Robert H. Lurie Comprehensive Cancer Center
Protocol Review and Monitoring System (PRMS) Accrual Policy

Purpose	The purpose of this policy is to describe the methods and benchmarks by which the Scientific Review Committee (SRC) of the Lurie Cancer Center (LCC) monitors scientific progress.
Scope	Applies to all cancer relevant interventional clinical trials under the purview of the Lurie Cancer Center.
Applicable Regulations & Guidance	• Data and Safety Monitoring Plan of the Robert H. Lurie Comprehensive Cancer Center • PAR-13-386: CCSGs for NCI-designated Cancer Centers (P30)

Detailed Policy	**New Projects and Initial Disease Team (DT) and Scientific Review Committee (SRC) Review** At the time of initial submission to the PRMS, the DT provides the annual and total accrual goals for the LCC as part of the endorsement process and confirms competing and/or overlapping trials within their portfolio along with justification if required. The projected accrual goals are reviewed during SRC within the context of the DT's existing portfolio. Any concerns regarding projected accrual goals and feasibility are communicated to the PI and respective DT leaders to be addressed prior to final SRC approval. Studies endorsed by the DT are evaluated for potential rare disease designation. The LCC utilizes the definition of a rare cancer per the NIH: a rare disease is generally considered to have a prevalence of fewer than 200,000 affected individuals in the United States or an incidence of fewer than 150 per million per year (i.e., 15 per 100,000 per year), roughly corresponding in the U.S. to 40,000 new cases per year or fewer. All pediatric cancers are considered rare by this definition. The LCC PRMS will consider other data in support of a rare disease designation (e.g. information pertaining to a particular sub-type or category of disease) on a case by case basis. NOTE: protocols designated as rare disease are not exempt from accrual review, although additional context regarding the available patient population at the time of review may be requested from the DT to support the projected annual accrual goal. **Monitoring & Review of Accrual** The SRC Sub-Committee for Comprehensive DT Progress Review meets quarterly to review each DT portfolio in full. The SRC portfolio review outcome letter, outlining any actions or determinations as well as information requested or recommendations issued, is communicated back to the DT leaders. DT leaders are expected to review and respond in writing on behalf of the DT as a whole. This process ensures that all active LCC interventional clinical trials are reviewed at least annually for scientific progress, including annual and overall accrual, regardless of rare disease designation. The committee has authority to close studies not meeting minimum accrual expectations. NOTE: protocols designated as rare disease are not exempt from accrual review, although additional context regarding the available patient population at the time of review may be requested from the DT to support the projected annual accrual goal. The projected annual and overall accrual goals provided at time of initial SRC submission will be used to enforce the accrual policy. For LCC-led IITs, the SRC will consider accrual progress across all participating institutions. The SRC considers multiple factors when reviewing a clinical trial for progress. These may include current annual and overall accrual as compared to the projected rate(s) at study submission, existence of studies with competing and/or overlapping patient populations, slot-based enrollment, rare disease designation, and/or national leadership of a trial by an LCC investigator. A study may be flagged as Under Monitoring, Risk of Closure, and/or Closure if it is not meeting at least 50% of the projected annual or overall accrual goals. In addition, any study that has not enrolled for a period of 6-12 months may be flagged for lack of progress. As a part of the annual DT portfolio review, the SRC will consider the team's screening and registration history, enrollment history to other current and prior trials of a similar population, changes in study enrollment status (e.g. lengthy suspensions by the study

sponsor or other regulatory authority), continued scientific relevance and the current treatment guidelines and disease landscape, and dialogue with the PI and DT leadership.

The SRC will generate a portfolio review letter which may include both study-specific and overall portfolio outcomes or actions taken. Individual study determinations may require a corrective and preventative action plan (CAPA) to address progress concerns. All portfolio review letters are distributed to the DT leaders on behalf of the DT as a whole. The DT leaders are expected to review all SRC letters, look critically at any poorly accruing trials, and respond as appropriate regarding justification or actions taken (e.g. DT closure of trials, adjustments to projected accrual, and/or-re-prioritization of their portfolio).

- For studies designated as Under Monitoring, no action may be required, however the SRC may recommend re-review prior to the next annual review (e.g. after 6 months). Any specific questions asked or suggestions made by the SRC should be responded to in the letter.

- For studies designated at Risk of Closure, the SRC typically requires a CAPA to be submitted within a specified timeframe. If no response and/or the CAPA is deemed unacceptable, the SRC may decide to elevate the outcome to Closure.

- For studies determined to meet criteria for Closure, notice is given in the letter with a set date for closure. Generally speaking, further appeal at this stage is not considered, however any urgent information should be communicated promptly to the SRC upon receipt of the outcome letter (e.g. patient was consented that day).

Note: any time a protocol revision is received or is being considered (for a LCC IIT), the implications of the proposed changes on projected accrual rates, study relevance, and/or feasibility should be discussed at the DT and communicated to SRC as needed.

Studies with the rare disease classification are not held as strictly to the 50% standard outlined above in this policy. However, as noted above these are not entirely exempt from review and are expected to demonstrate progress towards the projected accrual goals provided at initial endorsement. Rare disease trials may receive outcome determinations or requests for information if the SRC deems it appropriate.