1. BACKGROUND:

The Scientific Review Committee (SRC) is responsible for monitoring the accrual and evaluating the scientific merit and progress of all DF/HCC human subject research trials. The committee utilizes risk-based methodology for this monitoring process. Under the NCI Cancer Center Core Grant requirements, prioritization of protocols must be reviewed and approved by the SRC.

Evaluation of the scientific progress of the trial, and how that fits into overall progress in that specific area of research, is important to ensure that the trial is continuing to address an important scientific question.

Monitoring of zero and slow-accruing trials maximizes subject contributions by minimizing the likelihood that research will fail to complete its objectives; promotes efficient use of resources and maximizes the likelihood that research supported by DF/HCC Institutions will be completed, reported, and published.

Monitoring of rapidly accruing trials identifies research that requires close monitoring to ensure adequate resources, prospective data collection and appropriate safety review.

The SRC along with DF/HCC leadership has established specific criteria to assess whether trials are deemed slow or rapidly accruing and when trials trigger closure or additional follow-up assessment due to accrual progress.

2. ASSOCIATED DF/HCC POLICIES:

2.1. COM-100

3. DEFINITIONS:

3.1. **Target Accrual Rate:** The Target Accrual Goal divided by the Expected Duration (in days) of the trial.

3.2. **Actual Accrual Rate:** The accrual to date divided by the current number of days the trial has been open.

3.3. **Rare Cancer:** Defined per the NCI as a cancer with an incidence of ≤ 6 newly diagnosed persons out of a population of 100,000 persons per year.

4. PROCEDURE:

4.1. Accrual Monitoring

4.1.1. An automated monthly report will be run in OnCore identifying trials that trigger immediate closure or a 3-month closure warning based on the criteria outlined below.

4.1.2. All rare cancer trials will be excluded from the accrual monitoring report based on their "rare" OnCore annotation and/or documented communication between the PI or their designee and Accrual Monitoring Coordinator confirming the rare status of the trial.

4.2. **Zero and Slow Accrual Monitoring Criteria for Trials Triggering Closure**

4.2.1. Any ADULT trial open at 6+ months with zero accrual.

4.2.2. Any ADULT trial open at 24+ months with an accrual rate under 25% of the target rate.

4.2.3. Any COG PEDI trial open at 12+ months with zero accrual.

4.2.4. Any COG PEDI trial open at 36+ months with under 50% of the target accrual rate achieved.

4.2.5. Any PI-Initiated or NON-COG PEDI trial open at 6+ months with zero accrual

4.2.6. After a trial has triggered closure based on the criteria above, the following will occur:

4.2.7. The trials will be closed via a closure form submitted to the Office for Human Research Studies (OHRS) by the Accrual Monitoring coordinator. The PI and SRC Chair will be copied on this submission.

4.2.8. A summary of the closed trials will be sent to the SRC Chair for review.

4.2.9. A standardized letter will be sent from the SRC to each Overall PI informing them that their trial has closed due to accrual and that they may appeal this closure via a written response to the SRC.

4.2.10. Any appeal submitted should include a detailed explanation for the lack of accrual, a corrective action plan for increasing accrual, and justification for the trial remaining open.

4.2.11. Any appeal submitted will be reviewed by the committee at the following SRC meeting. The committee will decide whether to recommend to the IRB reopening the trial or deny the appeal. The Overall PI will be notified of the committee's decision.

4.2.12. Approved appeals will be submitted to the IRB with the SRC's recommendation to re-open the closed trial.

4.3. **Zero and Slow Accrual Monitoring Criteria for Trials Triggering a 3-Month Warning**

4.3.1. Any ADULT trial open at 3 months with zero accrual.

4.3.2. Any ADULT trial open at 12+ months with an accrual rate of 25-50% of the target rate.

4.3.3. Any ADULT trial that has not met accrual goals within 2x the expected duration of the trial.

4.3.4. Any COG PEDI trial open at 9 months with zero accrual.

4.3.5. Any COG PEDI trial open at 12-35 months with under 50% of the target accrual rate achieved.

4.3.6. Any PI-Initiated or NON-COG PEDI trial open at 12-35 months with under 50% of the target accrual rate achieved.

4.3.7. After a trial has triggered a 3-month warning based on the criteria above, the following will occur:

4.3.8. A standardized letter will be sent from the SRC to each Overall PI informing them that their trial has been identified as zero or slow-accruing and is in jeopardy of automatic closure based on the SRC automatic closure rules.

4.3.9. No response is required from the Overall PI regarding trials triggering a 3-month warning.

4.4. **Rapid Accrual Monitoring Procedures (Adult Trials)**

4.4.1. Monthly, the Accrual Monitoring coordinator will run a report identifying adult protocols meeting the rapidly accruing trial criteria:

4.4.2. An expected duration of less than one year

4.4.3. An expected duration of greater than one year and having an accrual rate 1.5 times faster than expected

4.4.4. A standardized letter will be sent from the SRC to the Overall PI, informing him or her that the trial has been identified as rapidly accruing and reminding them to closely monitor the trial's progress, including toxicities, adverse event reporting and data.

4.5. **SRC Scientific Progress Review**

4.5.1. Annually each DF/HCC trial will be reviewed by the SRC. The review will include but not be limited to accrual performance, scientific merit, trial completion and publication.

4.5.2. The SRC Chair will receive a list of all trials approved by the SRC Reviewer.

4.5.3. Any trial the SRC Reviewer wishes to disapprove will be sent to the full SRC for review and determination.

4.6. **Protocol Priority Lists**

4.6.1. Protocols must be prioritized within the appropriate disease program by the Disease Program Leader.)

4.6.2. The SRC must approve all initial protocol prioritization, and subsequent prioritization updates which are then reflected in the Priority List and maintained by OHRS on the Oncology Protocol System (OncPro).