ATTACHMENT 7

NIH Scientific Management Review Board

Translational Medicine and Therapeutics Working Group

November 10, 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, M.D., Ph.D.

Stephen Katz, MD, PhD

Griffin Rodgers, MD MACP

Susan B. Shurin, MD

Harold Varmus, MD

Francis Collins, MD, PhD *(ex officio)*

Working Group Charge

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

- **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 therapeutic development program.**

Working Group Deliverables

- **The Working Group's report to the full board will include:**
  - **Description of attributes, activities, and associated functional capabilities of a translational medicine program optimized to enhance therapeutics development;**
  - **Recommendations for organizing the Agency's existing components to optimize a translational medicine and therapeutics program; and**
  - **Metrics for evaluating successes and any untoward consequences of organizational and/or management changes, in particular consequences for the progress of research in areas affected by the proposed changes.**

Working Group Process and Timeline

DATE	MEETING OBJECTIVES
May 2010	**Full SMRB Meeting:** *Receive TMAT charge*
July 2010	**Full SMRB Teleconference:** *Briefing on TMAT charge*
	TMAT WG Teleconference: *Identify data needs*
September 2010	**Full SMRB Meeting:** *Hold stakeholder consultation & public forum*
October 2010	**TMAT WG Teleconference:** *Discuss NIH Director's vision & functions and activities of TMAT program*
November 2010	**TMAT WG Teleconference:** *Identify optimal organization of TMAT program*
	Full SMRB Teleconference: *Review findings & draft recommendations*
	TMAT WG Teleconference: *Review draft report*
December 2010	**Full SMRB Meeting:** *Vote on recommendations*

Overview of TMAT Deliberative Process

- Apply framework and process for considering change, as outlined by the DOCE Working Group:
  - Guiding principles for considering change at NIH
  - Three step process
    - Assess the need for change
    - Evaluate options for change
    - Implement and evaluate the change
  - Underpinning attributes of transparency, communication, and accountability
- Preliminary conclusions
  - There is a need and opportunity for change in order to optimize TMAT research at NIH
  - A range of options is under consideration, with a preferred option emerging

Deliberative Process *(framework developed by DOCE)*

GUIDING PRINCIPLES

Strengthen ability of NIH to carry out mission

Provide environment for collaboration, coordination, and interaction

Bring together synergies

Enhance public understanding, confidence, and support

Increase operational efficiency

STEPS AND CONSIDERATIONS

Step 1. Assess the need for change → Step 2. Evaluate options for change → Step 3. Implement and evaluate the change

UNDERPINNING ATTRIBUTES

Transparency | Communication | Accountability

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?

Deliberative Process *(framework developed by DOCE)*

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Deliberative Process: 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

Deliberative Process: 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.**
- **PASSAGE OF HEALTH CARE REFORM**
  - **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)**

Deliberative Process: 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?

Yes, but there are opportunities to streamline the therapeutics development pipeline, bridge gaps in the pipeline, and provide key resources to the research community.

Yes. TMAT research could benefit from a reorganization at NIH to capitalize on emerging scientific opportunities, recent changes in therapeutics development, existing resources and programs, and the recently-authorized Cures Acceleration Network.

Assessing Need: Functional Capabilities and Activities of TMAT Program

FUNCTION: **Conduct, support, and strengthen translational research**

ACTIVITIES:

- **Develop programs to conduct and support research**
  - **Identify and bridge gaps**
  - **Employ novel approaches to NIH support (e.g., adjust review processes and funding timelines to provide more flexibility for this area of research)**
  - **Recruit project managers with necessary expertise to identify promising projects (and terminate those unlikely to yield benefits) and provide guidance to investigators navigating the therapeutics development process**
  - **Incentivize research in areas where the private sector may not be able to make sufficient progress alone and where there is little interest on the part of the private sector (e.g., rescue and repurposing research, products for rare and neglected diseases)**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(cont.)*

***FUNCTION:* Conduct, support, and strengthen translational research** *(cont.)*

ACTIVITIES:

- **Develop and provide scientific resources (e.g., chemical libraries, high-throughput screening, repositories, unique research facilities, etc.)**
- **Coordinate and strengthen therapeutics development effort 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 and initiatives**
- **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**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(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 programs at NIH**
- **Offer expertise and advice needed to advance concepts from discovery to translation and assist efforts to navigate the therapeutics development process**
- **Develop programs to assist 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**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(cont.)*

FUNCTION: **Serve as catalyst and convener for collaborative 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 actors**
- **Eliminate silos and foster team science**
- **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**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(cont.)*

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

ACTIVITIES:

- **Promote and facilitate open exchange of information**
- **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 for sharing 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)**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(cont.)*

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

ACTIVITIES:

- **Brand a discipline for translational research**
- **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**
- **Identify mechanisms to incentivize careers in translational medicine**
- **Reinvigorate the discipline of clinical pharmacology**

Assessing Need: Functional Capabilities and Activities of TMAT Program *(cont.)*

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

ACTIVITIES:

- **Enable increased communication within NIH**
- **Identify opportunities to engage traditional NIH grantees**
- **Foster greater communication and collaboration with other government agencies (e.g., FDA, CMS, and PTO)**
- **Increase outreach to the public, patient advocacy groups, Congress, and others**

Deliberative Process *(framework developed by DOCE)*

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Organization Options: Goals and Objectives

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

Organization Options: Goals and Objectives *(cont.)*

- **It is proposed that a new TMAT program be established at NIH in the form of a new Institute/ Center (IC) to:**
  - ***Establish new and innovative approaches to conducting research*** **to advance the science of process engineering of the therapeutics development pipeline, in the context of strengthening and streamlining the process itself; and**
  - ***Serve as a catalyst, resource, and convener for collaborative interactions*****, 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.**

Organization Options: Considerations

- Any new IC should not duplicate, consume, or undermine the successful activities already underway within the NIH ICs – however, several trans-NIH programs and centers are ideally suited to the functions and aims of a new entity
- Once the appropriate infrastructure has been established, NIH can determine what additional resources are needed to fill the gaps hindering rapid translation
- In establishing the new IC, 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

Organization Options: Considerations *(cont.)*

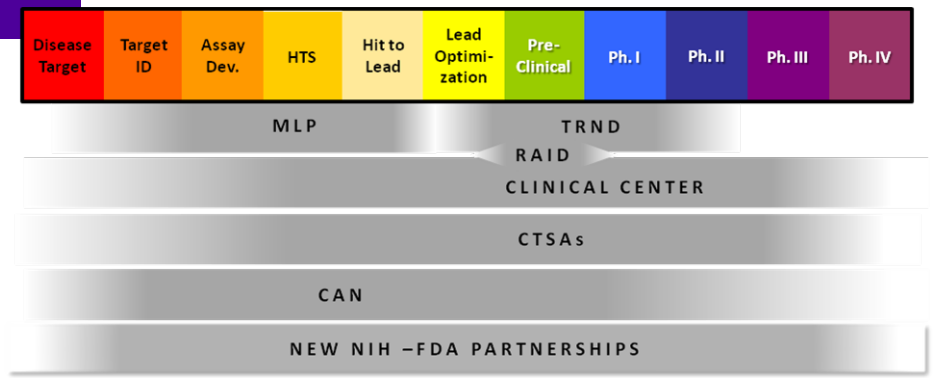
- **The bulk of the new IC's activities should focus on providing and supporting resources, training, and tools to enable translational and therapeutics development research**
- **The new IC should house targeted activities to perform its functions (e.g., implement the Cures Acceleration Network)**

Organization Options: Considerations *(cont)*

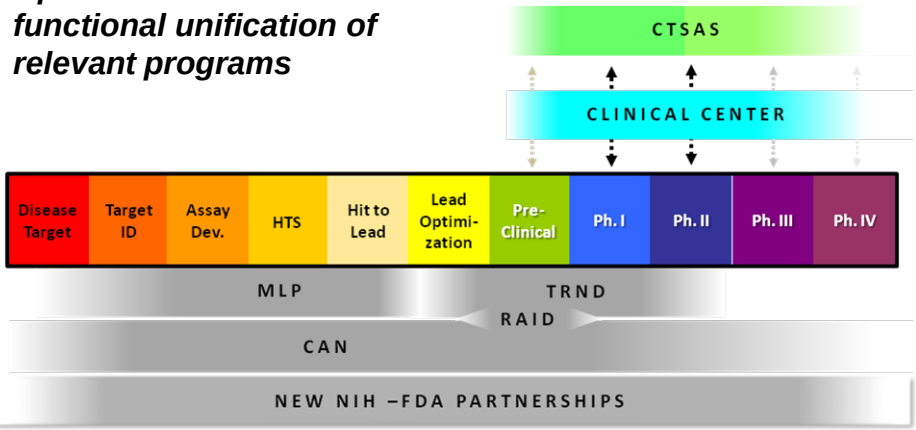
- **The new Institute or Center should:**
  - **Have sufficient infrastructure necessary to develop, maintain, and deploy its resources and activities**
  - **Amplify the connection between basic discovery and translation**
  - **Employ new models for issuing funding opportunities and reviewing applications**
  - **Foster and maintain strong communication with stakeholder communities, including other ICs, the Clinical Center, and CTSA institutions**
  - **Engage in partnerships with industry and other government agencies, especially FDA**

Potential Options for Organization

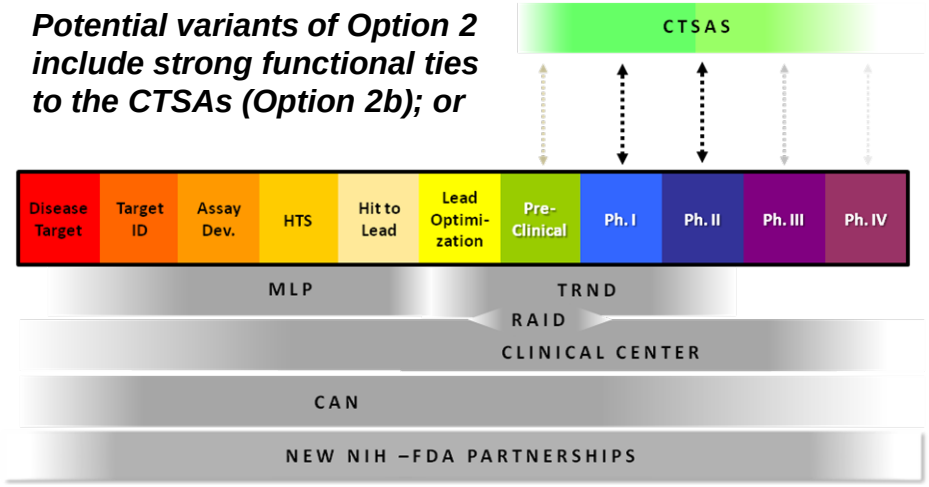
Option 1: Structural unification of relevant programs



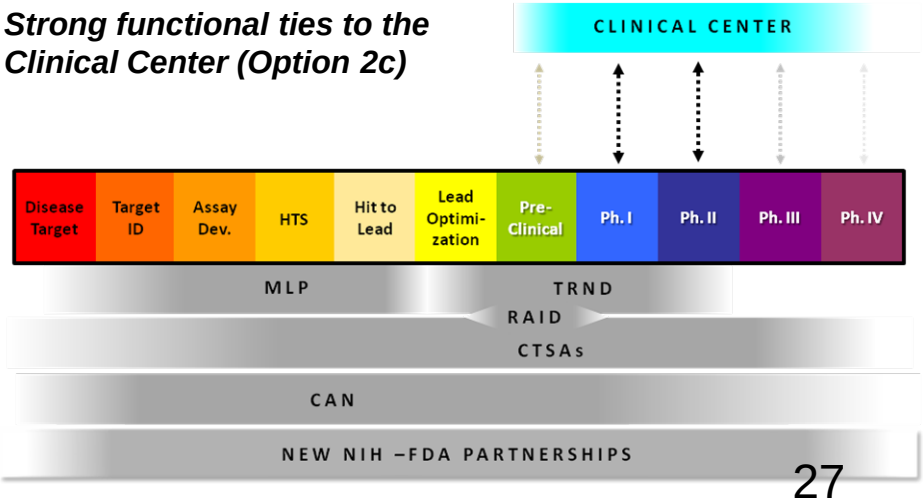
Option 2: Structural and functional unification of relevant programs



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

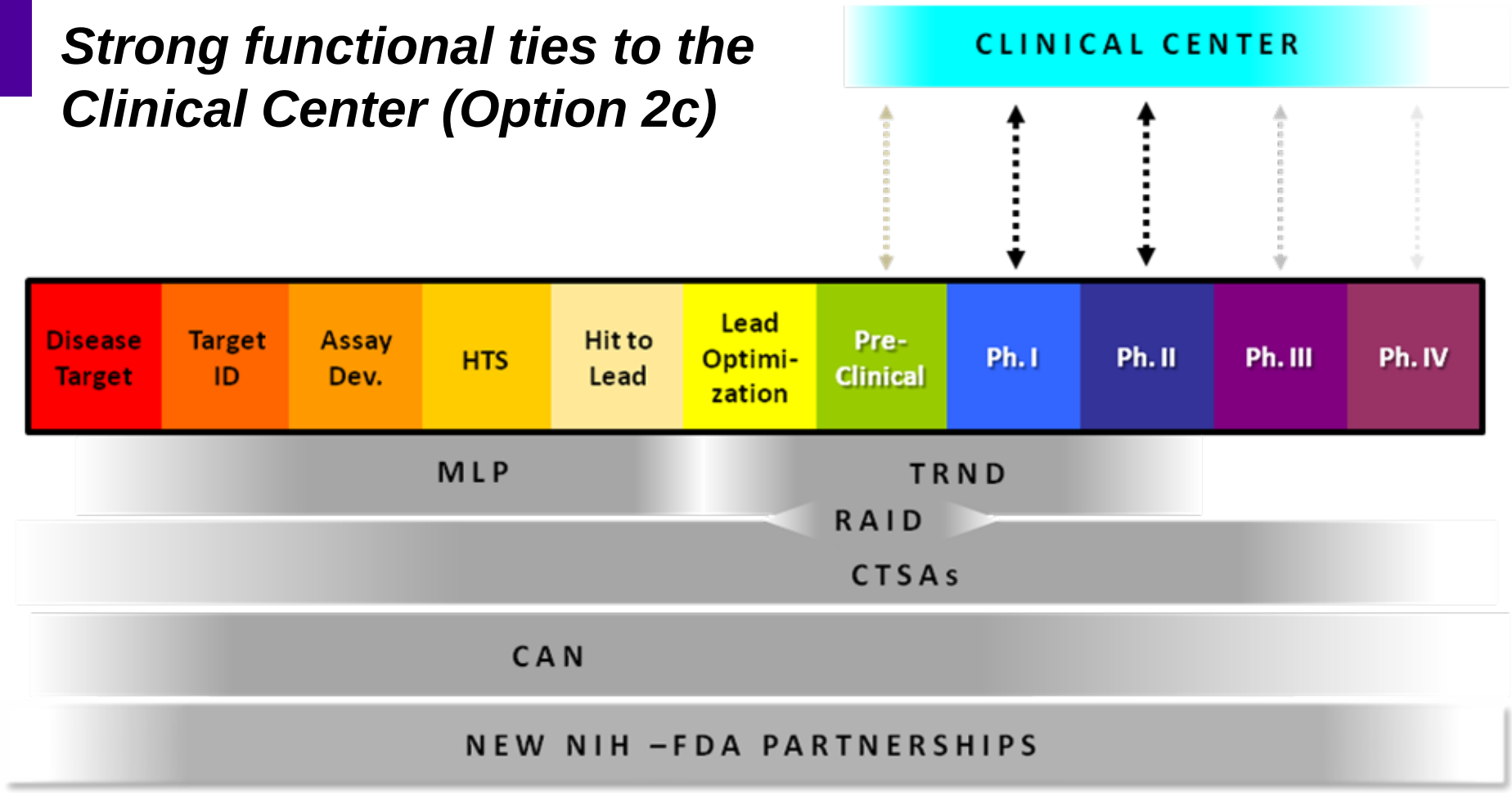


Strong functional ties to the Clinical Center (Option 2c)



Working Group's Preferred Option

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



Working Group's Preferred Option: Role of the NIH Clinical Center

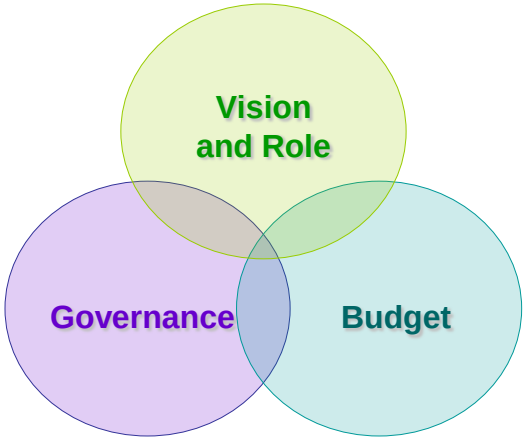
- The Clinical Center is a valuable resource and essential component of both the NIH Intramural Research Program and NIH's translational medicine portfolio
- The Clinical Center should have a strong functional connection to a new IC devoted to translational medicine, but should not be structurally encompassed within the entity
- The Clinical Center already has strong ties and communication with other NIH ICs and the CTSAs, which can be augmented through new governance models

Intramural Research Program (IRP) Working Group of the SMRB

- Charge: to recommend whether any change in the organization and/or management of NIH intramural research could further optimize the opportunities available in a central research program at NIH and maximize human health and/or patient well being
  - Given the urgency of addressing the fiscal sustainability and utilization of the Clinical Center, the IRP Working Group first developed recommendations regarding the vision and role, budget, and governance of the Clinical Center
- 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 December 2010 Board meeting
- In December, the Board will consider specific recommendations regarding the Clinical Center in light of the findings of the TMAT Working Group

IRP Working Group: Recommendations Regarding the NIH Clinical Center

Recommendation #1: *Clinical Center as a National Resource*



Role of the CC should be to serve as a state-of-the-art national resource, with resources optimally managed to enable both internal and external investigator use.

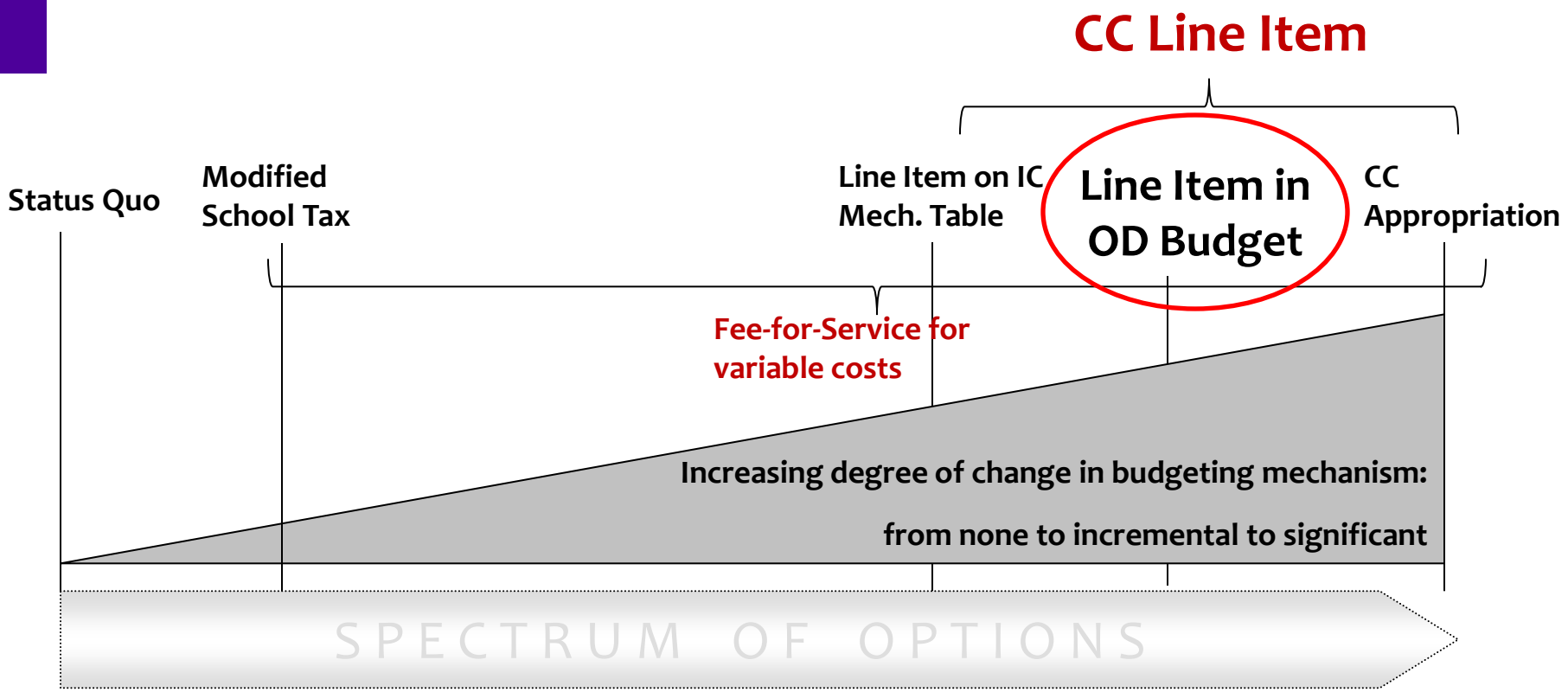
Recommendation #2: *Streamlined Governance Structure*

Governance should have a simplified structure, capable of developing and overseeing a clear, coherent plan for clinical research.

Recommendation #3: *Stable, Responsive Budget Underpinned by Priority Setting*

Budget should be linked to a strong planning process, remain stable (in source) and equitable (in distribution), be effective in attracting and supporting a high quality workforce, and assure efficient use.

IRP Working Group: Recommended Funding Option for NIH Clinical Center



TMAT Deliberations: Re-examining IRP Working Group Recommendations

- 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
- Strong functional ties to a new IC for translational medicine and therapeutics may also strengthen the role of the Clinical Center as a national resource