

# National Institutes of Health Advisory Committee to the Director

## Proposed National Center for Advancing Translational Sciences Working Group

### SUMMARY OF FINDINGS

Members: Maria Freire (chair), Julian Adams, Lee Babiss, Brook Byers, William Chin, Susan Desmond-Hellmann, David Ginsburg, Victoria Hale, Helen Hobbs, Robert Langer, Stelios Papadopoulos, Mary Pendergast, Moncef Slaoui, Marc Tessier-Lavigne, David Valle (*full titles and affiliations can be found in Appendix A*)

Dr. Francis Collins convened a Working Group of the Advisory Committee to the NIH Director (ACD) to help identify innovative research areas and activities whereby the proposed National Center for Advancing Translational Sciences (pNCATS) can substantially contribute to catalyze, invigorate and streamline translational sciences nationally and globally (*the full charge to the Working Group can be found in Appendix B*).

The Working Group met four times over the course of nine months. Its first meeting, on February 4, 2011, was held with members of the NIH Institute and Center Directors Working Group on pNCATS in Bethesda, Maryland. The Working Group also met via teleconference on May 24, 2011, and September 14, 2011, and held an in-person meeting in San Francisco, California, on July 15, 2011, where the group hosted two panel sessions to consult experts in project management and cross-sector partnerships (*a list of participants can be found in Appendix C*). The following represents the summary findings of the ACD-pNCATS Working Group over the course of these meetings.

#### **Revolutionize the Process of Translation: Goals for NCATS**

The creation of NCATS affords NIH a historic opportunity to catalyze, enable, and implement ground-breaking advances in translational sciences – innovations that will benefit all invested in improving human health. NIH is uniquely positioned to assume this leadership role given the rich expertise housed within the Institutes and Centers and its unprecedented track record of advancing our fundamental knowledge of living things.

Translation of basic scientific findings, such as the discovery of a novel chemical entity, into products that benefit patients is a critical endeavor – a process that involves numerous constituencies, takes long periods of time and requires substantial investment. By identifying and overcoming the hurdles and bottlenecks that decrease the probability of success, NCATS can lead the reengineering of the processes by which we develop, test, and implement new diagnostics, therapeutics and devices. NCATS can maximize its probability of success by complementing existing efforts at NIH and other government agencies, academia, and the private sector, allowing NCATS to fill gaps in our understanding of the translational process.

Much can and should be done in this area. Keeping in mind that the new NCATS leadership will be responsible for prioritizing goals and activities, the following key areas are ideally suited for NCATS activities:

- *Catalyze translation by promoting innovative research.* Support and enable high-risk, high-reward projects that experiment with novel and innovative strategies for transforming, improving, and accelerating the process of discovery, development, and post-market research for diagnostics, therapeutics, and devices. Serve as an incubator for innovative science that is too risky or too early in development for commercial investment. Recruit diverse expertise to address scientific barriers and/or gaps.
- *Galvanize and support new partnerships.* Utilize convening power to stimulate communication and promote partnerships between and among the regulatory, academic, public, private, and nonprofit sectors to address challenges in translational sciences and provide bold solutions. Offer incentives for cross-sector partnerships by leveraging funds and providing access to tools, technologies, and innovative platforms.
- *Support and augment the discipline of regulatory science and its application.* Collaborate with the Food and Drug Administration (FDA) to design and undertake studies that inform the regulatory approval process and help develop regulatory pathways that incorporate innovative design, including, but not limited to, adaptive clinical trials, novel drug combinations, and companion diagnostics. Strengthen communication between regulatory agencies and researchers across sectors, and convene joint meetings and conferences in support of a more nimble regulatory process.
- *Expand the precompetitive space : promote information exchange and encourage the dissemination of research outcomes.* Promote and facilitate the open exchange of information regarding the scope, methods, analysis, results, and lessons learned from each scientific inquiry. Encourage grantees to submit data regarding project failures, collect and analyze data to capture lessons from such experiences. Encourage researchers in the private sector to investigate the causes of failed projects prior to disbanding teams. Establish an open-access repository for collecting such knowledge.
- *Harness the power of the Clinical and Translational Science Awards (CTSAs) Program.* Capitalize on the remarkable capabilities of the CTSA program. Afford individual CTSAs flexibility in cultivating their unique strengths and provide incentives for the formation of a strong national CTSA consortium. Develop programs that train clinicians in translational sciences, including implementation research, which is the study of methods for implementing evidence-based practices and programs into clinical care.
- *Transformation through training.* Catalyze educational programs in translational sciences, especially in under-represented fields, such as clinical pharmacology. Promote novel training mechanisms such as a drug development apprenticeship for early-stage investigators; provide incentives for physician scientists to seek cross training in human biology and drug discovery; and explore cross-training of physicians and scientists between industry, academia, and government labs.

- *Streamline administrative process.* Review NIH and NCATS administrative processes to identify and overcome roadblocks to rapid and effective funding, management, and termination of projects. Establish clear pathways for developing agreements between NIH and other sectors that allow for prompt turnaround and timely funding.

**Points to Consider:**

At inception, NCATS will have limited resources. Such resources would not be utilized most efficiently by duplicating translational research efforts existing in and/or funded by NIH Institutes and Centers or already underway throughout industry. Rather, NCATS is poised to form strategic collaborations with these sectors to minimize scientific and administrative redundancy by leveraging NIH’s considerable infrastructure.

By focusing efforts on areas of research that broadly and profoundly impact the entire discipline, NCATS can transform the translational sciences landscape, spurring the creation of platform technologies, and generating innovative methods to develop and test diagnostics, therapeutics, and devices. As an example, rather than funding individual projects through the entire therapeutics development pipeline, projects should be supported only until they become compelling enough to garner subsequent commercial investment.

Examples of areas of translational science that are ripe for innovation and could be part of the NCATS portfolio are listed in Table 1. The list is not meant to be exhaustive and the prioritization of these and other areas of inquiry will be the responsibility of the new NCATS leadership.

Table 1 | Examples of Areas Amenable to Reengineering

<i>Target Validation</i>	<ul style="list-style-type: none"> <li>• Investigate both rare and common diseases</li> <li>• Increase support for use in both pre-clinical and clinical settings</li> <li>• Encourage use in the precompetitive space</li> <li>• Develop more robust disease models and <i>in vitro</i> assays to better predict efficacy</li> <li>• Leverage NIH expertise to develop appropriate disease models that can serve as the basis for power-analysis studies</li> </ul>
<i>Toxicology</i>	<ul style="list-style-type: none"> <li>• Generate a deeper understanding of the mechanisms of toxicity</li> <li>• Develop more efficient models and technologies for predicting toxicity such as cell-based organoids and induced pluripotent stem cells</li> </ul>
<i>Pharmacology</i>	<ul style="list-style-type: none"> <li>• Encourage the study of systems pharmacology</li> <li>• Develop an in-depth understanding of how pharmacological agents affect cellular networks and contribute to pathology</li> </ul>
<i>Biomarkers</i>	<ul style="list-style-type: none"> <li>• Facilitate studies on biomarkers and disease phenotyping</li> <li>• Define disease subsets</li> <li>• Encourage use of biomarkers and companion diagnostics in the drug development process</li> <li>• Develop imaging as a biomarker for chronic disease to support non-</li> </ul>

	invasive monitoring
<i>Imaging</i>	<ul style="list-style-type: none"> <li>Support the development of imaging technologies that generate non-invasive data about drug response, metabolism, and distribution</li> </ul>
<i>New Uses for Established Compounds</i>	<ul style="list-style-type: none"> <li>Serve as an honest broker between and among constituencies to facilitate partnerships for rescue and repurposing efforts</li> <li>Create and maintain datasets and databases containing information about drug failures and project terminations</li> <li>Support neglected and orphan/rare disease research groups in application of off-patent drugs or compounds for new indications</li> </ul>
<i>Devices and Diagnostics</i>	<ul style="list-style-type: none"> <li>Encourage the development of companion diagnostics</li> <li>Support toxicology research for new and nano materials</li> <li>Expand tissue-specific delivery systems</li> <li>Address regulatory science issues</li> <li>Act as a liaison between diagnostic companies and academia to help incorporate the newest markers into tests</li> </ul>
<i>Implementation Science</i>	<ul style="list-style-type: none"> <li>Develop more effective ways to incorporate FDA-approved medical products into patient care</li> </ul>
<i>Chemical space</i>	<ul style="list-style-type: none"> <li>Seek opportunities to collaborate with entities experimenting with the chemical space, including clean/green chemistry, inorganic chemistry, and combinatorial chemistry</li> </ul>

### **Ensuring Success: Qualities of Effective Leadership, Governance, and Staff**

NCATS leadership – its staff and its governing body – will play a defining role in the new Center’s success. The director of NCATS will need to have a unique blend of expertise and experience that transcends a single field or discipline. Ideally, an NCATS director should be experienced in both academia and the private sector, possess the ability to identify and overcome hurdles, demonstrate political sensitivity when working with diverse stakeholders and constituencies, and be able to convene multiple partners working toward common goals. The new leader should be a visionary who is willing to engage in “disruptive innovation.”

To achieve success, the new director must be advised and supported by individuals who understand the unique mission and role of NCATS. NCATS research staff must be innovative thinkers, technically sophisticated, and able to work independently and collaboratively in teams; their primary responsibility should be on the team’s project and not on the administrative functions of operating NCATS. The NCATS advisory board should be composed of stakeholder representatives with expertise in sectors of relevance to the NCATS mission.

### **Concluding Remarks: Moving Forward**

Creation of a new Center primed to address the significant obstacles facing the discipline of translational sciences is timely, important, and highly relevant to today’s challenges. With visionary leadership, Agency support, and in collaboration with the NIH Institutes and Centers, the FDA, and industry, NCATS can transform the way we develop new medicines, diagnostics, and devices that attack human disease and disability in the U.S. and around the globe.

## APPENDIX A

### ACD-pNCATS WORKING GROUP ROSTER

**Maria C. Freire, Ph.D. (Chair)\***

President  
The Albert and Mary Lasker Foundation

**Julian Adams, Ph.D.**

President of Research and Development  
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**Susan Desmond-Hellmann, M.D.,  
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**David Ginsburg, M.D.**

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**Moncef Slaoui, Ph.D.**

Chairman of Research & Development  
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**Marc Tessier-Lavigne, Ph.D.**

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**David L. Valle, M.D.**

Professor and Director of the Institute of  
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Johns Hopkins University School of  
Medicine

## APPENDIX B

### ACD-pNCATS WORKING GROUP CHARGE

The proposed National Center for Advancing Translational Sciences (pNCATS) Working Group of the ACD has the following charge:

- Identify specific areas and activities whereby NIH can substantially contribute to streamlining therapeutic and diagnostic development nationally and globally;
- Recommend possible ways in which pNCATS can maximally tap the strengths of extant programs, the authorities under CAN, and the vast capabilities of potential partners;
- Propose new models for how pNCATS could build partnerships with external entities, including biotechnology and pharmaceutical companies, to achieve its mission of accelerating translational research;
- Recommend the subset of scientific and technical challenges along the drug discovery pipeline that pNCATS should address;
- Recommend potential areas of translational research that fall outside the drug development process that pNCATS should consider addressing; and
- Suggest a framework for metrics and timelines by which success of pNCATS can be measured.

The ACD-pNCATS Working Group will:

- Hold deliberations on a quarterly basis, or more often if agreed-upon by the Working Group, with the intent of meeting at a minimum three times before Oct. 1 2011;
- The Chair of the Working Group will present preliminary findings to the full ACD at the June meeting of the ACD in 2011. The work of this Working Group will be complete when the Advisory Council for pNCATS is formally in place, which is expected by October, 2011.

## APPENDIX C

### ACD-pNCATS WORKING GROUP – EXPERT PANELISTS

**Jeffrey Bluestone, Ph.D.**

Executive Vice Chancellor and Provost  
University of California, San Francisco

**Jennifer Cook, M.S., M.B.A.**

Senior Vice President, Genentech  
Immunology and Ophthalmology  
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Branch, and  
Director of Chemistry  
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**Jack D. Newman, Ph.D.**

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