will be sent to the study team notifying the study team of the DISC review determination
  - ▶ PI or study team should acknowledge or respond to each memorandum released by the DISC.
  - ▶ The PI is responsible for reporting DISC correspondence to the IRB of record per the IRB reporting policy.
- ▶ PI Response for Stipulations and/or modifications
  - ▶ If stipulations were requested and a response is required, the study team will have 8 weeks after receipt of the DISC review memo to respond.
  - ▶ The DISC has the authority to require the creation and implementation of a Corrective and Preventative Action (CAPA) plan or recommend protocol modifications to the PI to address toxicity or other clinical issues.
  - ▶ When CAPAs are required, the PI will be responsible for drafting a plan and submitting it in writing to the DISC.

# Reporting Requirements for DISC

- ▶ **Major study deviations, including regulatory and protocol noncompliance.**
- ▶ **All SAEs, regardless of expectedness or relatedness.**
  - ▶ This applies to all SAEs that occur from the time any study intervention is initiated until 30 (thirty) days following the last protocol intervention, at a minimum.
  - ▶ Extended SAE reporting intervals may be required as defined per protocol.
- ▶ **How to report events:**
  - ▶ Use [UFHCC-DSMB@ahc.ufl.edu](mailto:UFHCC-DSMB@ahc.ufl.edu) to report serious adverse events and instances of major deviations.

# How to Report to DISC

- ▶ Report within 5 business days of discovery
- ▶ Use [UFHCC-DSMB@ahc.ufl.edu](mailto:UFHCC-DSMB@ahc.ufl.edu) to report serious adverse events and instances of major deviations.
- ▶ Include the following information for reportable events:
  - ▶ Event Date
  - ▶ Event End Date (if available)
  - ▶ Discovery Date
  - ▶ Event Narrative [description]
  - ▶ AE/Deviation Details
  - ▶ Any effect on patient safety
  - ▶ Unexpected [SAE only]
  - ▶ DLT [SAE Only]
  - ▶ Attribution [SAE Only]
  - ▶ Outcome
  - ▶ Event Report to IRB?



# DISC Resources

- ▶ The following resources are available on the DISC webpage:  
<https://cancer.ufl.edu/research/clinical-trials-office-2/data-integrity-and-safety-committee/>
- ▶ DISC Charter
- ▶ DISC Monitoring Report Template
- ▶ Deviations Table Template
- ▶ AE Table Template
- ▶ DISC Data & Safety Monitoring Plan
- ▶ DISC FAQ

# Contact Us!

- ▶ You can contact the DISC listserv ([UFHCC-DSMB@ach.ufl.edu](mailto:UFHCC-DSMB@ach.ufl.edu)) for any additional questions/concerns
- ▶ Thank you!