

FOLLOWING ARE THE SPECIAL TERMS AND CONDITIONS OF ROLES AND RESPONSIBILITIES (ITEMS 1-9) STANDARD TO EACH SCREENING CENTER IN THE MOLECULAR LIBRARIES SCREENING CENTERS NETWORK. ITEMS 2-9 WERE REFERENCED BY TITLE AND NUMBER ONLY IN THE NOTICE OF GRANT AWARD.

1. AWARDEE RIGHTS AND RESPONSIBILITIES

The PI of the center will coordinate project activities scientifically and administratively at the awardee institution. The PI will have primary responsibility for defining the details for the projects within the guidelines of this RFA RM-04-017, and for performing all scientific activities. The PI will agree to accept the close coordination, cooperation, and participation of the NIH staff (Program Official(s), Scientific Program Manager(s), the Network Science Officer(s), the NIH Project Team Director, and the NIH Project Team) in those aspects of scientific and technical management of the project as described below.

The NIH Intramural Research Program's NIH Chemical Genomics Center (NCGC) will participate in the MLSCN research network with the same rights and responsibilities, and within the same governing structure, as the extramural awardees.

Specifically, the PI of this MLSCN center will:

- 1) Determine experimental approaches, design protocols, set project milestones, conduct experiments, and analyze and interpret research data.
- 2) Provide goals for assay optimization, screening throughput, quality, and cost to the NIH Program Official and Scientific Program Manager as requested (usually at the outset of the award and in six-month progress reports, but also at other times as requested by the NIH Program Official and Scientific Program Manager).
- 3) Serve on the MLSCN Steering Committee, and participate, along with critical staff, in the MLSCN Steering Committee meetings held twice annually in the metropolitan Washington, DC area.
- 4) Adhere to MLSCN policies regarding data release, intellectual property, publications, and other policies that might be established during the three-year pilot period, as agreed upon by the MLSCN Steering Committee and the NIH Project Team.
- 5) Ensure that primary and secondary screening data and assay protocols are deposited in a centralized public database (e.g., PubChem or other, as specified by the NIH Program Official and Scientific Program Manager) according to the timeline agreed upon by the MLSCN Steering Committee and the NIH Project Team, and that resources developed as a part of this project (e.g., information about assays and chemical probes) are made publicly available according to MLSCN policies.
- 6) Accept and implement all scientific, practical, and policy decisions approved by the MLSCN Steering Committee and the NIH Project Team.
- 7) Submit data for quality assessment in any manner specified by the MLSCN Steering Committee, NIH Project Team, or External Scientific Panel.
- 8) Submit periodic (e.g., quarterly) progress reports in a standard format, as agreed upon by the MLSCN Steering Committee and NIH Project Team.
- 9) Share research resources, tools, and data of interest with other MLSCN centers, as agreed upon by the MLSCN Steering Committee and NIH Project Team.
- 10) Agree not to disclose confidential information obtained from other members of the MLSCN network.
- 11) May choose to establish a Center Steering Committee (CSC) consisting of key center personnel and external scientific advisors to review progress and provide advice on strategies for assay automation, screening, chemical probe optimization, etc.; prepare a concise summary of CSC meetings within 14 days to the NIH Program Official and Scientific Program Manager. The NIH Scientific Program Manager and the NIH Network Science Officer(s) may observe the proceedings at the discretion of the PI.
- 12) Be prepared for annual administrative site visits by NIH staff.

2. NIH SCIENTIFIC PROGRAM MANAGER RESPONSIBILITIES

The NIH Scientific Program Managers are scientist members of the NIH extramural staff who will have substantial scientific involvement during the conduct of this activity, through technical assistance, advice, and coordination above and beyond normal program stewardship for grants. This includes functioning as a collaborator with the PIs, facilitating the partnership relationship between NIH and the MLSCN centers funded under this RFA, helping to maintain the overall scientific balance in the program commensurate with new research and emerging research opportunities, and ensuring that the activities of the MLSCN centers are consistent with the mission of the NIH Molecular Libraries and Imaging Initiative. However, the role of the Scientific Program Manager will be to facilitate and not to direct. Each MLSCN center will have one designated NIH Scientific Program Manager, and a given Scientific Program Manager may be assigned to multiple centers.

The NIH Scientific Program Managers will have the following substantial involvement:

- 1) Provide ongoing coordination and tracking of the activities of individual MLSCN centers.
- 2) Provide relevant scientific expertise and overall knowledge.
- 3) Assist in the integration of the individual MLSCN centers into a research network, including coordinating regular conference calls for sharing of approaches and fostering inter-center collaborations.
- 4) Participate, as a voting member, with the other MLSCN Steering Committee members in the group process of setting research priorities and milestones, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted. The Scientific Program Manager will assist and facilitate the group process and not direct it.
- 5) Observe the proceedings of Center Steering Committee (CSC) meetings at the discretion of the center's PI.
- 6) Develop, with input from the MLSCN Steering Committee and the NIH Project Team, progress report formats (quarterly and annual) for both individual centers and for the Network.
- 7) Participate in the External Scientific Panel meetings.
- 8) Serve as scientific liaison between the awardees, other NIH program staff, and the NIH Project Team.
- 9) Report periodically (e.g., monthly) on the progress of the MLSCN pilot program to the NIH Project Team.
- 10) Assist in developing timelines for the wide distribution of screening data to the scientific community in accordance with the decisions of the MLSCN Steering Committee and the Project Team.
- 11) Assist in avoiding unwarranted duplication of effort across the MLSCN network, and help coordinate collaborative research efforts that involve multiple centers.
- 12) Review and comment on critical stages of MLSCN development for presentation to the NIH Project Team and External Scientific Panel before subsequent stages are implemented.
- 13) Retain the option to recommend, with the advice of the External Scientific Panel, additional research endeavors within the constraints of the approved research and negotiated budget to the NIH Project Team.
- 14) Retain the option to recommend, with the advice of the External Scientific Panel, re-allocation of NIH support among awardees, as scientific goals evolve.
- 15) To help carry out these duties, Scientific Program Managers may consult with non-NIH experts in the field.

3. NIH NETWORK SCIENCE OFFICER RESPONSIBILITIES:

The NIH Network Science Officers are scientist members of the NIH extramural staff who will work as a team with the NIH Scientific Program Managers to: 1) provide a broad base of scientific expertise to assist in oversight of the MLSCN research network in areas such as HTS approaches, detection platforms, assays, lead optimization chemistry, cheminformatics, and

compound management of the repository at the programmatic management level; and 2) serve as a resource to other NIH extramural staff about the procedures and progress of the MLSCN program.

The NIH Network Science Officer will have the following involvement:

- 1) Assist the awardees, in conjunction with the Scientific Program Managers, as needed.
- 2) Provide relevant scientific expertise and overall knowledge about specific aspects of MLSCN operations to the Scientific Program Managers.
- 3) Serve as subject matter experts to assist other NIH extramural staff in providing advice to investigators about the MLSCN program.
- 4) Assist the Scientific Program Managers in reviewing critical stages of development in the research program for presentation to the NIH Project Team and External Scientific Panel to make determinations regarding the implementation of subsequent stages.
- 5) Facilitate interactions between the awardee and investigators at other institutions.
- 6) Provide information about ongoing NIH-supported research and resources, and recommend the development of Molecular Libraries and Imaging related initiatives to the NIH Project Team.
- 7) Participate with the other MLSCN Steering Committee members in the group process of setting research priorities and milestones, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted in a non-voting liaison member role.
- 8) Two representatives of the Network Science Officers will participate in External Scientific Panel meetings to review and evaluate the progress of the centers in meeting their individual and collective milestones as non-voting liaison members.

4. NIH PROGRAM OFFICIAL RESPONSIBILITIES:

The NIH Program Official is an extramural staff scientist who will have responsibility for normal program oversight and stewardship of the MLSCN centers on behalf of the NIH Project Team.

The NIH Program Official will have the following involvement:

- 1) Approval of progress reports and support for out-years, on behalf of the NIH Project Team, for the cooperative agreements that support the MLSCN network.
- 2) Have the option to recommend, following consultation with the Scientific Program Managers, the NIH Project Team Director, the NIH Project Team, and the External Scientific Panel, the withholding or reduction of support from any center that substantially fails to achieve its goals according to the milestones agreed to at the time of the award, fails to maintain state-of-the-art capabilities, or fails to comply with the Terms and Conditions of the award.
- 3) Have the option to recommend, following consultation with the Scientific Program Managers, the NIH Project Team Director, the NIH Project Team, and the External Scientific Panel, an increase in support for any center that substantially exceeds its goals according to the milestones agreed to at the time of the award and substantially improves state-of-the-art capabilities.
- 4) Participate in the MLSCN Steering Committee meetings as an ex officio (non-voting) member.
- 5) Carry out continuous review of all activities to ensure objectives are being met.

5. NIH PROJECT TEAM DIRECTOR RESPONSIBILITIES:

The NIH Project Team Director is an extramural staff scientist who will have responsibility for coordinating the activities of the NIH Project Team and interactions with the MLSCN centers and NCGC. The Project Team Director may also serve as a Program Official.

- 1) Chair the NIH Project Team.
- 2) Participate in the MLSCN Steering Committee meetings as an ex officio (non-voting) member.

- 3) Provide materials to the External Scientific Panel needed to review and evaluate the progress of the centers in meeting their individual and collective milestones. Provide a concise summary of the External Scientific Panel meetings within 14 days to the panel members, center PIs, Program Officials, Scientific Program Managers, Network Science Officers, and NIH Project Team.
- 4) Carry out continuous review of all activities to ensure objectives are being met.

6. NIH PROJECT TEAM RESPONSIBILITIES:

The NIH Project Team will serve as the trans-NIH body overseeing and coordinating MLSCN activities. Project Team membership will include one or more representative(s) from each of the NIH Institutes and Centers participating in the Molecular Libraries and Imaging Initiative. Program Officials, Scientific Program Managers and Network Science Officers can be members of the NIH Project Team. Each participating IC and Center will have a single vote on the Project Team, no matter how many members from the IC or Center are involved. The Project Team Leader will chair meetings and serve as the Project Team Director of the MLSCN centers and NCGC on behalf of the NIH Project Team. The Project Team will receive recommendations from the MLSCN Steering Committee and will be overseen by the MLIIG.

The NIH Project Team will have the following involvement:

- 1) Review and implement MLSCN guidelines and policies based on recommendations from the MLSCN Steering Committee.
- 2) Communicate, through its chair, policy information to the MLSCN Steering Committee, Small Molecule Repository, PubChem, and the MLIIG.
- 3) Review the recommendations of the Assay Access Review Committee and prioritize the recommended assays for implementation within the Network to develop a balanced portfolio consistent with NIH-wide programmatic needs.
- 4) Review the recommendations of the MLSCN Steering Committee regarding the choice and distribution of assays to specific centers within the MLSCN and make final assignments of these assays to specific centers on a timetable that will ensure efficient operation of the Network.
- 5) Monitor the progress of HTS and probe development for individual assays to determine the appropriateness of the use/continued use of MLSCN resources (e.g., for implementing particularly difficult assays, or developing chemical probes)
- 6) Oversee the addition of new compounds to the Small Molecule Repository.
- 7) Evaluate progress of the MLSCN program in consultation with the External Scientific Panel and the MLIIG Working Group.
- 8) Attend the External Scientific Panel meetings and MLSCN Network meetings.

7. COLLABORATIVE RESPONSIBILITIES: MLSCN STEERING COMMITTEE FUNCTIONS:

The MLSCN Steering Committee is the operational group responsible for coordination of the activities of the MLSCN screening centers and the committee through which the NIH Project Team interacts with the MLSCN Network. The MLSCN Steering Committee will identify scientific and policy issues that need to be addressed at the Network level, develop recommendations to the NIH Project Team for addressing such issues, coordinate the primary recommendations for assay distribution within the Network, and coordinate the dissemination of screening data, assay protocols, and other materials with the wider scientific community.

The MLSCN Steering Committee membership will include the PI of each of the extramural centers and the NCGC (the NIH intramural center), the NIH Scientific Program Managers, and two representatives of the NIH Network Science Officers; the PI of the Small Molecule Repository, the PubChem designee, the NIH Program Officials, and the NIH Project Team Director will be *ex officio* (non-voting) members.

The PI of each center (or designee) will have one vote on the MLSCN. The NIH Scientific Program Managers and Network Science Officers may vote, but the total votes will count as a maximum of one-third of the total MLSCN votes. Membership on the Steering Committee

becomes effective upon issuance of the Notice of Grant Award. The MLSCN Steering Committee may establish additional subcommittees or workgroups for specific tasks. The NIH Program Officials, Scientific Program Managers, NIH Network Science Officers, and NIH Project Team Director may not chair any committee or subcommittee.

The MLSCN Steering Committee will:

- 1) Convene at least twice yearly. The purpose of these meetings is to assess scientific progress, identify new research opportunities, establish priorities, consider policy recommendations, and discuss strategies. One of the meetings will be in conjunction with the annual meeting of the External Scientific Panel to allow the MLSCN center Directors to meet directly with the External Scientific Panel.
- 2) Make decisions by a majority vote of a quorum, with an attempt for a consensus. A quorum will be the presence of a majority of the center PIs or their designees, at least one Scientific Program Manager, one Program Official, and the NIH Project Team Director. Outside consultants/experts may be asked to participate in these discussions as nonvoting advisors.
- 3) Establish a chair, subcommittees, or workgroups for specific tasks; the NIH Program Officials, Scientific Program Managers, NIH Network Science Officers, and NIH Project Team Director may not chair any committee or subcommittee.
- 4) Hold conference calls of the full committee and any subcommittees as needed; monthly calls are anticipated in the first year of the program.
- 5) Develop a plan for distribution of assays to specific centers within the Network on the basis of peer assessment of assay proposals received in response to PAR-05-060 by the MLSCN Assay Access Review Committee, the NIH Project Team's prioritization of assays acceptable for implementation, and information about available capacity and expertise of each center. The NIH Project Team will give final approval for assay assignments.
- 6) Develop recommendations for guidelines and policies for quality control and quality assurance of assay validation, screening, data reliability and quality, and chemical probe optimization; implement and monitor quality control/quality assurance procedures to assure consistency across centers.
- 7) Develop recommendations for a set of minimal characteristics that will have to be met in order to designate a compound as a "chemical probe," which is operationally defined as the final product of the MLSCN center's activity in the context of the MLSCN program.
- 8) Develop recommendations for guidelines for optimization of candidate compounds within the goals of the MLSCN program.
- 9) Develop recommendations for guidelines for standardizing the reporting of screening data and protocols for different types of assays to PubChem; develop policies to facilitate the timely deposition of screening data and protocols to PubChem in accordance with the MLSCN program's data release policy.
- 10) Serve as a venue for coordination on improving the state-of-the-art HTS in the academic sector by reporting progress, disseminating best practices, and collectively evaluating new procedures, resources, and technologies.
- 11) Identify opportunities to increase the inter-operability of centers in the Network; centers will be expected to have a high degree of flexibility and be willing to adopt uniform policies and procedures recommended by the Steering Committee and approved for implementation by the NIH Project Team.
- 12) Develop recommendations for guidelines for publication of screening data, assay protocols, chemical probe optimization, HTS technology development, and global data analyses, etc. resulting from the MLSCN effort.
- 13) Address recommendations made by the External Scientific Panel and approved for implementation by the NIH Project Team.
- 14) Each MLSCN Center will be expected to use the model agreement language approved by the MLSCN Steering Committee for transfer of assays and materials into the individual MLSCN Centers.

8. EXTERNAL SCIENTIFIC PANEL:

The External Scientific Panel will be responsible for reviewing and evaluating the progress of the MLSCN centers in meeting their individual and collective milestones and goals, and making recommendations about the progress and directions of the MLSCN network and individual centers to the NIH Project Team and the MLIIG. The External Scientific Panel will be composed of 6-8 senior non-federal scientists who are not directly involved in the activities of the MLSCN. The NIH Project Team will appoint members with concurrence from the MLIIG Working Group. The NIH Project Team will select one member as chair. The NIH Program Officials, NIH Scientific Program Managers, NIH Project Team Director, NIH Network Science Officers, and NIH Project Team members may attend the External Scientific Panel meetings as non-voting participants.

The External Scientific Panel will have the following involvement:

- 1) The chair will schedule, develop agendas, and oversee the annual meetings and conference calls. The membership of the Panel may be enlarged permanently, or on an ad hoc basis by action of the original members.
- 2) The External Scientific Panel will meet at least once a year and quarterly by conference call. During part of this meeting, there will be a joint meeting with the MLSCN Steering Committee to allow the Panel members to interact directly with the MLSCN center Directors, including the PI of the NCGC, and the PIs of the Small Molecule Repository, and PubChem.
- 3) The External Scientific Panel will review progress of the MLSCN network and individual centers, and make recommendations regarding any changes that may be needed in the direction of the MLSCN program to the NIH Project Team and the MLIIG Working Group.
- 4) The External Scientific Panel will be consulted by the NIH Scientific Program Managers and NIH Project Team Director when changes in a center's funding level are being considered because of either outstanding or poor technical performance, or for other reasons.
- 5) Any MLSCN center PI who considers a MLSCN Steering Committee decision unacceptable may appeal to the External Scientific Panel.

9. MLIIG STEERING COMMITTEE/WORKING GROUP:

The Molecular Libraries and Imaging Implementation Steering Committee (hereafter referred to as MLIIG Working Group) will provide overall guidance for the MLSCN program, and coordination with other components of the Molecular Libraries initiative. The MLIIG Working Group is composed of the Team Leaders (lead NIH staff) for each component of the Molecular Libraries and Imaging Roadmap Initiatives, and is co-chaired by the Directors of NHGRI, NIMH, and NIBIB.

