Contents

Harvard-MIT Center for Regulatory Science Annual Symposium

Schedule

9:00 – 9:15am	**Registration/Breakfast**
9:15 – 9:30am	**Welcome and Introduction – Peter Sorger**, HMS
9:30 – 10:40am	**Session 1 – The Science of Evaluation**
	Chair: Peter Sorger, HMS
	Ariel Stern, HBS, *Regulatory Incentives for Pharmaceutical Innovation: the FDA's Breakthrough Therapy Designation*
	Scott Kennedy, Novartis, *Precision Medicine in the Non-Oncology World*
10:40 – 11:00am	**Coffee Break**
11:00 – 12:45pm	**Aaron Kesselheim**, BWH, *How Does the 21st Century Cures Act Change the FDA Drug and Device Approval Paradigm?*
	Brian Alexander, DFCI, *Rationale For and Development of Disease-Specific Platform Trials*
	Jerry Avorn, BWH, *Pharmacoepidemiology on the Front Lines: Addressing Current Issues in Drug Effectiveness, Safety, and Affordability*
12:45 – 2:00pm	**Special Lunch Session – Perspectives on Partnering to Advance Regulatory Science**
	Chair: Bruce Chabner, Massachusetts General Hospital
	York Tomita, FDA, *Regulatory Science at FDA*
	Elazer Edelman, MIT, *The Role of Academic Centers in Regulatory Science*
2:00 – 3:05pm	**Session 2 – Applied Computation to Streamline Drug Development**
	Chair: Aaron Kesselheim, Brigham and Women's Hospital
	John Burke, Applied BioMath, *Model Aided Drug Invention: De-risking and Accelerating Drug R&D Using Systems Approaches*
	Adam Palmer, HMS, *The Impact of Patient-to-Patient Variability on Combination Cancer Therapies*
3:05 – 3:25pm	**Coffee Break**

3:25 – 6:05pm	**Session 3 – Measuring Safety and Mitigating Toxicities**
	Chair: Brian Alexander, Dana Farber Cancer Institute
	Jay Mettetal, AstraZeneca, *Innovation in Drug Safety through Collaboration: Industry Perspective*
	Jay Han, MIT, *Micro-Nanofluidic Real Time Quality Monitoring for Biologics*
	Gerald Feldman, FDA, *Unraveling the Efficacy and Toxicity of Immune Checkpoint Inhibitors in Combination Therapy*
	Susi Ramm, HMS, *Integrating Multi-Omics Techniques to Predict and Classify Toxicity in Vitro*
	Tony Sinskey, MIT, *A Multiplexed Nanosensor Platform for the Real Time Monitoring of Food and Water-Borne Contaminants*
6:05 – 6:20pm	**Closing Discussion**
6:20pm	**Drinks and Reception**

Speaker Bios

Peter Sorger, Harvard Medical School

Peter Sorger received his AB from Harvard College and PhD from Trinity College, Cambridge University U.K., working under the supervision of Hugh Pelham. He trained as a postdoctoral fellow at the University of California, San Francisco with Harold Varmus and Andrew Murray. Prior to coming to HMS Peter served as a Professor of Biology and Biological Engineering at MIT. Sorger was cofounder of Merrimack Pharmaceuticals and Glencoe Software and is an advisor to multiple public and private companies and research institutes in the US, Europe and Japan.

Peter's research focuses on signal transduction networks controlling cell proliferation and death, dysregulation of these networks in cancer and inflammatory diseases and mechanisms of action of therapeutic drugs targeting signaling proteins. His group uses mathematical and experimental approaches to construct and test computational models of signaling in human and murine cells as a means to understand and predict the responses of cells and tumors to drugs applied individually and in combination. The Sorger group also develops open-source software for analyzing biological networks and it participates in multiple collaborative programs working to improve data reproducibility.

As head of the Laboratory of Systems Pharmacology (LSP) Peter leads a multi-institutional effort to advance the basic and translational science used to develop new medicines, create novel drug combinations and identify potentially responsive patients. The LSP also applies systems biology approaches to understanding and mitigating adverse drug effects. The recently established Harvard-MIT Center of Regulatory Sciences focuses on improving how drugs are evaluated in clinical trials, brought to market and used in diverse patient populations. HiTS includes faculty from seven institutions.

Ariel Stern, Harvard Business School

Ariel Dora Stern is an Assistant Professor of Business Administration in the Technology and Operations Management Unit at Harvard Business School. She teaches the Technology and Operations Management course in the MBA required curriculum.

Ariel's research focuses on the management of innovation in health care, with a focus on the medical device and pharmaceutical industries. Her projects seek to understand the drivers of innovation among firms and the determinants of how medical technologies are adopted and used in practice. Ariel is particularly interested in the intersection of the regulation, firm strategy, and economics of health care. She also researches the digital transformation of medical technology and health care delivery, investigating the policy and managerial questions raised by the growth of "digital health." Her research has been cited by Bloomberg, The New York Times, and National Public Radio.

Professor Stern received her Ph.D. in Public Policy from Harvard, where she was a National Bureau of Economic Research Predoctoral Fellow in the Economics of Health and Aging and was honored with the Harvard Kennedy School Dean's Award for excellence in student teaching. She holds an undergraduate degree in economics from Dartmouth College, where she was a Presidential Scholar and a two-time U.S. national collegiate figure skating champion. Before beginning her academic career, she worked as an economist on Wall Street and at the Federal Reserve Bank of New York, the German Institute for Economic Research (DIW), the German Development Bank (KfW), and LeapFrog Investments, an impact investment fund.

Ariel is currently a faculty affiliate of the Harvard Business School Health Care Initiative and a Research Associate at Ariadne Labs, a joint center between the Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health, which focuses on scaling health care delivery innovation.

Scott Kennedy, Novartis

Dr. Scott Kennedy is Vice President and Global Head of Biomarker Development, Translational Medicine, for Novartis Institutes for Biomedical Research.

Scott leads a global group of scientists who work in partnership with Novartis and external translational biologists, physicians and companies to develop stratified medicines for all stages of clinical development. His group applies state of the art imaging, proteomic, genetic, genomic, cellular and computational approaches to address clinical and biological biomarker questions.

After completing a post-doctoral fellowship at Yale University School of Medicine Department of Pathology, Scott joined Alexion Pharmaceuticals, a biotechnology start-up company focusing on treatments for transplant rejection and inflammatory diseases. He moved to Pfizer Global Research and Development where he assumed increasing levels of responsibility, including Head of Biology Research, Vice President of Development in Drug Safety Research and Development, and Head of Pfizer's External Research Network. Prior to joining NIBR in 2010, Scott served as Chief Scientific Officer for RainDance Technologies, a biotechnology start-up company focusing on microdroplet technology applications in next generation sequencing and single cell analysis.

Scott received his B.S. Biochemistry from Trinity College and Ph.D. Immunology from the University of Connecticut Health Center.

Aaron Kesselheim, Brigham and Women's Hospital

Aaron Kesselheim MD JD MPH is an Associate Professor of Medicine at Harvard Medical School and a faculty member in the Division of Pharmacoepidemiology and Pharmacoeconomics in the Department of Medicine at Brigham and Women's Hospital (BWH). His work addresses a number of topics at the intersection of law, medicine, and ethics, including FDA regulatory policies and the approval process for prescription drugs and medical devices, and the costs, availability, and evidence-based use of prescription drugs. He graduated from Harvard College and received his postgraduate training at the University of Pennsylvania School of Medicine and Law School, and most recently at the Harvard School of Public Health. He is Board Certified in Internal Medicine, and serves as a primary care physician at the Phyllis Jen Center for Primary Care at BWH. Within the Division, Aaron created and leads the Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research core focusing on intersections among prescription drugs and medical devices, patient health outcomes, and regulatory practices and the law. Currently, PORTAL has two full-time faculty, 5 post-docs, and numerous affiliated faculty and students, and is funded from government grants and contracts, private foundations including the Laura and John Arnold Foundation, Engelberg Foundation, and Commonwealth Fund, and through the Harvard Medical School Program in Therapeutic Science. He is a member of the New York State Bar and is a Patent Attorney.

Aaron has received wide recognition for his work. He has testified before Congress on pharmaceutical policy, medical device regulation, generic drugs, and modernizing clinical trials, and served as a consultant for the NIH, FDA, National Academies of Science, Engineering, and Medicine, USPTO, and numerous state government offices. In 2010, he received the prestigious Alice S. Hersh New Investigator Award from AcademyHealth, the leading professional organization for health services/policy research. The Hersh award is given annually to an outstanding health services researcher under age 40 in the US. In 2013, Aaron was named a Greenwall Faculty Scholar in Bioethics by the Greenwall Foundation, which supports innovative empirical research in bioethics. In 2016, he was presented with the Research Leadership Award from Brigham and Women's Hospital, and Harvard Medical School's young mentor award.

Aaron also serves as a faculty supervisor for the Petrie-Flom Center for Health Law Policy, Biotechnology, and Bioethics at Harvard Law School, a faculty member of the Harvard Center for Bioethics, and a Research Associate in the Department of Health Policy and Management at the Harvard T. H. Chan School of Public Health. In 2014-2015 and again in 2016-2017, he has served as Visiting Associate Professor of Law at Yale Law School, where he teaches Food and Drug Administration Law. In 2012, he was named to the Perspectives Advisory Board of the New England Journal of Medicine.

Brian Alexander, Dana Farber Cancer Institute

Brian Alexander, MD, MPH, is an Associate Professor of Radiation Oncology at Harvard Medical School and the Disease Center Leader for Radiation Oncology, Center for Neuro-Oncology, at the Dana-Farber/Brigham and Women's Cancer Center. He also serves as the Head of the Program for Innovations in Therapeutic and Biomarker Development at the Dana-Farber Cancer Institute and the Deputy Director for Regulatory Science at the Harvard/MIT Center for Regulatory Science.

Brian received his BA from Kalamazoo College, MD from the University of Michigan Medical School, and MPH from the Harvard School of Public Health. He completed his training in radiation oncology at the Harvard Radiation Oncology Program.

Brian's research interests focus on innovations in clinical evidence generation to support the development of therapeutics, biomarkers, and novel endpoints. During his residency, he published a book on the use of Bayesian approaches to clinical decision-making and his work applying such approaches to clinical trial designs was supported by a Burroughs-Wellcome Innovations in Regulatory Science Award. Brian is currently the Principal Investigator and sponsor of INSIGhT, a multi-institutional genomic biomarker-based, Bayesian adaptively randomized trial for patients with glioblastoma. He is also co-PI and on the Executive Committee of GBM AGILE, a novel global clinical research environment currently in development. Brian's research also includes evidence generation from patient-derived preclinical models and the statistical modeling and synthesis of therapeutic development data from multiple sources.

Prior to his faculty appointment at HMS, Brian was a White House Fellow and Special Assistant to the Secretary of Veterans Affairs. In that role, he helped prepare VA for the transition of administrations, worked to develop a public reporting system for quality, and served as a health policy advisor to the Secretary. Brian organized the standup of the VA's Coordinating Council on National Health Reform and directed the activities of its multi-team Health Reform Working Group. He was also a member of the Institute of Medicine's Committee on the Governance and Financing of Graduate Medical Education.

Jerry Avorn, Brigham and Women's Hospital

Jerry Avorn, M.D. is Professor of Medicine at Harvard Medical School and Chief of the Division of Pharmacoepidemiology and Pharmacoeconomics in the Department of Medicine at Brigham and Women's Hospital. Dr. Avorn did his undergraduate work at Columbia University, received the M.D. from Harvard Medical School in 1974, and completed a residency in internal medicine at the Beth Israel Hospital. He joined the HMS faculty in 1978. While at the B.I., he was certified in Geriatric Medicine and helped to establish the Harvard Medical School program on aging, building a research program on the use and outcomes of medications in the elderly.

His research group was among the first to use large electronic datasets of medication use and clinical outcomes, beginning in the early 1980s. His current work centers on the intended and adverse outcomes of prescription drugs, physician prescribing practices, and medication policy. He founded the Division of Pharmacoepidemiology and Pharmacoeconomics in 1998; it currently includes 70 people, including 21 faculty members representing clinicians from various medical specialties, epidemiologists, lawyers, health services researchers, and biostatisticians, as well as programmers, graduate students, and reseasrch support staff.

In addition to his work in pharmacoepidemiology and medication policy, Dr. Avorn originated the "academic detailing" approach to continuing medical education, in which non-commercial, evidence-based information about drugs is provided to doctors through educational outreach programs run by public-sector sponsors. He served as a member of the Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines and is the author or co-author of over 500 papers in the medical literature on medication use and its outcomes, and of the book, Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs, now in its 11th printing. In 2015 he was recognized as one of the most highly cited reseaerchers in medicine and social sciences (epidemiology).

York Tomita, Food and Drug Administration

Dr. Tomita is a Science Advisor in the Office of Regulatory Science and Innovation (ORSI) within the office of the Chief Scientist and the Office of the Commissioner for the US Food and Drug Administration. At FDA, he has been working to build regulatory science initiatives in a global environment based on his broad knowledge and expertise in translational and regulatory science.

Dr. Tomita's experience includes development of translational and regulatory science tools including structural biology, systems biology and BigData analysis based on omics research, biomarker discovery, analytical chemistry and biochemistry, cancer drug discovery and cancer biology, and biophysics. At FDA, he has been involved in the development and promotion of regulatory science initiatives and policies such as intramural research coordination, Center of Excellence in Regulatory Science and Innovation (CERSI), Broad Agency Announcement (BAA) and international outreach.

After obtaining his Ph. D. from Columbia University in New York City, he completed his five year postdoctoral training at the National Institutes of Health (NIH) in Bethesda, Maryland. He continued his scientific career as an Assistant Professor of Oncology at Lombardi Cancer Center, Georgetown University Medical Center, where he developed and managed independent research programs with federal and private supports, and trained medical, undergraduate, and graduate students as well as fellows and technicians. His research at Georgetown University was focused on cancer drug discovery forging multidisciplinary team of investigators including experts in clinical oncology, bioinformatics, cancer biology and medicinal chemistry.

Elazer Edelman, Massachusetts Institute of Technology

Elazer R. Edelman, MIT Cabot Professor of Health Sciences and Technology, and Harvard Medical School Professor of Medicine, is a cardiac care unit cardiologist at Brigham and Women's Hospital and director of MIT's Biomedical Engineering Center. His research melds clinical and medical training, focusing on how tissue architecture and local biochemical regulation maintain homeostasis. Edelman and his students were amongst the first to validate that vascular diseases are the sum of effects from endogenous growth promoters like heparin and suppressors like heparin-binding growth factors, to define the nomenclature and kinetics of the FGF-2 receptor complex, and demonstrate that mode of growth factor or inhibitor delivery determines biologic effect.

Applied research flows from recapitulating natural regulation. The development and mathematical characterization of perivascular and stent-based drug delivery mimicked natural control of chemomediators, and design of endovascular stents from first principles leveraged understanding of vascular repair and innovations in computational modeling. Basic and applied aspects are intimately joined as exemplified by work with antisense oligonucleotides, HDL receptor biology and tissue engineered endothelial implants in vascular and cancer diseases. More than 330 students and fellows have passed through Edelman's laboratory.

Edelman is fellow of the American College of Cardiology, American Heart Association, American Institute for Medical and Biological Engineering, American Society for Clinical Investigation, American Academy of Arts and Sciences, National Academy of Medicine, National Academy of Engineering and National Academy of Inventors. As Chief Scientific Advisor of Science: Translational Medicine and member of the FDA Scientific Board he has set the tone for the national debate on translational research and innovation. He has received multiple awards and honors including most recently the Clemson Award for Basic Research from the Society for Biomaterials, the Dean's Distinguished Lecture, Weill-Cornell Medical School, the Massimo Calabresi Lecturer, Yale University, the Flexner Discovery Lecturer, Vanderbilt University Medical Center, Plenary Lecture, Irish Royal Society, Galway, Ireland, and Order of Civil Merit of Spain. As an avid ice hockey goalie Dr. Edelman's most impressive accomplishment involves passing three levels of coaching licensure from the Massachusetts Youth Hockey league and coaching his sons' Brookline Bantam B team.

John Burke, Applied Biomath

Dr. Burke is President, CEO and Co-founder of Applied BioMath, LLC., a Systems Biology and Pharmacology company. Dr. Burke's BS and MS are in Applied Mathematics, University of Massachusetts, Lowell. His PhD degree is in Applied Mathematics, Arizona State University, where he studied dynamical systems, singular perturbation theory, and control of signal transduction networks and protein expression. Prior to Applied BioMath, Dr. Burke joined Boehringer Ingelheim (BI), as Global Head of Systems Biology and Pharmacology, where he started, developed and managed the group, portfolio, and strategy. The group was responsible for applying systems techniques across all of Research, Development and Medicine. His group supported over 200 projects in five years, and over 11 transitions into Development or Clinical Trials.

Prior to BI, he was a Senior Scientist at Merrimack Pharmaceuticals. Prior to Merrimack he was a postdoc in Douglas A. Lauffenburger's lab, Biological Engineering Department, MIT; and a postdoc and Co-Scientific Director of the Cell Decision Processes Center, in Peter Sorger's lab, Systems Biology Department, Harvard Medical School. While at MIT and HMS, Dr. Burke studied apoptosis and growth factor pathways, and he provided systems pharmacology consulting or advising services for companies, including AstraZeneca, Pfizer, Momenta, and Matlab (Simbio). Research interests include dynamical systems theory, singularly and randomly perturbed differential equations, bifurcation theory, understanding how cells and tissues make decisions in human disease, predicting optimal drug properties and mechanistic PK/PD modeling. He presented at the NIH-Academic-Industry Target Validation Consortia and presently he serves on advisory boards for the MIT "Human Physiome on a Chip" MIT-DARPA Program, the MIT NIH/NCATS "Translational Center of Tissue Chip Technologies" grant, and the Mathematics Department at the University of Massachusetts, Lowell.

Adam Palmer, Harvard Medical School

Adam Palmer is a postdoctoral fellow with Prof. Peter Sorger at the Harvard Medical School Laboratory of Systems Pharmacology, where he applies experiments and computation to understand and to develop combination therapies in oncology. Previously Adam received his Ph.D in Systems Biology from Harvard University, where he studied mechanisms of antibiotic drug action and the evolution of antibiotic resistance with Prof. Roy Kishony.

Jay Mettetal, AstraZeneca

Dr Jerome "Jay" Mettetal leads the Modeling and Simulation function in Drug Safety and Metabolism at AstraZeneca and is responsible for application of quantitative and bioinformatics approaches to translating drug safety from discovery to the clinic. Prior to joining AZ, Jay was a modelling and simulation team leader at Millennium/Takeda Oncology working in oncology and a principal scientist at Pfizer developing biologics. He also worked at CombinatoRx as a computational biologist discovering novel combination therapies. He earned his PhD in Physics at MIT on an NSF Graduate Fellowship, and has undergraduate degrees in physics and mathematics from Virginia Tech.

Jay Han, Massachusetts Institute of Technology

Dr. Jongyoon Han is currently a professor in the Department of Electrical Engineering and Computer Science and the Department of Biological Engineering, Massachusetts Institute of Technology. He received B.S.(1992) and M.S.(1994) degree in physics from Seoul National University, Seoul, Korea, and Ph.D. degree in applied physics from Cornell University in 2001. He was a research scientist in Sandia National Laboratories (Livermore, CA), until he joined the MIT faculty in 2002. He received NSF CAREER award (2003) and Analytical Chemistry Young Innovator Award (ACS, 2009). His research is mainly focused on applying micro/nanofabrication techniques to various problems, such as biosample preparation, biodetection, desalination / water purification, and even neurotechnology.

Gerald Feldman, Food and Drug Administration

Dr. Feldman is a Senior Investigator in the Division of Biotechnology Research and Review-IV, Office of Biotechnology Products, CDER. He received his doctorate in Immunology and Infectious Diseases from the Johns Hopkins University in Baltimore, MD. In 1989, after several years of post-doctoral work in the Laboratory of Immunology at the NIDR, NIH, Dr. Feldman joined the staff of the Division of Cytokine Biology in the Office of Therapeutics Research and Review at CBER, receiving tenure in 1996. In 2002 Dr. Feldman became a Senior Investigator in the Office of Biotechnology Products, CDER, and in 2015 he became Chief of the Laboratory of Immunobiology in DBRR- IV, Office of Biotechnology Products, CDER. He has been involved in all phases of the regulatory process, from pre-IND product development through licensing and post-licensure inspections. Dr. Feldman has also been involved in guidance document development, and has represented the Agency internationally on a wide range of issues ranging from assay validation to TSE's. His active research interests involve mechanisms of receptor signaling, with a current laboratory emphasis on monoclonal antibody structure-function relationships and their role in predicting potential adverse events.

Susanne Ramm, Harvard Medical School

Susanne Ramm is a Research Associate at Harvard Medical School, Boston in the Laboratory of Systems Pharmacology and at the Renal Division of Brigham and Woman's Hospital. Dr. Ramm obtained her Bachelor's (2007) and Master's degree (2009) in Food Chemistry, and Doctoral degree (2012) in Toxicology from the University of Wuerzburg, Germany.

From 2013 to 2016, Dr. Ramm conducted her postdoctoral fellowship in Vishal S. Vaidya's laboratory at Harvard Medical School. During that time, she developed innovative tools to predict whether novel drugs or chemicals might be toxic to the kidney, without the need for testing in animals. Given the possible applications of these models, Dr. Ramm's work has garnered interest from a number of parties including pharmaceutical companies (Merrimack, AstraZeneca, and Pfizer), the US Food and Drug Administration, and academic collaborators (Dana-Farber Cancer Institute and Massachusetts Institute of Technology). More recently, her research interests have expanded to include the development of new screening assays to identify small molecules that help regenerate kidney tissue after acute damage, with the goal of preventing the progression to chronic kidney failure.

Dr. Ramm has published several first-authors papers in the toxicology and nephrology literature. Her work was highlighted by the National Institute of Environmental Health Sciences and has been awarded prizes at each of the international annual scientific meetings of the Society of Toxicology since 2015. Her accomplishments have culminated in her election as officer for the "In Vitro and Alternative Methods" Specialty Section of the Society of Toxicology.

Dr. Ramm is passionate about the use of artistic imagery to convey scientific concepts. Recently, her designs have been featured on the covers of the esteemed journals Cancer Cell (03/16, for a paper which she co-authored) and Nature Medicine (07/16). Dr. Ramm harbors a strong interest in teaching and providing mentorship to others. She has given several lectures to pharmacy and medical students in Germany, and served as a supervisor to undergraduate and graduate students at Harvard. Her long-term goal is to establish a career that combines scientific endeavor and teaching, with the ultimate aims of preventing kidney disease and improving the lives of patients with kidney failure.

Tony Sinskey, Massachusetts Institute of Technology

Anthony J. Sinskey, Sc.D., is a Professor of Microbiology and Engineering Systems at the Massachusetts Institute of Technology, and Professor of Health Sciences and Technology at the Harvard-MIT Division of Health Sciences & Technology. Professor Sinskey also holds positions as Co-Director of the Malaysia-MIT Biotechnology Partnership Program and as Faculty Director of the MIT Center for Biomedical Innovation (CBI). He conducts interdisciplinary research in metabolic engineering focusing on the fundamental physiology, biochemistry and molecular genetics of important organisms. Professor Sinskey is well known in the biopharmaceutical industry and has been a Scientific Co-founder of several biotechnology companies, including Genzyme Corporation, Natural Pharmaceuticals, Metabolix, Merrimack Pharmaceuticals, and Tepha. Dr. Sinskey has given more than 300 presentations at U.S. and International scientific meetings and congresses. He has received 31 issued patents, has made more than 30 invention disclosures and has published more than 300 scientific papers in leading peer-reviewed journals for biology, metabolic engineering, and biopolymer engineering. Dr. Sinskey received his undergraduate degree from the University of Illinois at Urbana-Champaign and his Sc.D. in Microbiology and Food Science from the Massachusetts Institute of Technology. His post-doctoral work was done at the Harvard School of Public Health.