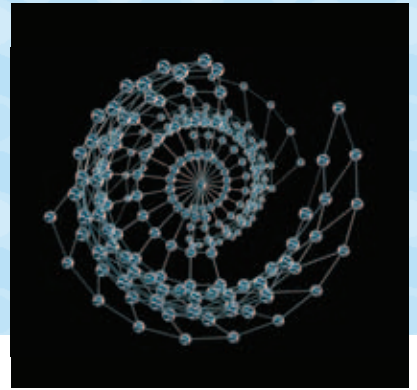


Forum on Drug Discovery, Development, and Translation

2013 Annual Report



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the nation • Improving health

Message from the Co-Chairs

Jeffrey Drazen and Steven Galson

The Institute of Medicine's (IOM's) Forum on Drug Discovery, Development, and Translation was created in 2005 by the IOM's Board on Health Sciences Policy to foster communication and collaboration and to provide ongoing opportunities to discuss and act on issues of mutual interest in a neutral setting. The Forum brings attention and visibility to important issues in drug development; explores new approaches for resolving problem areas; helps define the scope of the field and thus sets the stage for future policy action; provides a catalyst for collaboration on topics where there is synergy among potential partners; and elevates the general understanding of drug discovery, development, and translation among the research, public policy, and broader communities. The Forum membership includes leaders from the pharmaceutical and biotech industries, academia, federal agencies, foundations, and patient groups. The group is self-governing, with Forum members convening several times each year to identify and prioritize the topics they wish to address.

The Forum recognizes that although breakthroughs in biomedical research have led to an increased understanding of human disease, the translation of these discoveries into therapies for patients has not kept pace with medical need. The pharmaceutical innovation enterprise faces continued and mounting pressures, strained from all sides by increasing costs, reducing productivity, regulatory and economic uncertainties, and accelerating complexity. The Forum views such great challenges as opportunities and has used collaborative approaches to address these complex issues.

In 2013, the Forum provided a focused venue for stakeholders to take stock of the needs and priorities in the drug discovery and development “ecosystem” and to encourage meaningful information sharing and collaboration across sectors and stakeholder groups. The Forum contributed to broad conversations on biomedical research and policy, including convening a workshop with multi-national participants from the regulatory and pharmaceutical development sectors to help foster more harmonized regulatory standards for pharmaceutical product development. The Forum membership also continued its focused effort to address challenges in the U.S. clinical trials enterprise, facilitating an action-oriented, collaborative dialogue to advance development of a national accreditation system for clinical trial sites.

In this pivotal time of enormous change and opportunity for pharmaceutical innovation, sustaining and growing the biomedical research enterprise requires a renewed intellectual, business, scientific, and public policy climate in which effective collaboration in research and translation can flourish. The Forum has proposed new paradigms for discovering and developing drugs that bridge the ever-widening gap between scientific discoveries and translation of those discoveries into life-changing medications. Worldwide, patients, industry, federal agencies, academia, and foundations bring a broad array of new tools and approaches in response to this challenge with the understanding that thoughtful partnership and collaboration can create results that would be impossible alone.

In 2014, the Forum will foster innovative efforts to identify and highlight potentially breakthrough ideas and visionary approaches to the “drug development and translational science enterprise of the future.” Through working group discussions and workshops, solicited and original qualitative research and collaborative writing, and broad outreach, the Forum will serve as a hub and catalyst for new ideas and directions. As a neutral convening venue for stakeholders and collaborators, the Forum provides a unique setting in which complex issues of health science policy can be tackled collegially, and in which partnerships may be formed and nurtured.

We look forward to another groundbreaking and productive year for the Forum in 2014.



A handwritten signature in black ink, appearing to read "Jeff M Drazen MD".

Jeffrey Drazen
Co-Chair



A handwritten signature in black ink, appearing to read "Steven Galson".

Steven Galson
Co-Chair

Reflecting Back

Forum Activities in 2013

Forum Meetings

The Forum membership met three times in 2013. Discussions at these meetings focused on diverse topics relating to the Forum's priorities, including grand challenges in drug discovery, development, and translation; reproducibility issues confronted in therapeutics development; harnessing information science; clinical trial data transparency and sharing; and policy developments and needs in the landscape of the bioinnovation ecosystem. In addition, the Forum convened public workshops and collaborative meetings, described below.

The Global Crisis of Drug-Resistant Tuberculosis and Leadership of China and the BRICS: Challenges and Opportunities—Workshop (January 2013)

The Forum convened a multiyear international initiative on multidrug-resistant tuberculosis (MDR TB), which began with a foundational workshop in Washington, DC, in 2008, and international workshops in the high-burden countries of South Africa (2010), Russia (2010), India (2011), and China (2013). The final workshop in the MDR TB series was held in Beijing, China, in January 2013 in collaboration with the Institute of Microbiology, Chinese Academy of Sciences (IMCAS). This workshop addressed the current status of drug-resistant (DR) TB in China and across the globe; highlighted key challenges to controlling the spread of DR strains; and discussed innovative strategies to advance and harmonize local and international efforts to prevent and treat DR TB. The meeting focused on various aspects of DR TB, including epidemiology, diagnostics and preventive therapies, treatment, transmission and infection control, pediatric TB, innovative approaches to TB control, and drug procurement and supply issues.

FORUM ACTIVITIES TIMELINE

2000–2004

2005

Clinical Research Roundtable,
predecessor to the Drug Forum



MDR TB in China and the BRICS Workshop co-chairs Gail Cassell and Barry Bloom with speakers and IMCAS staff

International Regulatory Harmonization Amid Globalization of Biomedical Research and Medical Product Development—Workshop (February 2013)

The last several decades have seen a rapid globalization of commerce, including within the medical product and technology sectors. Investigational studies for products intended for use in U.S. populations are increasingly being conducted outside the United States, often in countries with limited regulatory

March 23-24
Forum Meeting #1

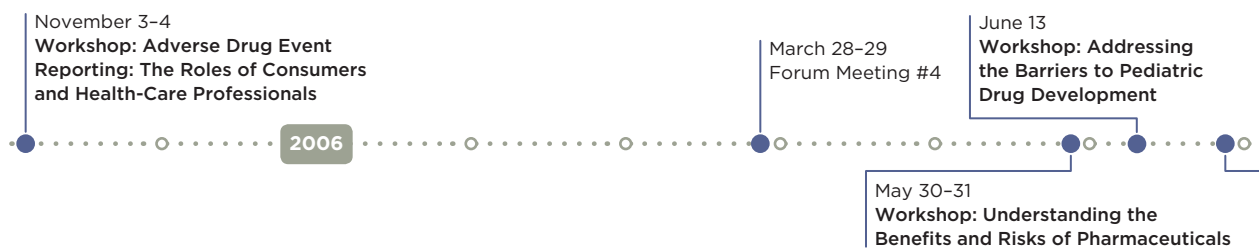
June 29-30
Forum Meeting #2

September 8-9
Forum Meeting #3

capacity. Moreover, biopharmaceutical companies seeking global markets for a single product face requirements for regulatory submissions in numerous international jurisdictions that could introduce scientific requirements that are discordant with U.S. standards. Discordant data requirements could result in additional clinical trials and animal studies, exposing more patients to experimental drugs and increasing the use of laboratory animals. There is a need for globally harmonized, science-based standards for the development and evaluation of safety, quality, and efficacy of medical products—both to enhance the efficiency and clarity of the drug development and evaluation process and ultimately to promote and enhance



Lawrence Tabak speaking to the Forum about NIH reproducibility efforts, pictured with James Shannon, GlaxoSmithKline; Kathy Hudson, NIH; and Rusty Kelley, Burroughs Wellcome Fund



product quality and the public's health. There is also need for harmonization of standards for ongoing safety and quality surveillance of marketed biomedical products. This public workshop identified needs for international harmonization of regulatory standards to support the development, evaluation and surveillance of biomedical products. The workshop identified principles and potential approaches to the development or evolution of more harmonized regulatory standards.



International Regulatory Harmonization Workshop speaker Peter Honig, AstraZeneca

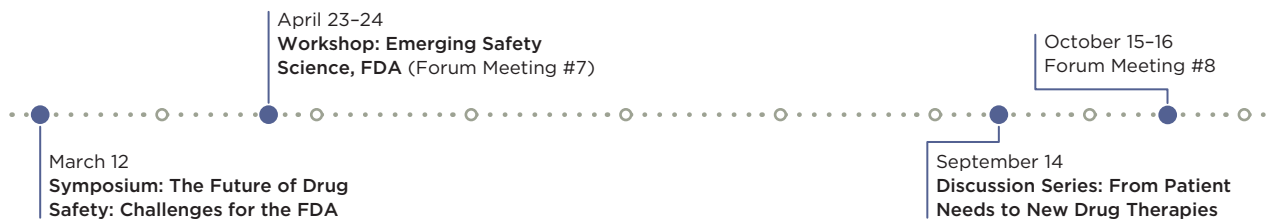
Developing a National Accreditation System to Improve Clinical Trial Performance—Action Collaborative (August 2013)

The Forum continued to devote time and attention to issues around clinical trials, convening an Action Collaborative to foster development of a national accreditation system for clinical trial sites. The Action Collaborative, a convening activity under the auspices of the Forum, provides a venue for joint and collaborative activities among participants to advance development of standards or a system to improve clinical trial



Forum Director Anne Claiborne with, from left to right: Jeffrey Drazen (Forum co-chair), Steven Galson (Forum co-chair), Paul Seligman, Bernard Munos, and Rusty Kelley

performance through accreditation of clinical trial sites. Participants, who are drawn from multiple sectors and disciplines, met for the second time on August 21, 2013, and convened working groups to discuss their perspectives on a process for standards development, and on the establishment of a mechanism to facilitate coordination of an experimental approach to develop and implement standards reporting and monitoring.



Looking Forward

Forum Activities in 2014

Forum Meetings

The Forum membership will meet in March, June, and October 2014 to continue its discussions of key problems and strategies in the discovery, development, and translation of drugs. Forum working groups are convening to discuss and explore potential research, publication, and workshop topics in the areas of envisioning and characterizing **transformation and disruptive innovation** in the drug development enterprise, strengthening the effectiveness and impact of **collaboration**, advancing **pharmaceutical safety monitoring**, and supporting a **translational science workforce**. In addition, the Forum is convening the public workshops and collaborative meetings described below.

Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks of Pharmaceutical Products—Workshop (February and May 2014)

There is increasing attention to the need for enhancing the evaluation and communication of the benefits and risks associated with pharmaceutical products, thereby increasing the predictability, transparency, and efficiency of pharmaceutical regulatory decision making. In 2006, the IOM's Forum on Drug Discovery, Development, and Translation held a workshop to explore the complex tradeoff between drug benefits and risks and examine approaches for better quantifying this balance and informing the public and the medical community. Since that time, FDA has worked to develop an enhanced structured approach to the assessment of benefits and risks in drug regulatory decision making to better communicate this aspect of the human drug review process. An extensive body of evidence informs regulatory decisions on

November 30
Discussion Series: A Conversation
with Tony Fauci

2008

February 20–21
Discussion Series: Comparative
Effectiveness (Forum Meeting #9)

April 21
Discussion Series:
Science at FDA: Challenges
and Opportunities

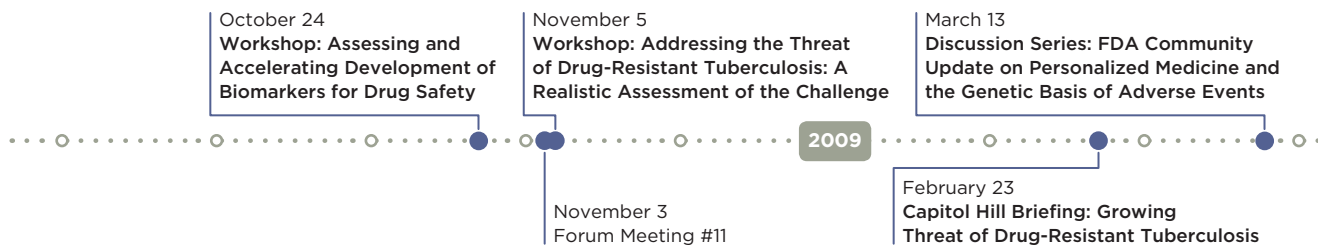
June 23–24
Symposium: Diseases and Individualized
Therapies (Forum Meeting #10)

June 23
Workshop: Breakthrough
Business Models: Drug
Development for Rare
and Neglected Diseases



Clinical Trial Site Accreditation Action Collaborative meeting, August 2013

the safety and efficacy of a proposed product, but in many cases, FDA must draw conclusions from imperfect data. This two-part public workshop series is being convened at the request of FDA to address the opportunity to advance the development of more systematic and structured approaches to characterize and communicate: (a) the sources



of uncertainty in the assessment of benefits and risks, and (b) their implications for pharmaceutical regulatory decisions. Specifically, the workshops will explore potential analytical and communication approaches and identify key considerations on their development, evaluation, and incorporation into the assessment of benefits and risks in pharmaceuticals.

Developing a National Accreditation System to Improve Clinical Trial Performance—Action Collaborative (March 2014)

The members of the Clinical Trial Site Accreditation Action Collaborative will meet for the third time on March 11, 2014, to discuss the findings of the working groups on a process for standards development, and on the establishment of a mechanism to facilitate a process to align and improve clinical trial site standards. Participants are preparing a Perspective paper to be published by the IOM.

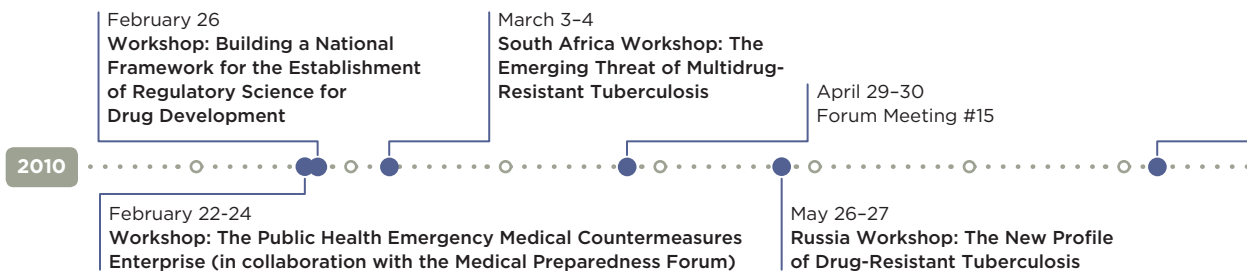


Forum Themes and Priorities

*The Forum addresses key problems in the discovery, development, and translation of drugs, covering the full translational continuum from basic discovery to the approval and adoption of new therapies into clinical practice. As an overarching and cross-cutting theme, the Forum fosters innovative efforts to identify and highlight potentially breakthrough ideas and visionary approaches to the “**drug development and translational science enterprise of the future.**” The Forum has also identified four core components of translational science across this continuum that serve as thematic pillars to frame the Forum’s focus areas and activities: Drug Development Enterprise **Infrastructure**; **Workforce Needs** for Drug Discovery, Development, and Translation; **Science and Technology** for Drug Development; and Drug **Regulatory Science and Evaluation**.*

Transformational Innovation in the Drug Development and Translational Science Enterprise

Despite exciting scientific advances, the pathway from basic science to new therapeutics faces challenges on many fronts. New paradigms for discovering and developing drugs are being sought to bridge the ever-widening gap between scientific discoveries and translation of those discoveries into life-changing medications. The Forum has explored these issues from many perspectives—emerging technology platforms, regulatory efficiency, intellectual property concerns, the potential for precompetitive collaboration, and innovative business models that address the “valley of death.” Evidence suggests that industries are almost always disrupted from the outside by new technologies they were slow to embrace, new business models they wrongly dismissed, or policy changes they thought they could keep at bay. Many argue that the current paradigm for drug discovery and development requires disruptive innovation to break out of a crisis in R&D productivity.



The Forum hosts collaborative efforts to stimulate and inform a discussion that could help chart a course through the turbulent forces of disruptive innovation in the drug discovery and development “ecosystem.”

Drug Development Enterprise Infrastructure

Considerable opportunities remain for enhancement and improvement of the infrastructure that supports the drug development enterprise. That infrastructure, which includes the organizational structure, framework, systems, and resources that facilitate the conduct of biomedical science for drug development, faces significant challenges. The economic and institutional framework for biomedical discovery and translation is inefficient and insufficiently funded, and the nurturing and collaborative research environment necessary for a robust biomedical research enterprise has eroded. There is increasing recognition of the need for new models and methods for drug development and translational science, and “precompetitive collaborations” and other partnerships, including public–private partnerships, are proliferating. Through its activities, the



Forum member Christopher Austin, participating in a Forum member discussion

August 5–6
Discussion Series:
Conflict of Interest
(Forum Meeting #16)

October 29
Discussion Series: Administrative and Regulatory
Inefficiencies in Clinical Trials (Forum Meeting #17)

2011

March 28
Forum Meeting #18

April 18–19
**India Workshop: Facing the
Reality of Multidrug-Resistant
Tuberculosis**

March 29–30
**Workshop: Advancing Regulatory Science for Medical Countermeasure
Development (in collaboration with the Medical Preparedness Forum)**

Forum offers a venue to discuss and develop best practices and principles for effective collaboration in the drug discovery and development enterprise. Among other projects, Forum collaborative participants have addressed core needs for the U.S. clinical trial infrastructure.

Workforce Needs for Drug Discovery, Development, and Translation

Biomedical product innovation requires the expertise of many kinds of scientists and investigators, working across multiple sectors, including academia, industry, research sponsors, and regulatory agencies. The science of drug discovery and development, and its translation into clinical practice, is cross-cutting and multidisciplinary. Career paths can be opaque or lack incentives such as recognition, career advancement, or financial security. The Forum has considered workforce needs as foundational to the advancement of drug discovery, development, and translation. It has convened workshops examining these issues, including consideration of strategies for developing a discipline of innovative regulatory science through the development of a robust workforce. The Forum will also host a working group that will address infrastructure, resource, cultural, and training needs for a workforce across the translational science lifecycle.

Science and Technology for Drug Development

Despite breakthroughs in the basic biomedical sciences over the past several decades, those scientific advances have not translated into new therapeutics. Key gaps remain in our knowledge about science, technology, and methods needed to support drug discovery and development. These gaps represent a wide range of opportunity, including, for example, target identification and validation, biomarker development and validation, methods for predicting



toxicity, improved statistical methods, and other areas of emerging science. The Forum provides a venue to focus ongoing attention and visibility to these important drug development needs and facilitates exploration of new approaches. Among other topics, the Forum has addressed cutting-edge drug safety science, development of safety biomarkers, personalized medicine and clinical trial methodologies.

Drug Regulatory Science and Evaluation

There has been considerable and increasing attention to the need for robust science to underlay and serve as the basis for regulatory decision making. “Regulatory science” involves the development and application of scientific tools and methodologies to improve the development, review, and oversight of new therapeutics. Recent rapid advances in innovative drug development science present opportunity for revolutionary developments of new scientific techniques, therapeutic products, and applications. The Forum has focused considerable attention on the need to develop, support, and enhance a discipline of regulatory science as an essential component of the drug discovery enterprise and translational sciences. The Forum has held workshops that have contributed to the defining and establishment of regulatory science, including in-depth consideration of issues such as adverse event reporting and postmarketing safety surveillance, infrastructure and workforce needs, and collaborative approaches to support and sustain regulatory science and drug development. The Forum has also convened workshops to help inform aspects of drug regulatory evaluation, including discussion of principles and approaches to advance international regulatory harmonization, and methods and strategies for characterizing and communicating uncertainty in the assessment of benefits and risks.



Reports Released in 2013



Sharing Clinical Research Data: Workshop Summary

Released: March 29, 2013

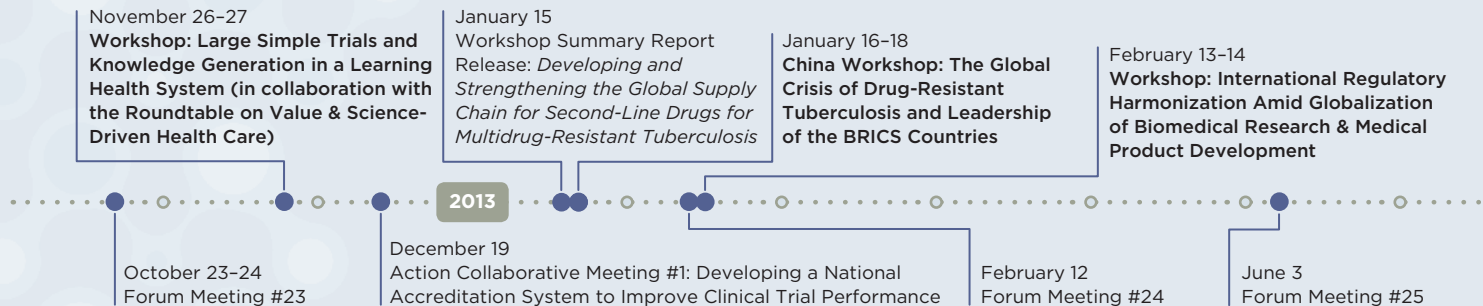
Pharmaceutical companies, academic researchers, and government agencies compile large quantities of clinical research data, which, if shared more widely both within and across sectors, could improve public health, enhance patient safety, and spur drug development. Despite several barriers to data sharing, there is increasing acknowledgment among researchers of the importance and potential benefits to sharing clinical research data at various stages of the research, discovery, and development pipeline. The IOM's Forum on Drug Discovery, Development, and Translation; Forum on Neuroscience and Nervous System Disorders; National Cancer Policy Forum; and Roundtable on Translating Genomic-Based Research for Health hosted a workshop to explore the benefits of sharing clinical research data, the barriers to such sharing, and strategies to address those barriers to facilitate the development of safe, effective therapeutics and diagnostics.



International Regulatory Harmonization Amid Globalization of Drug Development: Workshop Summary

Released: August 1, 2013

The past several decades have been a time of rapid globalization in the development, manufacture, marketing, and distribution of medical products and technologies. Demand has been increasing for globally harmonized, science-based standards to improve the efficiency and clarity of the drug development and evaluation process and, ultimately, to promote and enhance product quality and the public health. The IOM's Forum on Drug Discovery, Development, and Translation hosted a workshop to help identify principles, potential approaches, and strategies to advance the development or evolution of more harmonized regulatory standards for drug development.





Large Simple Trials and Knowledge Generation in a Learning Health System: Workshop Summary

Released: September 24, 2013

Despite a robust clinical research enterprise, a gap exists between the evidence needed to support care decisions and the evidence available. Streamlined approaches to clinical research provide options for progress on these challenges. Large simple trials (LSTs), for example, generally have simple randomization, broad eligibility criteria, and enough participants to distinguish small to moderate effects; focus on outcomes important to patient care; and use simplified approaches to data collection. Significant opportunities, including the widespread adoption of electronic health records, could accelerate the potential for the use of LSTs to efficiently generate practical evidence for medical decision making and product development. To address these opportunities, as well as challenges, the IOM's Roundtable on Value & Science-Driven Health Care and the Forum on Drug Discovery, Development, and Translation co-hosted a workshop to highlight the pros and cons of the design characteristics of LSTs, explore the utility of LSTs on the basis of case studies of past successes, and consider the challenges and opportunities for accelerating the use of LSTs in the context of a U.S. clinical trials enterprise.



The Global Crisis of Drug-Resistant Tuberculosis and Leadership of China and the BRICS: Challenges and Opportunities: Summary of a Joint Workshop

Released: December 19, 2013

Although antibiotics to treat TB were developed in the 1950s and are effective against a majority of TB cases, resistance to these antibiotics has emerged over the years, resulting in the growing spread of drug-resistant TB. Since 2008, the IOM's Forum on Drug Discovery, Development, and Translation has hosted or co-hosted six domestic and international workshops to address the global crisis of drug-resistant TB. The Forum, along with the Institute of Microbiology of the Chinese Academy of Sciences, held a workshop to address the current status of drug-resistant TB globally and in China as well as identify opportunities for Brazil, Russia, India, China, and South Africa (the BRICS countries) to lead efforts in TB control.

August 21
Action Collaborative Meeting #2:
Developing a National Accreditation System
to Improve Clinical Trial Performance

October 28-29
Forum Meeting #26

February 12
Workshop: Characterizing and
Communicating Uncertainty in the
Assessment of Benefits and Risks of
Pharmaceutical Products (Day 1)

March 11
Action Collaborative
Meeting #3: Developing
a National Accreditation
System to Improve Clinical
Trial Performance

March 3-4
Forum Meeting #27

2014

Forum Sponsorship

(as of December 31, 2013)

Financial support for the Forum is derived from private foundations, government agencies, industry sponsors, and nonprofit associations.

Private Foundations

Burroughs Wellcome Fund
CDC Foundation
Doris Duke Charitable Foundation
Eli Lilly & Co. Foundation
Fondation Mérieux

Other Nonprofit Organizations

American Diabetes Association
American Society for Microbiology
Association of American Medical Colleges
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Johnson & Johnson
Merck & Co.
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Pfizer Inc.
Sanofi



Forum Members

(as of December 31, 2013)

Membership in the Forum includes a diverse range of stakeholders from multiple sectors, including government, the pharmaceutical and biotechnology industries, biomedical research funders and sponsors, academia, and patient groups.

Jeffrey Drazen (Co-Chair)

New England Journal of Medicine

Steven Galson (Co-Chair)

Amgen Inc.

Russ Altman

Stanford University

Margaret Anderson

FasterCures

Hugh Auchincloss

National Institute of Allergy and Infectious Diseases

Christopher Austin

National Center for Advancing Translational Sciences

Ann Bonham

Association of American Medical Colleges

Linda Brady

National Institute of Mental Health

Gail Cassell

Harvard Medical School Department of Social and Global Medicine (Visiting)

Andrew Dahlem

Eli Lilly & Co.

James Doroshow

National Cancer Institute

Gary Filerman

Atlas Health Foundation

Mark Goldberger

AbbVie Inc.

Harry Greenberg

Stanford University School of Medicine

Peter Honig

AstraZeneca

Kathy Hudson

National Institutes of Health

Lynn Hudson

Critical Path Institute

S. Claiborne (Clay) Johnston

University of California, San Francisco

Michael Katz

March of Dimes Foundation

Petra Kaufmann

National Institute of Neurological Disorders and Stroke

Jack Keene

Duke University Medical Center

Rusty Kelley

Burroughs Wellcome Fund

Ronald Krall

University of Pennsylvania

Freda Lewis-Hall

Pfizer Inc.

Carol Mimura

University of California, Berkeley

Bernard Munos

InnoThink Center for Research in Biomedical Innovation

Elizabeth (Betsy) Myers

Doris Duke Charitable Foundation

John Orloff

Novartis Pharmaceuticals Corporation

Robert Ratner

American Diabetes Association

Michael Rosenblatt

Merck & Co., Inc.

James Shannon

GlaxoSmithKline

Janet Shoemaker

American Society for Microbiology

Ellen Sigal

Friends of Cancer Research

Lana Skirboll

Sanofi

Brian Strom

Rutgers, the State University of New Jersey

Janet Tobias

Ikana Health

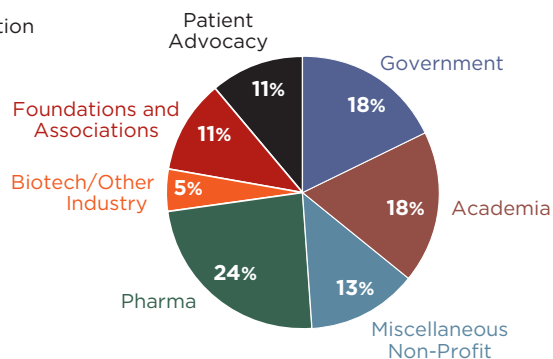
Joanne Waldstreicher

Johnson & Johnson

Janet Woodcock

FDA Center for Drug Evaluation and Research

Membership



About the Forum on Drug Discovery, Development, and Translation

The IOM's Forum on Drug Discovery, Development, and Translation was created in 2005 by the IOM's Board on Health Sciences Policy to provide a unique platform for dialogue and collaboration among thought leaders and stakeholders in government, academia, industry, foundations, and patient advocacy. The Forum brings together leaders from private-sector sponsors of biomedical and clinical research, federal agencies sponsoring and regulating biomedical and clinical research, the academic community, and patients, and in doing so serves to educate the policy community about issues where science and policy intersect.

The Forum convenes several times each year to identify and discuss key problems and strategies in the discovery, development, and translation of drugs. To supplement the perspectives and expertise of its members, the Forum also holds public workshops to engage a wide range of experts, members of the public, and the policy community in discussing areas of concern in the science and policy of drug development. The Forum also fosters collaborations among its members and constituencies. The Forum's public meetings focus substantial public attention on critical areas of drug development. Proceedings and speaker presentations are disseminated to the public through published summaries and the Forum website. For more information about the Forum on Drug Discovery, Development, and Translation, please visit our website at www.iom.edu/drug.

About the Institute of Medicine

The Institute of Medicine was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility assigned to the National Academy of Sciences by its congressional charter to serve as an advisor to the federal government and, upon its own initiative, to identify issues needing attention in the areas of medical care, research, and education.

Forum Staff

Anne B. Claiborne, J.D., M.P.H.

Forum Director

Rebecca A. English, M.P.H.

Program Officer

Elizabeth F. C. Tyson

Associate Program Officer

Robin Guyse (until January 2014)

Senior Program Assistant

Barret Zimmermann (as of January 2014)

Senior Program Assistant

Board on Health Sciences Policy

Andrew M. Pope, Ph.D.

Director



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Established in 1970 under the charter of the National Academy of Sciences, the Institute of Medicine provides independent, objective, evidence-based advice to policymakers, health professionals, the private sector, and the public. The mission of the Institute of Medicine embraces the health of people everywhere.