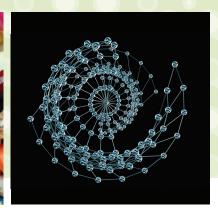
Forum on Drug Discovery, Development, and Translation

2014 Annual Report







INSTITUTE OF MEDICINE

OF THE NATIONAL ACADEMIES

Advising the nation • Improving health

Message from the Co-Chairs

Russ Altman 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, collaboration, and action in a neutral setting on issues of mutual interest relating to drug discovery, development, and translation. The Forum brings attention and visibility to important issues; 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 U.S. Food and Drug Administration (FDA) and the National Institutes of Health, the pharmaceutical and biotech industries, academia, foundations, and patient and disease advocacy organizations. 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. 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. Patients, industry, federal agencies, academia, and foundations can 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.

The Forum views such great challenges as opportunities and has used collaborative approaches to address these complex issues. In 2014, the Forum provided a focused and neutral venue for stakeholders to identify and characterize the needs and priorities in the drug discovery and development "ecosystem" and to encourage meaningful information sharing and collaboration across sectors. The Forum contributed to broad conversations on drug development research and policy, including convening a workshop at the request of FDA to advance the development of more structured approaches to characterize and communicate uncertainty in the assessment

of benefits and risks of drugs. 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 harmonized standards for clinical trial sites.

In 2015, a broad and deep policy conversation continues about how we can advance biomedical product innovation nationally and globally. Legislative initiatives in both U.S. chambers are considering reform of our nation's system for developing innovative new medicines. Presidential initiatives, including a "precision medicine" effort inspired in part by a National Academies report, have been announced and prioritized. The Forum will continue to convene its innovative action collaborative to identify and highlight potentially breakthrough ideas and visionary approaches to the "drug development and translational science enterprise of the future." Individual collaborative participants will provide a discussion paper that will outline a framework and define key terms and activities in the biomedical innovation ecosystem. Through these and other 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 2015.



Russ Altman



Steven Galson

Reflecting Back

Forum Activities in 2014

Forum Meetings

The Forum membership met three times in 2014. Discussions at these meetings focused on diverse topics relating to the Forum's priorities, including establishing a clinical trials network and enhancing clinical trial infrastructure; envisioning the translational science and drug development enterprise of the future; challenges in biomedical innovation; best practices and metrics for collaboration; mapping the biomedical innovation ecosystem; and strategies for responsible sharing of clinical trial data. In addition, the Forum convened public workshops and collaborative meetings, described below.

Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks of Pharmaceutical Products—Workshop Series (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. An extensive body of evidence informs regulatory decisions on 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 was 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 explored potential analytical and communication approaches and identified key considerations for their development, evaluation, and incorporation into the assessment of benefits and risks in pharmaceuticals. The workshop was covered in a story on NPR's *All Things Considered*, and workshop attendees



will create a Perspective paper summarizing the results of an innovative media analysis presented at the workshop.

Clinical Trial Site Standards Harmonization—Action Collaborative (March 2014)

Since sponsoring a workshop series on issues relating to the U.S. national clinical trials enterprise from 2009 to 2011, the Forum continues to devote time and attention to issues around clinical trials. This action collaborative is an ad hoc convening activity under the auspices of the Forum, which provides a venue for joint and collaborative activities among participants to advance development of standards or a system to improve clinical trial performance through accreditation of clinical trial sites. Participants, who are drawn from multiple sectors and disciplines, are preparing a Perspective paper, to be posted by the IOM, which will summarize their perspectives on a process for standards development, and on the establishment of a mechanism to facilitate coordination of an experimental approach to align existing standards and improve clinical trial site standards based on continuous data collection. Collaborative participants are also planning a second phase of the collaborative activity, which is expected to include the collection, analysis, and assessment of how clinical trial site standards that are currently in use by key stakeholders could be harmonized.

Looking Forward

Forum Activities in 2015

Forum Meetings

The Forum membership will meet in March, June, and October 2015 to continue its discussions of key problems and strategies in the discovery, development, and translation of drugs. Forum workshop planning committees, working groups, and action collaboratives will convene to discuss and act on the following topics:

Action Collaboratives:

Disruptive Innovation and the Transformation of the Drug Development and Translational Science Enterprise—Action Collaborative

Many argue that the current paradigm for drug discovery and development requires disruptive innovation to break out of a crisis in research and development (R&D) productivity. 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. The pharmaceutical industry offers many opportunities for disruption in each of these areas. The Forum has convened an action collaborative that has set out to identify and highlight potentially breakthrough ideas and visionary approaches to the "drug development and translational science enterprise of the future." The effort has addressed new technologies (e.g., biosensors, apps and telemetry, synthetic biology, new delivery technologies); new business models (e.g., crowdsourcing platforms, drug repurposing, virtual companies, or clinical trials); and policy issues (e.g., pricing/reimbursement, patent law, data transparency). The effort has included a data gathering phase, along with a review



May 30-31

Workshop: Understanding the

Benefits and Risks of Pharmaceuticals

phase, and includes the preparation of a Perspective. The Forum will convene one or more workshops in 2015 to further explore issues identified through this effort, including defining a drug development paradigm for the future and considering the impact of new technologies on drug development.

Mapping and Connecting the Biomedical Innovation Ecosystem—Action Collaborative

The biomedical innovation ecosystem is a dynamic network of activity. Standardizing and bringing clarity to this complex process could help to set a vocabulary and allow more fluid dialogue among ecosystem participants to encourage further innovation. It could also facilitate ongoing discussion to help frame, map, and synergize activities across the biomedical innovation ecosystem. Defining key terms and



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locating complex activities, such as translational science and regulatory science, within the biomedical innovation ecosystem landscape might help to articulate problem areas and provide opportunities to learn from local environments where the system is working more efficiently. The goal of this collaborative is to enable discussion and to identify these rate-limiting steps in order to facilitate process improvement efforts within the biomedical innovation ecosystem.

Sharing Clinical Trial Data—Action Collaborative

Sharing clinical trial data can facilitate more efficient and effective development of better medicines, diagnostics, and procedures for the ultimate benefit of patients. At the same time, sharing data presents risks, burdens, and challenges that need to be

April 23-24 Workshop: Emerging Safety Science, FDA (Forum Meeting #7)

October 15-16 Forum Meeting #8

March 12

Symposium: The Future of Drug Safety: Challenges for FDA September 14
Discussion Series: From Patient
Needs to New Drug Therapies

addressed by a broad set of stakeholders. These opportunities and challenges were laid out in the IOM report *Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk*. The report calls upon stakeholders to foster a culture of sharing and offers a blueprint for action within and across sectors. Four IOM forums provided momentum and a framework for initiating the IOM consensus study and are working together again to form a platform that could support coordination and collaboration among stakeholders engaged in data sharing initiatives through convening and other activities.

Workshops:

Priorities to Advance the Field of Regulatory Science: An Update on Progress and a Forward-Looking Agenda—Workshop

In the face of rapid advances in medicine and biomedical science, FDA faces pressure to keep pace with new technologies and develop the expertise necessary to regulate those technologies as they emerge. The Forum, in collaboration with the Burroughs Wellcome Fund, will convene a public workshop that will discuss issues related to the development of the discipline of innovative regulatory science, focusing on infrastructure, systems, and workforce. The workshop will explore current regulatory science priorities and strategies in federal, academic, and private sector settings; consider the current state of regulatory science as a discipline; explore the core components of a robust discipline of innovative regulatory science; consider gaps and key opportunities to address needs to support the discipline of innovative regulatory science; and examine needs and barriers to collaboration among, across, and within the public and private sectors.



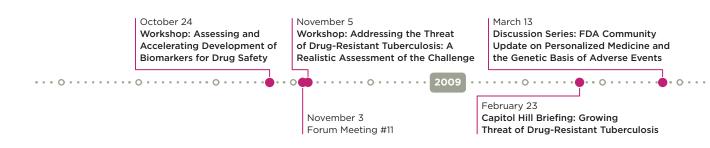
In addition, the Forum will co-convene the following workshops in collaboration with other IOM Forums:

Financial Incentives to Support Unmet Medical Needs for Nervous System Disorders—Workshop

The global burden of nervous system disorders is projected to significantly increase over time. Although there have been recent international initiatives to better understand the human brain in order to develop new therapeutics, several large pharmaceutical companies have decreased investment or even withdrawn from their neuroscience research programs. The perceived high risk and low probability of success has made the neuroscience sector less attractive than other therapeutics areas for R&D, despite the large market potential. As a result, patients are often left with few, if any, options for treatment; thus, there is a need to consider policy options to increase private-sector investment in R&D for nervous system disorders. The Forum, in collaboration with the IOM's Forum on Neuroscience and Nervous System Disorders, convened this public workshop, which explored opportunities to foster private-sector innovation by supporting new investments directed toward the development of novel therapeutics to meet unmet needs for nervous system disorders.

Enabling Rapid Medical Countermeasure Response to Emerging Threats—Workshop

With the global attention to recent large-scale outbreaks and their public health and medical consequences, it has become clear that the current medical countermeasure (MCM) response system is not well adapted to rapidly respond to a large number of diverse threats through adequate development and production of vaccines, therapeutics, diagnostic tools, and other nonpharmaceutical interventions. The Forum, in collaboration with the IOM's Forum on Medical and Public Health Preparedness for Catastrophic Events, will





co-convene a public workshop that will examine how to better enable rapid and nimble private-sector engagement in the discovery, development, and translation of MCMs. This meeting will explore what policies, guidance, and resources exist to guide decision making within the government and how the business and operational models employed by the private sector are affected by policies and guidance and available resources set forth by the U.S. government. Further, the discussions at this meeting will be designed to identify and discuss what is needed to ensure that the private sector can respond in a rapid, nimble manner to ensure the availability of MCMs and explore advances made by the Public Health Emergency Medical Countermeasures Enterprise to improve MCM development and translation.

April 27 Workshop: Streamlining Clinical Trial and Material Transfer Negotiations September 2 Discussion Series: FDA Community Update on Post-Market Drug Safety

October 15-16 Forum Meeting #14

July 10

Symposium: Drug Regulation with FDA Commissioner Peggy Hamburg (Forum Meeting #13) October 7-8
Workshop: Transforn

Workshop: Transforming Clinical Research in the United States

Forum Themes and Priorities

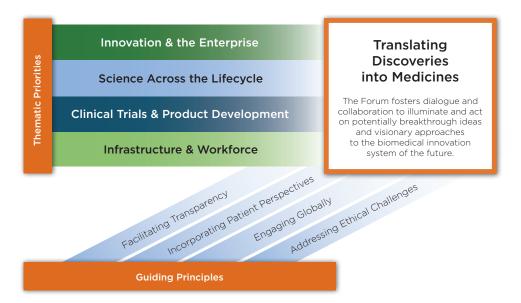
The Forum addresses key problems in the discovery, development, and translation of drugs, covering the full translational continuum from basic discovery to the approval and adoption of new therapies into clinical practice. As an overarching and cross-cutting theme, the Forum fosters innovative efforts 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: (1) Innovation and the Drug Development Enterprise; (2) Science Across the Drug Development Lifecycle (Basic, Translational, and Regulatory Sciences); (3) Clinical Trials and Clinical Product Development; and (4) Infrastructure and Workforce for Drug Discovery, Development, and Translation

Innovation and the Drug Development 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. There is also 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. The Forum offers a venue to discuss effective collaboration in the drug discovery and development enterprise and also hosts discussions that could help chart a course through the turbulent forces of disruptive innovation in the drug discovery and development "ecosystem."

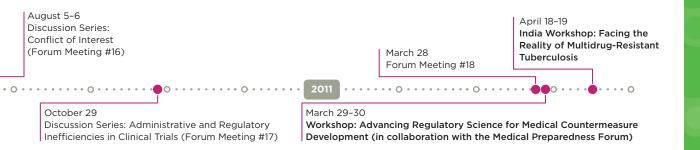


Substance—What We Aim For



Science Across the Drug Development Lifecycle

Key gaps remain in our knowledge about science, technology, and methods needed to support drug discovery and development. Recent rapid advances in innovative drug development science present opportunity for revolutionary developments of new scientific techniques, therapeutic products, and applications. The Forum provides a venue to focus ongoing attention and visibility to these important drug development needs and facilitates exploration of new approaches across the drug development lifecycle. The Forum has held workshops that have contributed to the defining and establishment of regulatory science and have helped inform aspects of drug regulatory evaluation.



Clinical Trials and Clinical Product Development

Clinical research is the critical link between bench and bedside in developing new therapeutics. Significant infrastructural, cultural, and regulatory impediments challenge efforts to integrate clinical trials into the health care delivery system. Collaborative, cross-sector approaches can help articulate and address these key challenges and foster systemic responses. The Forum has convened a multiyear initiative to examine the state of clinical trials in the United States, identify areas of strength and weakness in our current clinical trial enterprise, and consider transformative strategies for enhancing the ways in which clinical trials are organized and conducted. In addition to sponsoring multiple symposia and workshops, under this initiative, the



June 28–29 Forum Meeting #19 July 12 South Africa Workshop Summary Report Release: *The Emerging Threat of Multidrug-Resistant Tuberculosis: Global and Local Challenges and Solutions*

October 4-5 Forum Meeting #20 November 7-8
Workshop: Envisioning a Transformed
Clinical Trials Enterprise in the United
States: Establishing an Agenda for 2020

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June 27-28

Workshop: Public Engagement and Clinical Trials: New Models and Disruptive Technologies

September 20-21

Workshop: Strengthening a Workforce for Innovative Regulatory Science in Therapeutics Development Forum is fostering innovative, collaborative efforts to facilitate needed change in areas such as improvement of clinical trial site performance.

Infrastructure and Workforce for Drug Discovery, Development, and Translation

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

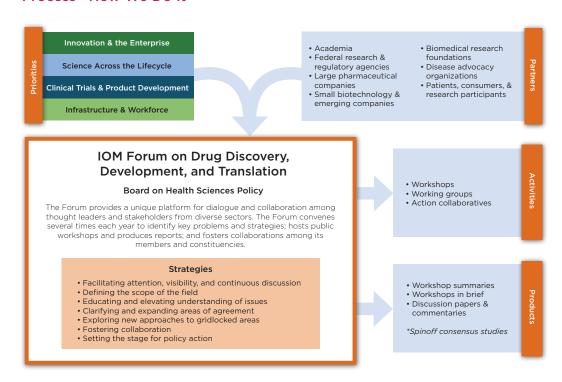


resources that facilitate the conduct of biomedical science for drug development, faces significant challenges. The science of drug discovery and development, and its translation into clinical practice, is cross-cutting and multidisciplinary. Career paths can be opaque or lack incentives such as recognition, 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.

March 13-14 Forum Meeting #21 June 4-5
Workshop: Maximizing the Goals of
the Cures Acceleration Network to
Accelerate the Development of New
Drugs and Diagnostics

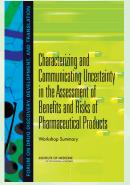
June 5 Forum Meeting #22 October 4-5
Workshop: Sharing Clinical
Research Data (in collaboration
with the Neuroscience Forum,
National Cancer Policy Forum,
and Genomics Roundtable)

Process-How We Do It





Reports Released in 2014



Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks of Pharmaceutical Products—Workshop Summary

Released: September 26, 2014

Despite the extensive body of evidence that informs regulatory decisions on pharmaceutical products, significant uncertainties persist. As a result, regulatory reviewers are consistently required to draw conclusions about a drug's safety and efficacy from imperfect data. Efforts are under way within the drug development community to enhance the evaluation and communication of the benefits and risks associated with pharmaceutical products, aimed at increasing the predictability, transparency, and efficiency of pharmaceutical regulatory decision making. On February 12 and May 12, 2014, the Institute of Medicine's (IOM's) Forum on Drug Discovery, Development, and Translation (the Forum) held public workshops at FDA Headquarters in White Oak, MD, to advance the develop-

ment of more systematic and structured approaches to characterize and communicate the sources of uncertainty in the assessment of benefits and risks, and to consider their implications for pharmaceutical regulatory decisions. This report is a summary of the workshops.



Characterizing Uncertainty in the Assessment of Benefits and Risks of Pharmaceutical Products—Workshop In Brief

Released: April 25, 2014

On February 12, 2014, the IOM's Forum on Drug Discovery, Development, and Translation held a public workshop as the first of a two-part series to advance the development of more systematic and structured approaches to characterize and communicate the sources of uncertainty in the assessment of benefits and risks, as well as their implications for pharmaceutical regulatory decisions. Workshop presentations and discussions were convened to explore the science of identifying and characterizing uncertainty in scientific evidence and approaches to translate uncertainties into decisions that reflect the values of stakeholders. This brief summary of the workshop provides highlights from the presentations and discussions.

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

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

Forum Meeting #27

2014

March 3-4

Forum Sponsorship

(as of December 31, 2014)

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

Private Foundations

Burroughs Wellcome Fund Doris Duke Charitable Foundation

Other Nonprofit Organizations

American Diabetes Association
American Society for Microbiology
Association of American Medical Colleges
Critical Path Institute
FasterCures
Friends of Cancer Research
March of Dimes Foundation

Government Sponsors

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National Institute of Neurological Disorders and Stroke (NIH)

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Forum Members

(as of December 31, 2014)

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) (until December 2014) *New England Journal of Medicine*

Steven Galson (Co-Chair)

Amgen Inc.

Russ Altman (Co-Chair) (as of January 2015) 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.

January 20-21

Workshop: Financial Incentives to Support Unmet Medical Needs for Nervous System Disorders

May 12

Workshop: Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks of Pharmaceutical Products (Day 2)

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Atlas Health Foundation

Harry Greenberg

Stanford University School of Medicine

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National Institutes of Health

Lynn Hudson

Critical Path Institute

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Dell Medical School at the University of Texas, Austin

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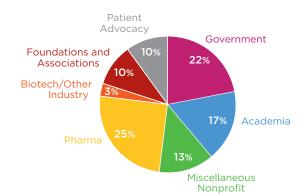
FDA Center for Drug Evaluation and Research

Liaison to the Board on Health Sciences Policy

Robert Califf

Duke University School of Medicine

Membership



March 26-27

Workshop: Enabling Rapid Medical Countermeasure Response to Emerging Threats October 20

Workshop: Priorities to Advance the Field of Regulatory Science

March 17-18 Forum Meeting #30 June 23-24 Forum Meeting #31 October 21 Forum Meeting #32

About the Forum on Drug Discovery, Development, and Translation

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 provide a unique platform for dialogue and collaboration among thought leaders and stakeholders in government, academia, industry, foundations, and patient advocacy with an interest in improving the system of drug discovery, development, and translation. 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. The Forum also fosters collaborations among its members and constituencies. 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.

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Associate Program Officer

Board on Health Sciences Policy

Barret Zimmermann (until July 2014)

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Senior Program Assistant



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The Institute of Medicine serves as adviser to the nation to improve health.

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.