Low Accrual Policy

1.0 OBJECTIVES

1.1 This procedure details the low accrual policy for the Robert H. Lurie Comprehensive Cancer Center’s (Lurie Cancer Center) Clinical Protocol Review & Monitoring System (CPSRMS).

1.2 This procedure is intended to comply with all federal regulations, National Cancer Center (NCI) guidelines and the Lurie Cancer Center’s Data and Safety Monitoring Plan (DSMP).

2.0 RESPONSIBILITY

2.1 This SOP applies to all CPSRMS members and attendees and to the Clinical Research Office (CRO) employees responsible for providing administrative support to the CPSRMS Committees.

2.2 This SOP applies to all Investigators that initiate or participate in studies at the Lurie Cancer Center.

3.0 APPLICABLE REGULATIONS AND GUIDELINES

3.1 May 9, 1997 International Conference on Harmonisation; Good Clinical Practice: Consolidated Guideline

3.2 Data and Safety Monitoring Plan of the Robert H. Lurie Comprehensive Cancer Center

3.3 PAR-13-386: CCSGs for NCI-designated Cancer Centers (P30)

4.0 REFERENCES TO OTHER APPLICABLE SOPs

4.1 DMC Administrative Guidelines and Processes

4.2 DMC Responsibilities

5.0 DEFINITIONS

5.1 Clinical Protocol Scientific Review and Monitoring System (CPSRMS): This system is comprised of three committees that work collaboratively to provide oversight of all aspects of clinical research conducted at the Lurie Cancer Center. These committees include: the Scientific Review Committee (SRC), the Data Monitoring Committee (DMC), and the Audit Committee.
5.2 **Clinical Research Office (CRO):** The CRO provides a centralized resource to facilitate the development, conduct, quality assurance monitoring, compliance with regulatory agency requirements, and evaluation of clinical trials at the Lurie Cancer Center. As such, the office coordinates clinical research conducted in medical oncology, malignant hematology, gynecologic-oncology, neuro-oncology, radiation oncology, surgical oncology, and chemoprevention.

5.3 **Data Monitoring Committee (DMC):** The DMC is a part of the Lurie Cancer CPSRMS and is an independent committee responsible for data and safety review of all institutional clinical trials. This responsibility includes the review of audit reports generated by the Audit Committee.

5.4 **Investigator-Initiated Trial (IIT):** A trial initiated by an investigator at Northwestern University (NU) or by an investigator at Lurie Children’s Hospital (LCH). All such trials must be monitored according to the Lurie Cancer Center’s DSMP.

5.5 **Rare Disease:** 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. The prevalence of a given stage and molecular profile, for example, will be taken into account when determining what qualifies as a rare disease.

5.6 **Scientific Review Committee:** The SRC is a part of the Lurie Cancer Center’s Clinical Protocol Scientific Review & Monitoring System (CPSRMS) and is an independent committee responsible for reviewing new clinical trials to ensure that they are scientifically sound. The SRC conducts a full scientific review of all cancer-relevant studies that have not received external peer review by a NIH-approved peer-review body.

### 6.0 PROCEDURES

6.1 The Scientific Review Committee (SRC) is responsible for monitoring accrual on all cancer-relevant trials. The Data Monitoring Committee (DMC) is responsible for monitoring accrual on all IITs that fall under the purview of the Lurie Cancer Center DSMP. The DMC will report study closures due to low accrual to the SRC. DMC will forward PI closure appeals to the SRC for review. SRC will vote on the appeal and will report the final decision to the DMC.

6.2 When a PI submits a new project to the CRO, he or she must provide the annual accrual goal for the trial, the total accrual goal for the trial, and the estimated amount of months he or she anticipates it will take to accrue the projected number of subjects (time from study opening to study closure) on the New Protocol Submission Form (NPSF). The NPSF also requires that the investigator provide data that supports a study’s classification as a rare disease, if applicable (see definition provided in 5.5).

6.3 During the initial protocol approval process, the SRC will review the accrual goals set by the PI to determine if they are reasonable and make any revisions as is necessary. A notification of a revised accrual goal will be sent to the PI. The SRC-approved accrual goals will be used to enforce this 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.

6.4 The SRC will also determine whether the trial is studying a rare cancer per the NIH definition. 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.

6.6 The following studies are exempt from rigorous ongoing progress review:
- Retrospective chart reviews,
- Individual, investigator initiated, federally funded studies, and
- Ancillary /correlative studies.

6.5 The CPSRMS will request a Corrective Action and Preventative Action plan (CAPA) for any trial for which 20% of the anticipated annual accrual has not been reached at 6 months from activation (e.g., if a trial was opened on 01/01/2012 and the PI estimates that a total of 10 participants will be accrued in the first year of a trial, a closure letter will be sent if 2 participants were not accrued by 06/30/2012).

6.6 The CPSRMS will generate a 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 01/01/2012 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 01/01/2013).

6.7 The CPSRMS will generate a closure letter for any trial for which 50% of the estimated total accrual has not been reached by the midpoint of the total estimated time to study closure (e.g., if the PI estimated that a trial will accrue a total of 40 participants and would take 4 years to accrue all participants, and the trial was formally opened at NU on 01/01/2012, the CPSRMS will generate a closure letter if the trial had not accrued 20 subjects by 01/01/2014).

6.8 If any of the time points listed (6 month, annual, or midpoint) coincide, the study will be held to the more rigorous accrual rule (e.g., if a trial is estimated to be open for 12 months, a closure letter will be sent if 50% of the estimated total accrual has not been reached by the 6 months from activation).

6.9 When a PI receives a request for a CAPA or a closure notice, the PI may respond by submitting a CAPA that satisfactorily addresses the accrual issues. The CPSRMS may approve the appeal, request further changes to the CAPA, 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 in any proposed amendment.
6.10 If the CPSRMS approves the appeal, the study will remain open and the study and CAPA will be reevaluated during the next 60-day period. If no additional subjects are registered in the 60-day period, the CPSRMS will generate a final closure letter and the study will be closed to further accrual.