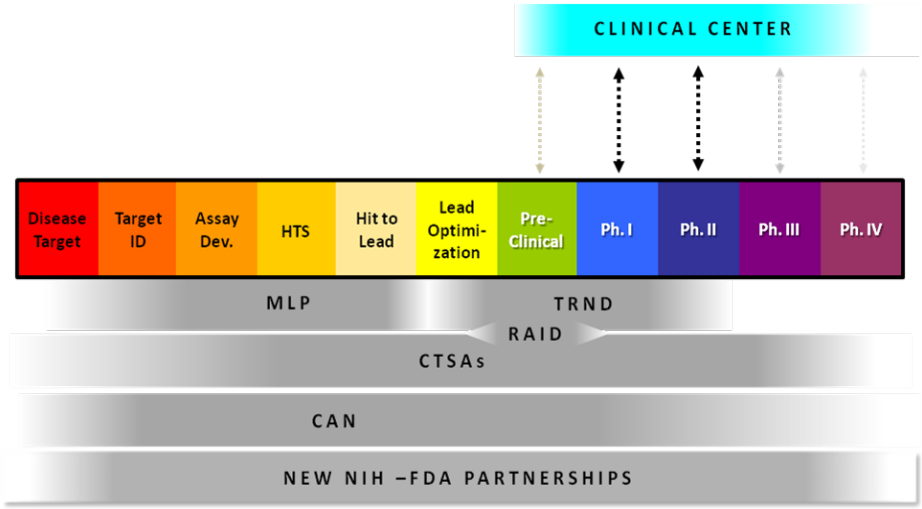
The NIH Clinical Center and the Proposed New Center

Opportunities for Partnership



Scientific Management Review Board

John I. Gallin, M.D.
Director, NIH Clinical Center

December 7, 2010

SMRB Recommendations on Clinical Center Budget and Governance

Provide stable support that will enable the expanded Clinical Center vision and new partnerships

Clinical Center as a National Resource

Core Strengths:

- **First-in-human clinical studies**
- **Investigation of rare diseases**

CC Specialized Services Enabling Clinical Research

- **Highly trained MD investigators and clinical research nurses**
- **Latest imaging technologies**
- **IT tools:**
  - ***Prototype: simplified protocol authoring***
  - ***BTRIS: warehousing and merging clinical and research data***
  - ***CRIS: patient care in the context of clinical trials***
- **Cell therapies**
- **GMP facility for drug formulation**
- **Metabolic chambers**
- **Biomechanics laboratory**
- **International clinical research training program**
  - ***New sabbatical program in clinical research management***

Interactions with the New Center

1) Developing new research partnerships

2) Making CC special resources available

3) Extending clinical research training programs

Clinical Center Planning
New Strategic Goal

To support the national translational research agenda through collaborative partnerships and new research programs to enrich clinical science

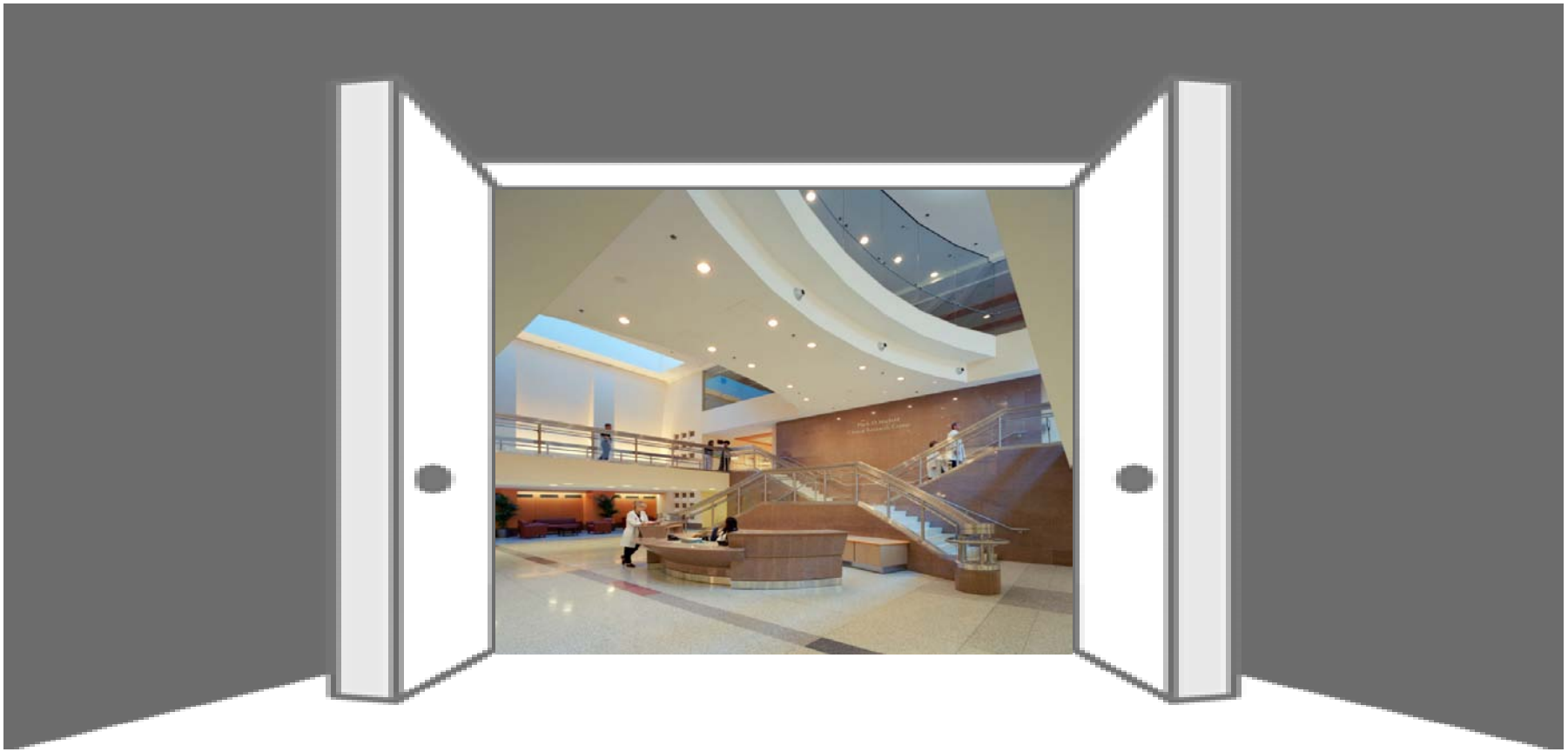
Comprehensive Plan Will Include…

- Inclusive stakeholder input
- Identification of a compendium of CC resources and catalogue on CC website
- Clarity of capacity and realistic expectations
- Assessment of resources needed
- Preserving the strong programs at the CC
- Developing policies and procedures for access:
  - application and review process
  - financial model for costing and reimbursement
  - plans for ongoing interface with the NIH extramural grants community

Other Key Considerations

- **Transparent and facile process for evaluating proposals**
- **Pool of funds to allow the Clinical Center and the new center to be nimble and responsive to high priority needs**
- **Stabilizing and expanding funding for bench-to-bedside awards**
- **CC/NCI/Damon Runyon Cancer Research Foundation pilot**

Conclusion



The Clinical Center is committed to enriching the collaborative environment for a strong continuum of translational research.

National Center for Research Resources
NATIONAL INSTITUTES OF HEALTH

Translating research from basic discovery to improved patient care

An Overview of NCRR: Presentation to the Scientific Management Review Board

December 7, 2010

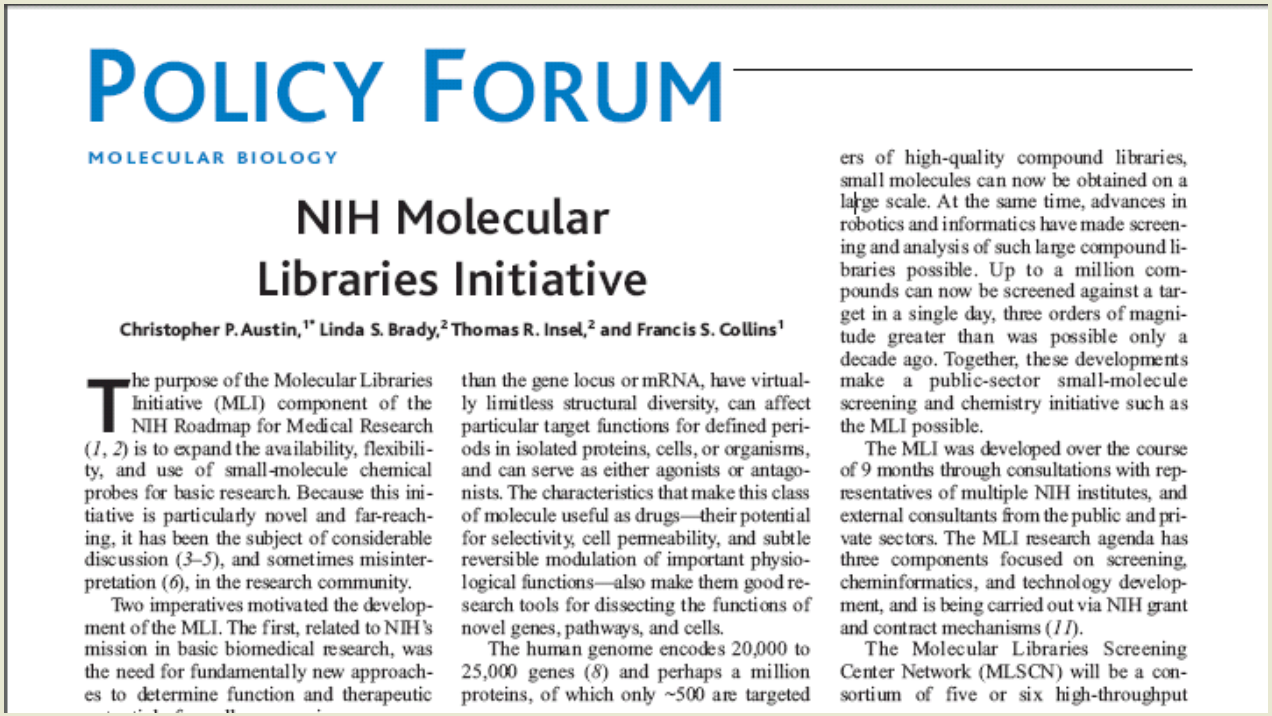
Barbara Alving, M.D., MACP
Director
National Center for Research Resources

NCRR Increases the Efficiency of Translation :
View from the Investigators and Academic Health Centers

- Transformative technologies
- Unique animal models
- Access to deep multi-disciplinary expertise
- Opportunities for minority – serving institutions
- Direct, hands-on training

Vision of Translational Research in 2004

Written by Drs. Austin, Brady, Insel and Collins



POLICY FORUM

MOLECULAR BIOLOGY

NIH Molecular Libraries Initiative

Christopher P. Austin,[1*] Linda S. Brady,[2] Thomas R. Insel,[2] and Francis S. Collins[1]

The purpose of the Molecular Libraries Initiative (MLI) component of the NIH Roadmap for Medical Research (*1*, *2*) is to expand the availability, flexibility, and use of small-molecule chemical probes for basic research. Because this initiative is particularly novel and far-reaching, it has been the subject of considerable discussion (*3*–*5*), and sometimes misinterpretation (*6*), in the research community.

Two imperatives motivated the development of the MLI. The first, related to NIH's mission in basic biomedical research, was the need for fundamentally new approaches to determine function and therapeutic

than the gene locus or mRNA, have virtually limitless structural diversity, can affect particular target functions for defined periods in isolated proteins, cells, or organisms, and can serve as either agonists or antagonists. The characteristics that make this class of molecule useful as drugs—their potential for selectivity, cell permeability, and subtle reversible modulation of important physiological functions—also make them good research tools for dissecting the functions of novel genes, pathways, and cells.

The human genome encodes 20,000 to 25,000 genes (*8*) and perhaps a million proteins, of which only ~500 are targeted

ers of high-quality compound libraries, small molecules can now be obtained on a large scale. At the same time, advances in robotics and informatics have made screening and analysis of such large compound libraries possible. Up to a million compounds can now be screened against a target in a single day, three orders of magnitude greater than was possible only a decade ago. Together, these developments make a public-sector small-molecule screening and chemistry initiative such as the MLI possible.

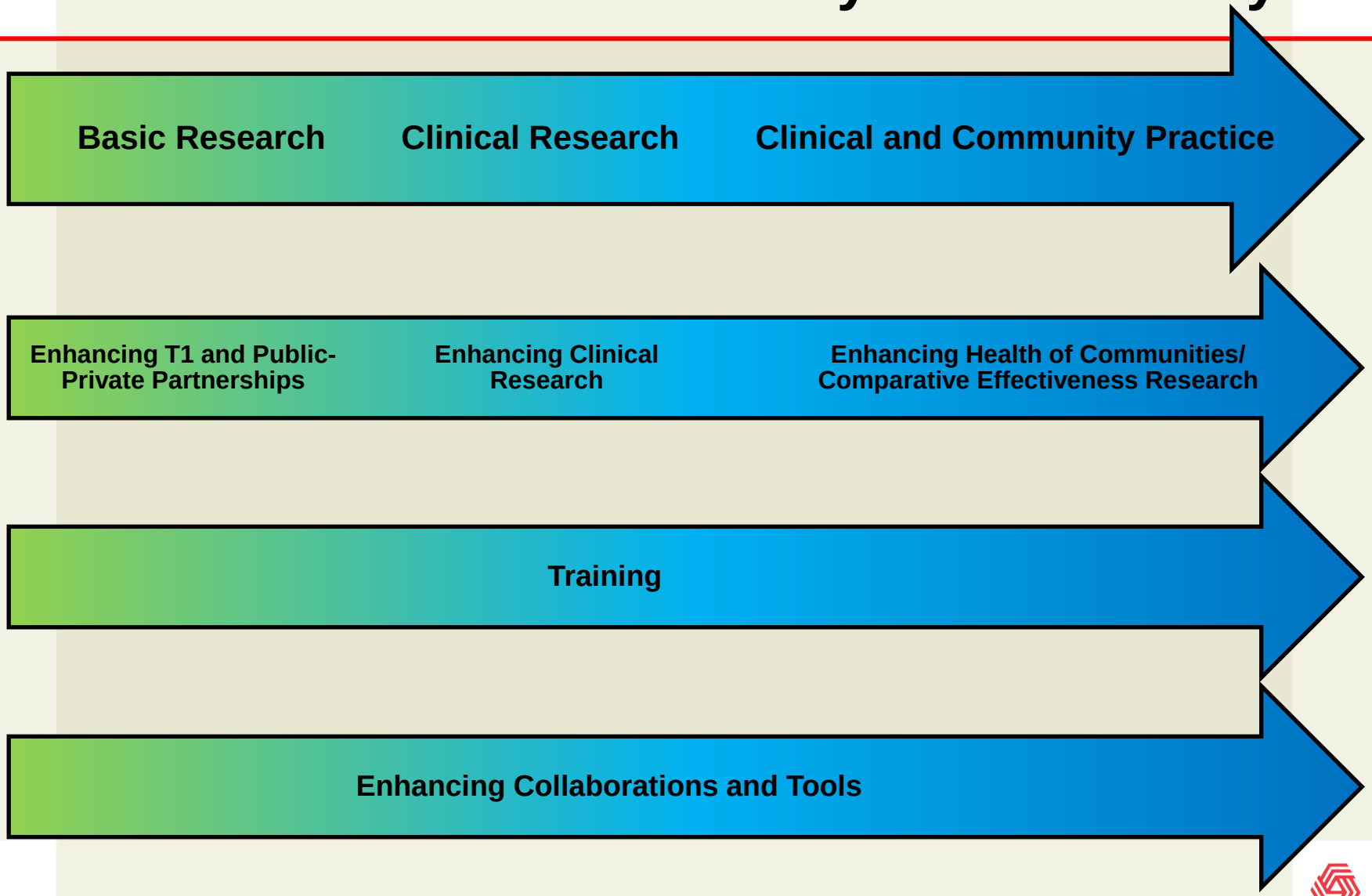
The MLI was developed over the course of 9 months through consultations with representatives of multiple NIH institutes, and external consultants from the public and private sectors. The MLI research agenda has three components focused on screening, cheminformatics, and technology development, and is being carried out via NIH grant and contract mechanisms (*11*).

The Molecular Libraries Screening Center Network (MLSCN) will be a consortium of five or six high-throughput

12 November 2004:.Volume 306: *Science*. www.sciencemag.org
Published by AAAS

NCRR

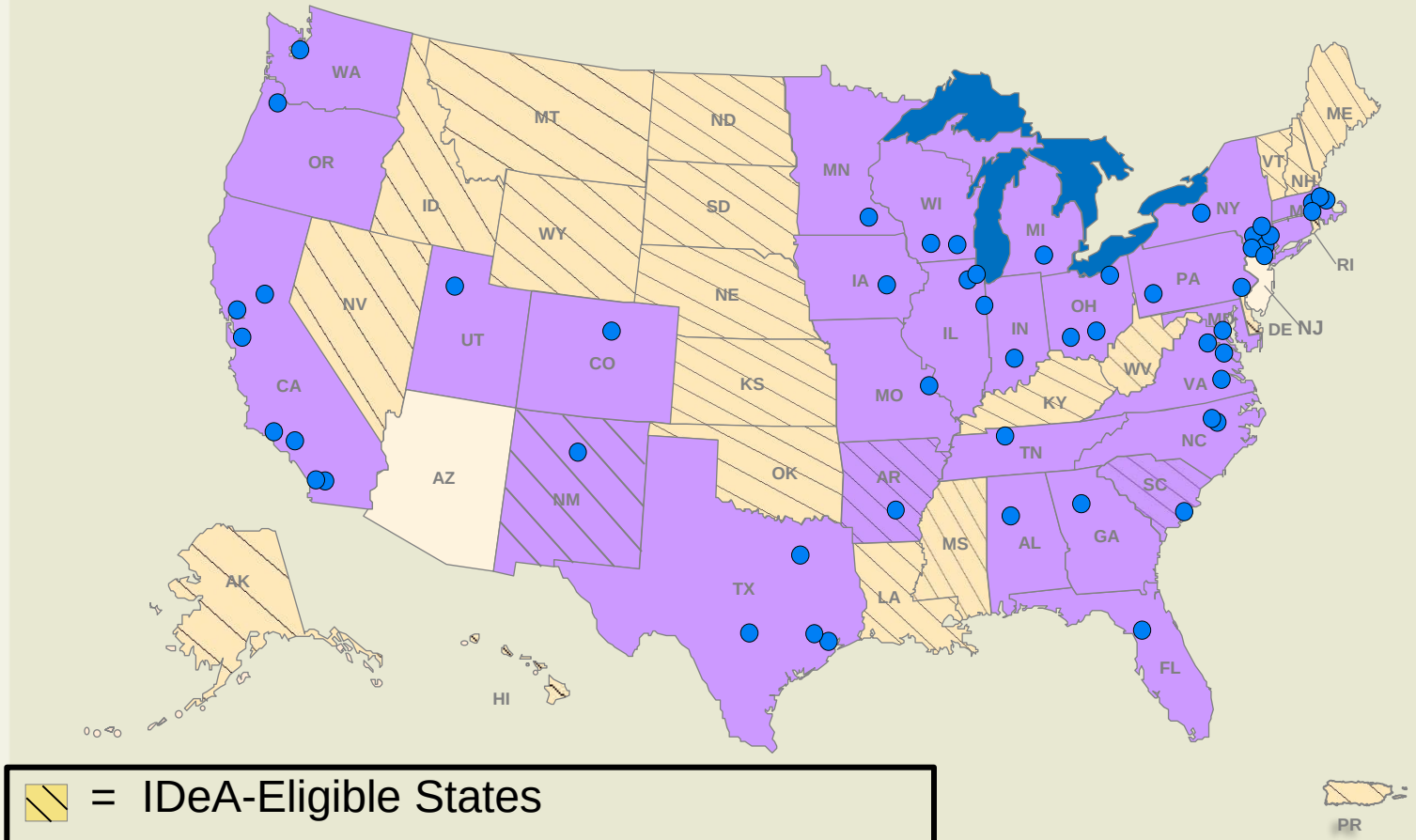
CTSA Consortium: Promoting Efficient Translation from Laboratory to Community



NCRR

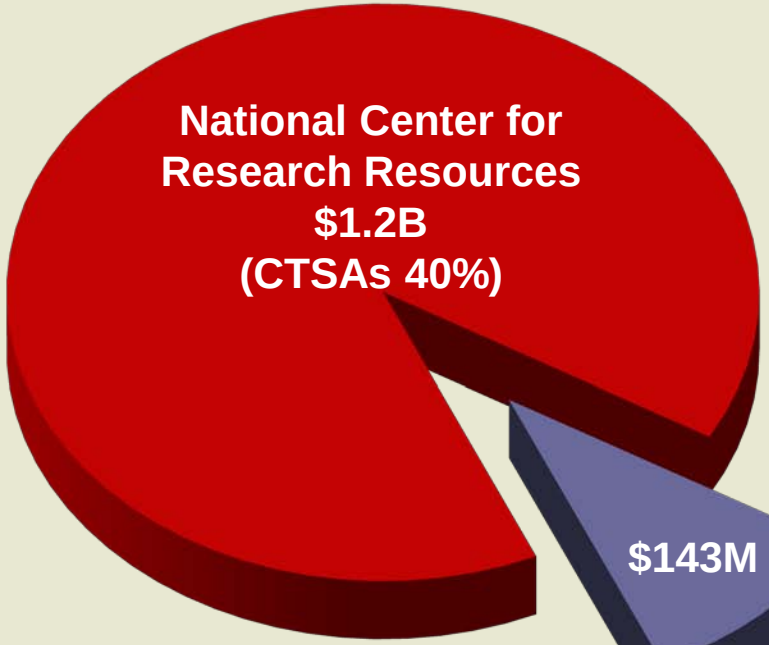
2010-Building a National CTSA Consortium

55 CTSA sites in 28 states and the District of Columbia



NCRR

Budgets of Molecular Libraries, RAID, and TRND Relative to Budget of NCRR (2010)



Proposed New Programs	
Molecular Libraries	$113M
Therapeutics for Rare and Neglected Diseases (TRND)	$25M
Rapid Access to Interventional Development (RAID)	$5M

NCRR

NCRR Recommendations

- Develop a financial and impact report that SMRB is charged by Congress to provide
- Engage in dialogue with stakeholders
- Consider :
  - Incorporating Molecular Libraries, RAID and TRND into NCRR after careful review of budget and accomplishments by expert advisory panel
  - Recruiting a new director for the newly-configured center that **CONTINUES** to address the full spectrum of translational medicine

NIH Scientific Management Review Board

Translational Medicine and Therapeutics Working Group

December 7, 2010

Arthur Rubenstein, M.B.B.Ch.

Executive Vice President, University of Pennsylvania for Health System and Dean, University of Pennsylvania School of Medicine

Working Group Roster

Non-Federal

Arthur Rubenstein, MBBCh
(Chair)

William Brody, MD, PhD

Gail Cassell, PhD

William Roper MD, MPH

Solomon Snyder, MD

Huda Zoghbi, MD

Norman Augustine
(ad hoc)

Federal

Josephine Briggs, MD

Anthony Fauci, MD

Eric Green, MD, PhD

Stephen Katz, MD, PhD

Griffin Rodgers, MD, MACP

Susan B. Shurin, MD

Harold Varmus, MD

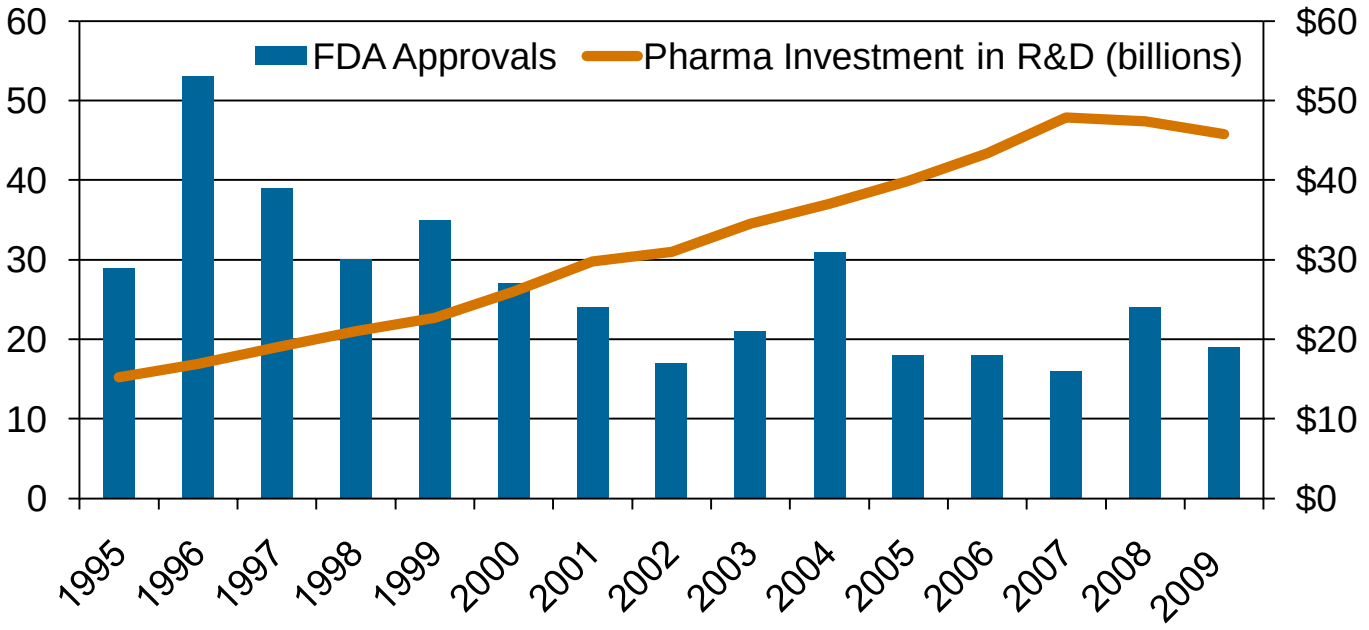
Francis Collins, MD, PhD
(ex officio)

Presentation Overview

- Impetus for Deliberations and TMAT Charge
- Deliberative Process
- Working Group Findings
- Working Group Recommendations

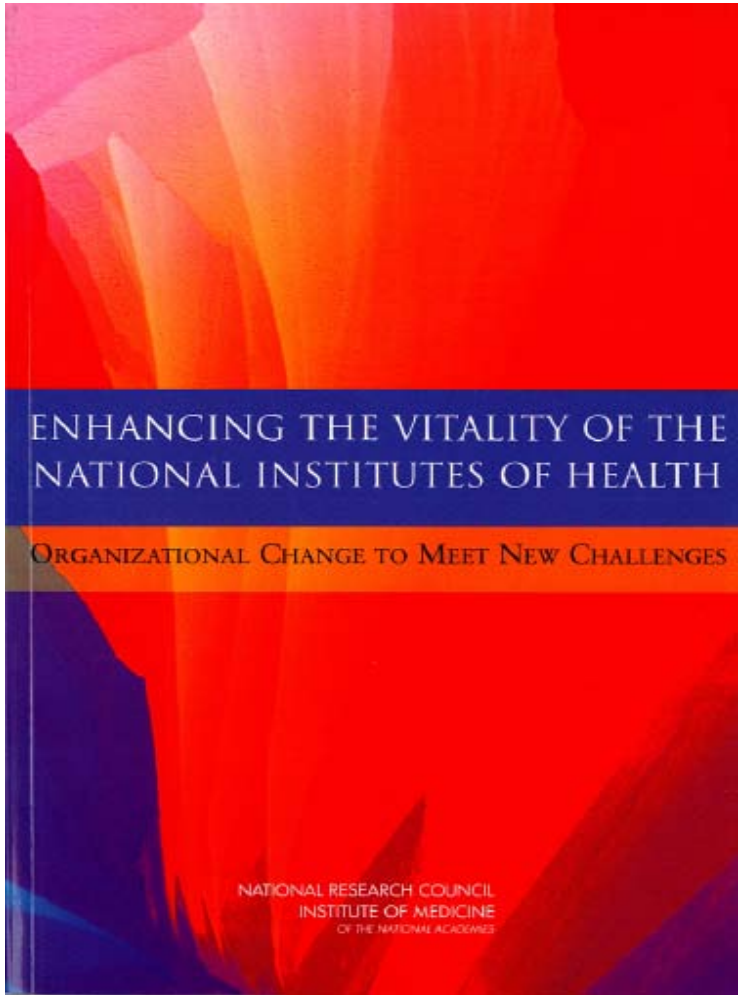
Impetus for Deliberations: Current Landscape

- **Despite greater investments in R&D by pharma, FDA approvals of new medical entities have declined**



- Pharmaceutical Research and Manufacturers of America; FDA

Impetus for Deliberations: Prior Recommendations



"…the Committee sees a critical lack of coordination and standardization across NIH in its clinical research programs that cause many opportunities for collaboration and data sharing across fields to be lost."

- **From the National Research Council and Institute of Medicine report titled *Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges (2003)***

Impetus for Deliberations: NIH Director's Opportunities

- Applying high throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases
- Translating basic science discoveries into new and better treatment
- Putting science to work for the benefit of health care reform
- Encouraging a greater focus on global health
- Reinvigorating and empowering the biomedical research community

- Collins, F.S., (2010). Science, 327: 36.

Working Group Charge

- Identify the attributes, activities, and functional capabilities of an effective translational medicine program for advancing therapeutics development

- Broadly assess, from a high-level view, the NIH landscape for extant programs, networks, and centers for inclusion in this program and recommend their optimal organization

- In addressing its charge, the Working Group will consider how the Agency could leverage and organize a wide range of existing NIH resources and effectively implement the Cures Acceleration Network (CAN) (assuming appropriation of funds)

Working Group Considerations

- **Additionally, in executing its charge, the TMAT Working Group should consider the following:**
  - **Current NIH-supported infrastructure, initiatives, and resources with direct relevance to the therapeutics development pipeline;**
  - **Methods to synergize, and avoid competition with, resources in the private sector;**
  - **Prior recommendations for strengthening the clinical and translational research enterprise at NIH, including recommendations of the IOM, and relevant lessons learned from industry, academia, non-profit organizations, etc.; and**
  - **Metrics and methodologies that could be used for evaluating the impact of changes in the organization and management of the therapeutics development program.**

Overview of TMAT Deliberative Process

- **Apply framework and process for considering change, as outlined by the Deliberating Organizational Change and Effectiveness (DOCE) Working Group:**

Deliberative Process *(framework developed by DOCE)*

Step 1.
Assess the Need for Change

Is TMAT research at NIH capitalizing on scientific opportunities and/or meeting public health needs?

Could reorganization better optimize TMAT research at NIH?

Step 2.
Evaluate Options for Change

What are the options for organizational change?

Which option would best optimize TMAT research at NIH?

Step 3.
Implement and Evaluate the Change

How should the change be implemented and navigated?

How should the effectiveness of the change be evaluated?

Working Group Activities

- **Since May 2010, the Working Group has held 5 teleconferences and 1 two-day stakeholder consultation, hearing from diverse groups and sectors, including:**
  - **Patient advocacy groups**
  - **Leaders of academic health centers**
  - **Clinical and Translational Science Awards recipients**
  - **Venture capitalists**
  - **Industry specialists**
  - **Non-profit organizations**
  - **NIH institute and center staff**
  - **Councils of NCRR and CC**

Working Group Findings: Assessing the Need for Change

- **EMERGING SCIENTIFIC OPPORTUNITIES**
  - Scientific discoveries have generated a large inventory of potential targets for new products
  - Rapid advances in innovative technology have made processes more efficient and affordable
  - Interest and expertise in therapeutics development are growing at academic institutions
- **EVOLVING LANDSCAPE OF THERAPEUTICS DEVELOPMENT**
  - Efforts by biotech and pharmaceutical companies have slowed due to lack of available venture capital and shrinking resources for R&D
  - A shift from a siloed approach towards one that is more integrated and modular is needed, capitalizing upon the respective strengths of the government and the private sector

Working Group Findings: Assessing the Need for Change *(cont.)*

- **SYNERGY IN LEVERAGING RESOURCES EFFECTIVELY**
  - Extant and emerging programs at NIH are increasingly well equipped to catalyze progress in therapeutics development
  - NIH possesses scientific and technological resources that can enable unique partnerships with diverse organizations, entities, sectors, etc.
- **AUTHORIZATION OF CURES ACCELERATION NETWORK**
  - Both Congress and the American public look to NIH to play a catalytic role in delivering on the promise of translational medicine, as reflected in the recent passage of the Patient Protection and Affordable Care Act (PL 111-148)
  - Legislation calls on NIH to establish a Cures Acceleration Network (CAN) to advance the development of “high need cures”

Working Group Findings: Assessing the Need for Change *(cont.)*

- **At the September 14-15, 2010 stakeholder consultation, participants identified the additional areas of opportunity:**
  - **Developing and enhancing appropriate collaborations**
  - **Training and supporting TMAT career paths**
  - **Communicating a clear mission**

Working Group Findings: Assessing the Need for Change *(cont.)*

Step 1.

Assess the Need for Change

Is TMAT research at NIH capitalizing on scientific opportunities and/or meeting public health needs?

Could reorganization better optimize TMAT research at NIH?

CONCLUSION OF THE TMAT WORKING GROUP

The current NIH structure related to TMAT should be reorganized to capitalize best upon emerging scientific opportunities, adapt to and help shape the evolving landscape, create a home for the recently authorized CAN, and leverage existing NIH resources to speed the delivery of new, more effective medical products to patients.

Working Group Findings: Goals and Objectives of Reorganization

- *GOAL:* To expand and augment the agency's efforts in advancing translational medicine and developing new therapeutics* and diagnostics
- Toward this end, it will be critical that NIH pursue a deliberate and rational approach that effectively:
  - Leverages existing efforts
  - Supports promising areas of research
  - Enhances synergy between public and private sectors

*Includes, but not limited to, drugs, biologics, and devices

Working Group Findings: Functional Capabilities and Activities

FUNCTION: Support and strengthen TMAT research

ACTIVITIES:

- Develop and provide scientific resources (e.g., chemical libraries, high-throughput screening, repositories, unique research facilities) and expertise
- Enhance therapeutics development efforts within and across NIH
  - Provide services and expertise to NIH ICs
  - Augment the strengths and experience of IC-based activities
  - Inform the development of trans-NIH strategies
  - Incentivize research in areas of little interest in the private sector
- Streamline and improve the therapeutics development process
  - Facilitate effective transition between steps
  - Learn from successes and failures of each product
  - Design innovative approaches to product development
- Identify and bridge gaps

Working Group Findings: Functional Capabilities and Activities *(cont.)*

FUNCTION: **Provide central locus for information on and access to resources, tools, and expertise related to TMAT**

ACTIVITIES:

- **Establish a visible home at NIH**
  - **Cluster and leverage core resources**
  - **Establish strong functional connections with relevant components of NIH**
  - **Publicize existing and new TMAT-related resources and activities at NIH**
- **Offer expertise and advice on advancing concepts from discovery to translation and assist efforts to navigate the therapeutics development process**
- **Develop resources for assisting in navigating regulatory pathways**
- **Develop and support data-sharing infrastructure**
- **Maintain knowledge of applicable resources, technology, programs, experts, partners, etc., at each phase of product development**

Working Group Findings: Functional Capabilities and Activities *(cont.)*

FUNCTION: **Serve as catalyst and convener for collaborative TMAT interactions and partnerships**

ACTIVITIES:

- **Facilitate and participate in partnerships, including identifying and matching potential partners**
- **Use convening power to promote mutual understanding of the cultures and goals of key sectors**
- **Facilitate effective hand-off of products to industry for further development and commercialization**
- **Establish mechanisms for navigating IP and COI concerns**
- **Incentivize sharing of abandoned products and the exploration of rescuing and repurposing products**

Working Group Findings: Functional Capabilities and Activities *(cont.)*

FUNCTION: **Expand the pre-competitive space**

ACTIVITIES:

- **Incentivize the publication of research failures and lessons learned**
- **Develop and incentivize use of informatics infrastructure for validation, curation, integration, and sharing pre-clinical data across sectors and distributing risk**
- **Engage in partnerships to conduct and support research in pre-competitive areas (e.g., advance disease understanding, biomarkers, disease models)**

Working Group Findings: Functional Capabilities and Activities *(cont.)*

FUNCTION: **Support training for translational research investigators**

ACTIVITIES:

- **Develop clear career tracks for TMAT research (including clinical pharmacology)**
- **Offer training grants for translational research education; including bioinformatics, systems biology, biomarker development, and cross-sector training (including FDA and pharma)**
- **Establish curriculum in regulatory science**

Working Group Findings: Functional Capabilities and Activities *(cont.)*

FUNCTION: **Enhance communication with and among all stakeholders regarding TMAT**

ACTIVITIES:

- **Identify opportunities to encourage NIH grantees to pursue the translation of their discoveries**
- **Foster greater communication and collaboration with other government agencies**
- **Increase outreach to the public, patient advocacy groups, Congress, and others**

Deliberative Process *(framework developed by DOCE)*

Step 1.
Assess the Need for Change

Is TMAT research at NIH capitalizing on scientific opportunities and/or meeting public health needs?

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How should the change be implemented and navigated?

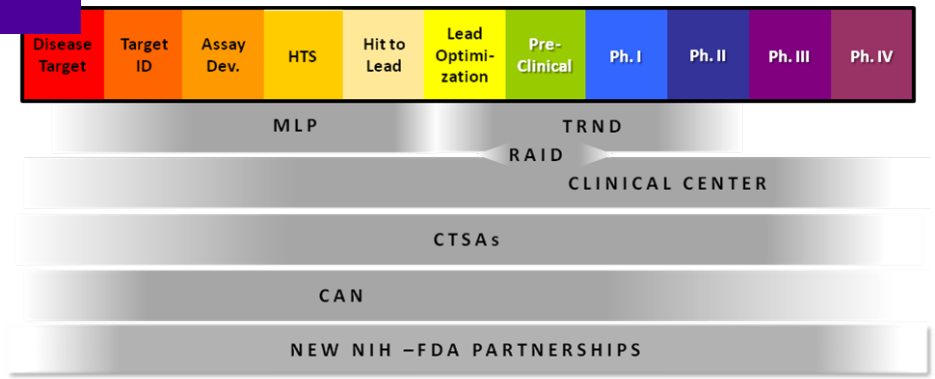
How should the effectiveness of the change be evaluated?

Working Group Findings: Relevant Extant NIH Resources for Consideration

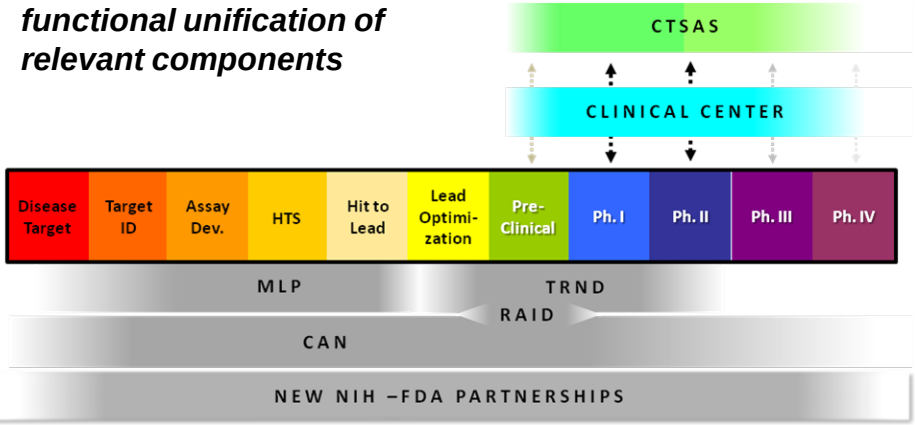
- Molecular Libraries Program (MLP)
- Therapeutics for Rare and Neglected Diseases (TRND) Program
- NIH Rapid Access to Interventional Development (RAID) Program
- NIH-FDA Regulatory Science Initiative
- Clinical and Translational Science Awards (CTSAs)
- NIH Clinical Center (CC)

Working Group Findings: Potential Options for Organization

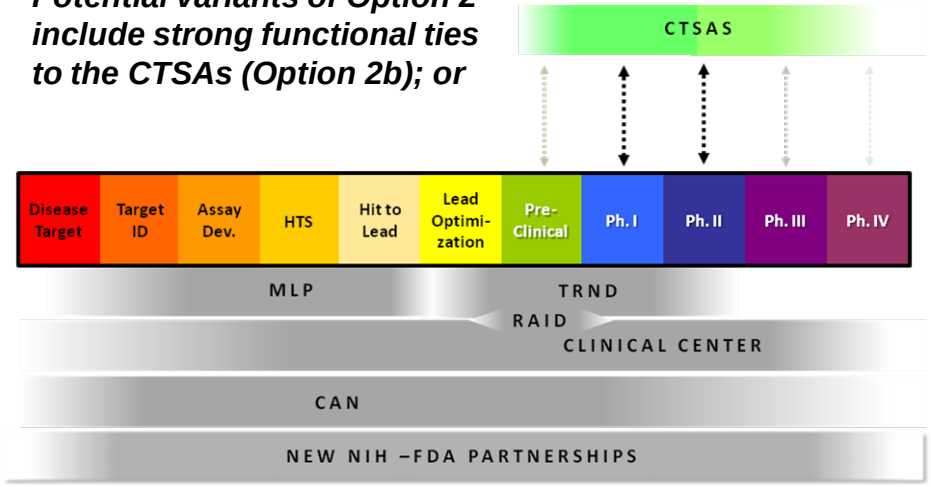
Option 1: Structural unification of relevant components



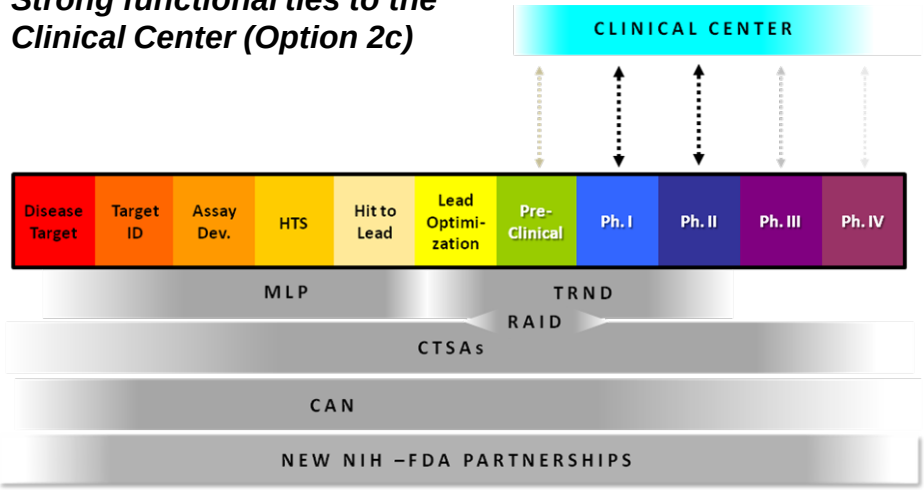
Option 2a: Structural and functional unification of relevant components



Potential variants of Option 2 include strong functional ties to the CTSAs (Option 2b); or



Strong functional ties to the Clinical Center (Option 2c)

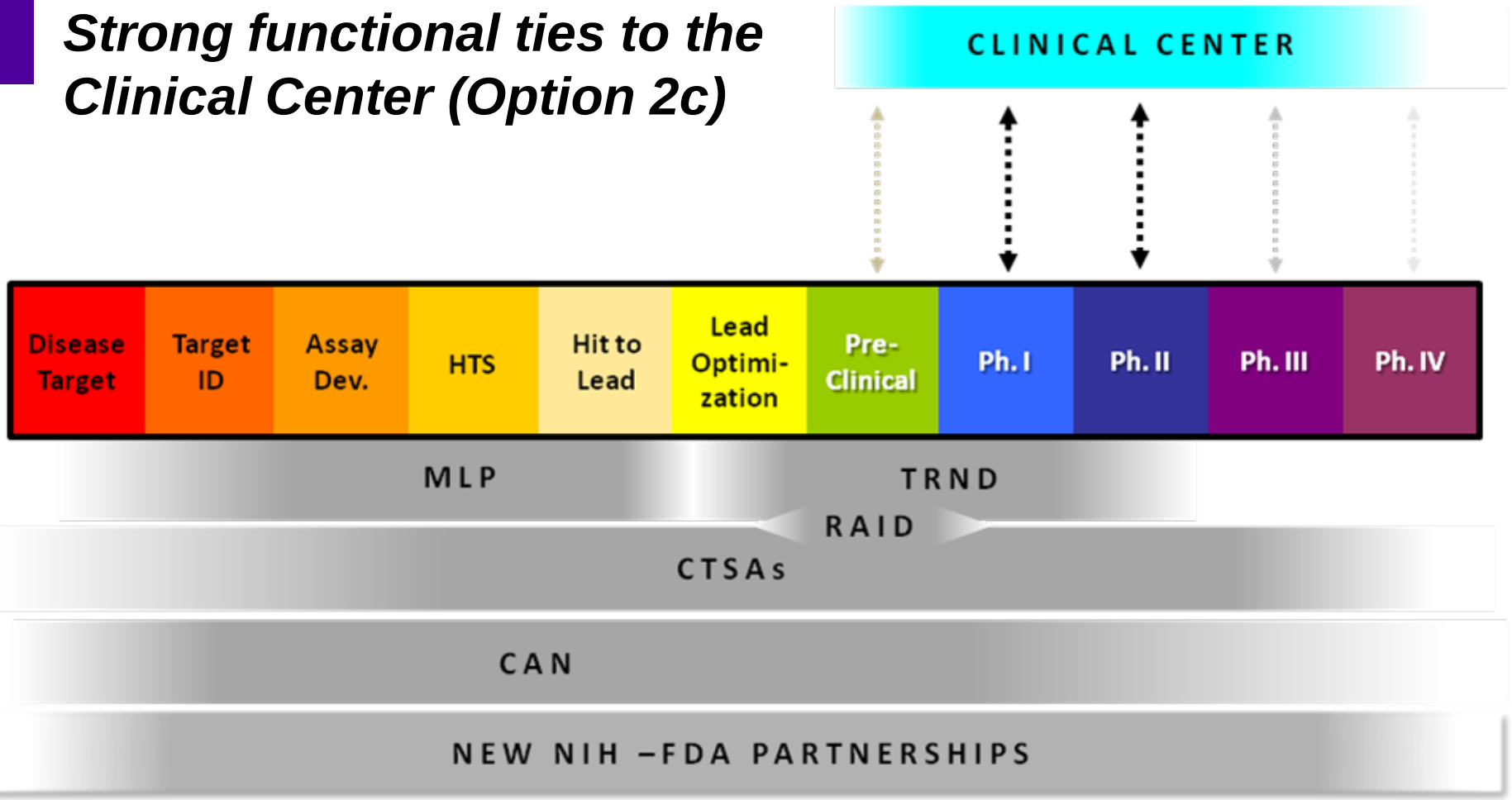


Working Group Recommendations

- **It is proposed that NIH establish a new Center to:**
  - ***Develop and provide research infrastructure*** **for advancing translational medicine and therapeutics development**
  - ***Foster new and innovative strategies for TMAT research*** **by advancing a process engineering approach to developing therapeutics, including strengthening and streamlining the process itself**
  - ***Serve as a catalyst, resource, and convener for collaborative TMAT interactions and partnerships,*** **capitalizing on the relative strengths of the extra- and intramural communities, private sector, government, and academia, to promote quick-win, fast-fail paradigms and further develop the pre-competitive space**

Working Group Recommendations: Organization of New Center

Strong functional ties to the Clinical Center (Option 2c)



Working Group Recommendations: Rationale for Organizational Structure

- Components of the core structure support activities, provide expertise, and enable access to resources (e.g., technologies) broadly applicable to a range of diseases

- CTSAs share a common vision for reducing the time it takes for laboratory discoveries to become treatments for patients, engaging communities in clinical research efforts, and training clinical and translational researchers—this consortium provides an existing national infrastructure for the conduct of translational research and is to be an essential component of the new Center

- The Clinical Center is a valuable resource and essential component of both the NIH Intramural Research Program and NIH's translational medicine portfolio and subsequently should have a strong functional connection to a new Center devoted to TMAT research, but should not be structurally encompassed within the entity

Working Group Recommendations: IRP Working Group Recommendations on CC

- At the SMRB meeting on September 14-15, 2010, members agreed to table the vote on IRP Working Group recommendations regarding the Clinical Center until the TMAT recommendations were finalized
- Members of the TMAT Working Group continue to support the IRP Working Group's recommendations regarding the vision and role, governance, and funding of the Clinical Center
- The TMAT Working Group finds that the IRP Working Group's recommendations regarding the Clinical Center are compatible with emerging TMAT recommendations
- The TMAT Working Group anticipates synergy between the proposed Center and the recommended vision and role for the Clinical Center as a national resource

Working Group Recommendations: Functions and Activities

- **Bulk of the new Center's activities should focus on providing and supporting resources, training, and tools to enable TMAT research**
- **As necessary, the new Center should house targeted activities to perform its functions (e.g., implement the Cures Acceleration Network)**
- **Functions and activities of any new Center should not duplicate, consume, or undermine the successful activities already underway within the NIH ICs**

Working Group Recommendations: Functions and Activities *(cont.)*

- **Specifically, the new Center should:**
  - **Support and strengthen research in translational medicine and therapeutics development;**
  - **Provide a central locus for information on and access to resources, tools, and expertise related to TMAT;**
  - **Serve as a catalyst and convener for collaborative TMAT interactions and partnerships;**
  - **Expand the pre-competitive space;**
  - **Support training for TMAT investigators; and**
  - **Enhance communication with and among all stakeholders.**

Working Group Recommendations: Attributes

- Promotes collaboration across sectors
- Streamlines and accelerates the translation of basic research
- Provides a visible home for resources and expertise
- Employs metrics, benchmarks, timelines, and milestones in planning, management, and decision-making
- Promotes and allows flexibility in decision-making and priority-setting
- Facilitates culture shifts, including in cross-sector collaborations and internal peer review processes

Working Group Recommendations: Implementation and Evaluation

Step 3.

Implement and Evaluate the Change

How should the change be implemented and navigated?

How should the effectiveness of the change be evaluated?

- **Successful implementation will require strong leadership, clearly delineated tasks, and cooperation from affected parties**
- **The new Center should be evaluated periodically to determine whether it is meeting its goals and address any untoward consequences.**

Working Group Recommendations: Metrics for Evaluation

- *Long-Term Metrics:* **Evidence that the new Center has made contributions to the development of new products (including the pace of their discovery)**
- *Interim Metrics:* **Given the lengthy timelines, high-risk nature, and difficulty associated with TMAT research, interim metrics will be critical to enabling short-term evaluation and making necessary adjustments. Metrics should include:**
  - **Evidence of a portfolio that enhances the breadth and depth of Agency's TMAT portfolio by complementing (and not duplicating or infringing on) successful IC initiatives**
  - **Evidence of increasing interdisciplinary and cross-sector research collaborations**
  - **Identification and support of new approaches and technologies enabling TMAT research**
  - **Evidence of increasing number of investigators participating in TMAT research**
  - **Evidence that TMAT efforts reveal new pathways and areas for basic discovery**
  - **Development and utilization of a TMAT-relevant web portal for internal and external stakeholder access**

Working Group Recommendations: Additional Considerations

- The Working Group noted that NCRR also possesses programs for establishing clinical research infrastructure, developing versatile new technologies and methods, providing access to state-of-the art technologies and instruments, and developing and providing access to critical animal models—many of which have significant collaborations and interactions with the CTSAs across the country
- Given that many of NCRR's resources are germane to the resource function of the proposed Center, the agency may choose to consider the incorporation of these relevant components

Working Group Recommendations: Additional Considerations *(cont.)*

- **Once the appropriate infrastructure has been established, NIH can determine what additional resources are needed to enhance rapid translation of basic discoveries into cures**
- **In establishing the new Center, it will be critical for NIH to analyze previous experience in implementing translational medicine and therapeutics development programs, including lessons learned from both successes and failures**

Conclusions

- NIH could enhance its efforts in translating basic discoveries into new diagnostics and treatments by establishing a focused, integrated pipeline for therapeutics development
- The mission of the new Center should complement the NIH's mission of advancing fundamental biomedical research and improving human health—it should not detract from the agency's emphasis on fundamental knowledge, but rather, stimulate the pursuit of new avenues of scientific inquiry
- Formation of this new Center should not be delayed in the absence of a CAN appropriation

Working Group Recommendation: Creation of a New Center

NIH should establish a new Center devoted to advancing translational medicine and accelerating therapeutics development.

The new Center should incorporate MLP, TRND, RAID, CTSAs, CAN, NIH-FDA Partnerships, and other existing components or new resources to be developed (as appropriate).