

Lung Program – Theme # 5: Enabling Therapeutic Trials and Translational Research

Introduction:

Vision: Improved respiratory health of the United States public through expedited discovery, testing, and implementation of treatments. This vision requires rapid translation of basic research to clinical care, wide participation of the population in research studies, and optimal knowledge diffusion and implementation.

To achieve this, NHLBI should take a leadership role in improving the current infrastructure for clinical research in the United States. These improvements should be designed to:

- promote the growth and maintenance of a skilled work force in clinical research
- promote investigator access to repositories containing standardized disease definitions, procedures for characterizing and analyzing lung, sleep and critical care phenotypes, and research data
- maximize efficient use of resources and production and implementation of research findings
- promote more participation by patients and health care providers in clinical research

Recommendations:

1. Improve clinical research infrastructure.

Rationale: Growth and efficiency of clinical research in the U.S. is limited by: non-standardized methods for defining and characterizing disease phenotypes; rudimentary databases that are not integrated or user friendly; regulatory requirements that are time-consuming and burdensome, and clinical research environments that do not attract scientists or research subjects.

NHLBI action: For lung, critical care, and sleep disorders, take long-term ownership and stewardship for:

- Development and maintenance of controlled vocabularies and ontologies.
- Standardization (with regular updates) of clinical and behavioral phenotypes, definitions of key diseases, exposures and outcomes; and maintenance of operational procedure documentation.
- Development of HIPAA-compliant, searchable patient databases for developing and testing hypotheses, determining trial recruitment and feasibility, and creating user friendly data sets for collaborative research and meta-analyses.
- Adoption of these standards within investigator-initiated research
- Development of infrastructure to support trials by cooperative groups and access to “virtual” or regional support centers for clinical trials and observational study methodologies.
- Facilitating cross-linkage of data within and across studies that address multiple diseases and disease processes.

- Facilitating efficient solutions across centers and countries for the complexities of and barriers to maintaining data confidentiality, acquiring informed consent, and obtaining IRB review in a timely manner (with other federal agencies, the international research community, and industry).

2. Enhance leadership skills of NHLBI clinical investigators

Rationale: Clinical researchers face specific challenges in building research programs. They must build links to sources of patients, comply with complex regulation, and lead large multidisciplinary research teams. These challenges demand leadership skills that can be taught.

NHLBI action: For lung, critical care, and sleep disorders, develop and offer:

- Training and retention programs for existing and future leaders in clinical research, fostering skills in leadership, management, communications, mentoring, and advocacy.
- Mechanisms to allow increased participation of developing investigators in study section, network, and multicenter study deliberations.

3. Offer funding mechanisms specifically-tailored to clinical research

Rationale: Funding and review mechanisms appropriate for animal or basic studies may be poorly suited to clinical research. For example, obtaining adequate preliminary data may require

years prior to award of funding, building of infrastructure, and creating the multi-disciplinary teams. Many study sections do not contain sufficient representation of experienced clinical researchers necessary for a balanced appraisal of the strengths and weaknesses of clinical research proposals.

NHLBI action: For lung, critical care, and sleep disorders, develop:

- Funding mechanisms that are better tailored to the needs of clinical investigators and research programs, such as planning grants, extended times on R21 and R03, clinically-oriented PPGs or center grants, supplemental funds to K08 and K23 mechanisms for larger data collection and to assist in transition to R awards, K and F mechanisms to support clinician and non-clinician scientists doing clinical research, and flexible caps on funding of clinical and population research.
- Funding to grow a clinical research infrastructure that promotes efficiency, enhances transdisciplinary interactions, and enhances training opportunities in pulmonary clinical research.
- Collaborations with other NIH institutes and government agencies, the international research community, professional societies, patient advocacy groups, and industry to address interdisciplinary problems such as critical care and sleep.
- A process for setting research priorities, assuring that funding mechanisms are available to support study designs and hypotheses that address knowledge gaps.

4. Expand community participation in, and benefit from, clinical research

Rationale: An important barrier to medical community and patient participation in clinical trials is the perception that the questions posed are not relevant to everyday clinical practice. More emphasis on research that impacts public health, partners with the practicing

clinician, and is appropriate to multiple health care settings will enhance clinical research participation by primary health care providers and patients.

NHLBI action: For lung, critical care, and sleep disorders, develop:

- Infrastructure and award systems that foster partnerships between investigators in academic environments and investigators in community settings.
- Formal mechanisms for community-based investigators to build the research agenda, set priorities, and design strategies for knowledge implementation.
- Mechanisms for accessing hard-to-reach and vulnerable populations.

5. Develop better fundamental understanding of the distribution and determinants of lung, critical care, and sleep disorders in the population, including children and underrepresented minorities.

Rationale: The impact of environmental and temporal exposures and genetic and ethnic variation on pulmonary disease expression affects the design and interpretation of clinical research, including therapeutic responses.

NHLBI action: To foster and encourage study designs that allow:

- Study of natural history and epidemiology of lung diseases, critical illness, and sleep disorders.
- Study of lung diseases, critical illness, and sleep disorders in existing observational studies.
- Inclusion of pulmonary, critical illness, and sleep phenotypes in ongoing observational studies.
- Inclusion of specific populations such as children and underrepresented minorities.

6. Educate the public about the value of clinical lung, critical care, and sleep disorders research

Rationale: The public's poor understanding of the burden of respiratory diseases and the role of clinical research in reducing this burden is a barrier to progress. A public better educated in the benefits of clinical research will be more likely to participate. Every opportunity should be taken to promote greater understanding of the role of research in improving respiratory health.

NHLBI action:

- Conduct public awareness campaigns on the value of clinical lung, critical care, and sleep disorders research, especially in populations who have not regularly participated in research.
- Develop incentives for hospitals and health care systems to educate patients about the value of and to participate in clinical research.

09/29/06