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

<table>
<thead>
<tr>
<th>Purpose</th>
<th>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).</th>
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<tbody>
<tr>
<td>Scope</td>
<td>Applies to all qualifying studies monitored by the Lurie Cancer ROS.</td>
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| 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. If a study is noted as a rare cancer trial, it is exempt from this policy. 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 of all clinical trials for progress. 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.

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 a risk of closure letter 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 risk of closure letter will be sent if 5 subjects were not accrued by 01/01/2017). All risk of closure letters 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 risk of closure notice, the PI may petition for the trial to remain open by submitting a Corrective Action Plan (CAP) that satisfactorily addresses the accrual issues. The SRC may approve the petition, request further changes to the CAP, may recommend that the PI amend the trial to reflect the actual accrual, or may deny the petition 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.

If a PI fails to respond to a risk of SRC closure letter 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 a petition for a trial to remain open, the study will remain open for a conditional period set by the SRC. If the CAP is not satisfactorily implemented, and the specified number of subjects are not registered during this conditional period, the SRC will generate a final closure letter and the study will be closed to further accrual.