Robert H. Lurie Comprehensive Cancer Center Research Oversight System Accrual Policy

Purpose	The purpose of this policy is to ensure that trial accrual for all cancer-relevant research conducted at and by Northwestern University is monitored appropriately by the Robert H. Lurie Comprehensive Cancer Center's Research Oversight System (ROS).
Scope	Applies to all qualifying studies monitored by the Lurie Cancer ROS.
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 and Scientific Review Committee (SRC) Review** When a PI submits a new project through the ROS, the annual accrual goal for the trial, the total accrual goal for the trial, and estimated time it will take to accrue the projected number of subjects (time from study opening to study closure) must be provided. If an investigator indicates that the trial studies a rare disease, data that supports a study's classification as a rare disease must also be provided. All cancer-relevant projects must initially be submitted to the appropriate disease team for endorsement. The disease team endorsement process, in part, affirms the project's potential to meet the projected accrual goals. During the initial protocol approval process, the SRC will review the accrual goals set by the PI and endorsed by the Disease Team to determine if they is reasonable and make any revisions as is necessary. A notification of any revisions accrual goal will be sent to the PI and the respective Disease Team Co-Leader. The SRC will also determine whether the trial is studying a rare cancer per the NIH definition. Generally, based on the National Institutes of Health (NIH) definition, 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 SRC 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. **Monitoring & Review of Accrual**

The SRC reviews all clinical trials for progress, regardless of rare disease classification. Accrual is monitored annually for all qualifying trials, and may be monitored more frequently, as is warranted. The committee has authority to close studies not meeting minimum accrual requirements. Special consideration is given to studies involving rare cancers, as it is understood that minimum accrual requirements often do not apply to these studies, but they will nonetheless be monitored for activity.

The SRC-approved accrual goals will be used to enforce the accrual policy. When reviewing the accrual goals for IITs monitored under the DSMP, the SRC will compare projected annual accrual goal and total accrual across all participating institutions. For all other trials, the SRC will compare projected annual accrual to the total NU accrual.

The following studies are exempt from rigorous ongoing progress review:

- Retrospective chart reviews,
- Individual, investigator initiated studies that are federally funded, and
- Ancillary /correlative studies.

The SRC will generate either a closure letter or a request for a corrective action plan (CAP) for any trial for which 50% of the estimated annual accrual has not been reached at the anniversary of the activation date and each anniversary thereafter (e.g., if a trial was opened on 01/01/2016 and the PI estimates that a total of 10 subjects will be accrued annually, a closure letter will be sent if 5 subjects were not accrued by 01/01/2017). All closure letters and/or requests for CAPs will be directed to the PI and will copy the disease team co-leaders. While the PI must respond, the respective disease team is expected to review all such letters, look critically at any poorly accruing trial, close trials, and/or re-prioritize their research portfolio based on these communications.

When a PI receives a request for a CAP or a closure notice, the PI may respond by submitting a CAP that satisfactorily addresses the accrual issues. The SRC may approve the appeal, request further changes to the CAP, may recommend that the PI amend the trial to reflect the actual accrual, or may deny the appeal and close the trial to accrual. The implications of this new accrual rate on study relevance and feasibility should be discussed at the disease team and included in any proposed amendment.

Studies with the rare disease classification are not held to the 50% accrual standard outlined above in this policy. However, these studies will also be reviewed on the anniversary of their activation date for overall activity and accrual health. As a part of this review the SRC will consider the study's screening and registration history, continued scientific relevance within the Cancer Center's portfolio, and dialogue with the PI and disease team membership. Following this review process the study may be subject to request for a CAP or may receive a closure letter. If a study with a rare disease classification has not accrued one patient within two years of the trial's activation date, it will warrant additional discussion with the PI and disease team to determine the feasibility of identifying patients within the institution that would qualify for the trial. The PI will be expected to provide a written response or corrective action to be reviewed by the committee. After discussion, the trial may receive a closure letter.

If a PI fails to a respond to a SRC closure letter or a request for a corrective action plan to address poor accrual by a specific due date, the SRC considers the PI to be in agreement with the decision to close the study to further accrual.

	If the SRC approves the appeal, the study will remain open for a conditional period set by the SRC. If no additional subjects are registered during this conditional period, the SRC will generate a final closure letter and the study will be closed to further accrual.