Guruprasad Aithal is the Professor of Hepatology in the University of Nottingham, UK and the Co-Director of NIHR Nottingham Digestive Diseases Biomedical Research Unit, one of the only two BRUs funded to research on liver diseases in the UK. He has been a Consultant Hepatobiliary Physician at Nottingham University Hospitals NHS Trust since 2001.

Guru Aithal was introduced to research in 1996 when he took a position of research fellow which led to PhD in the area of Hepatotoxicity. His studies on pharmacogenetics of warfarin and its clinical relevance stimulated the identification of striking genetic factors explaining a large part of the inter-individual variation in dose requirement. In 2007, FDA updated the prescribing information for warfarin to add that genetic information improves dosing. Further studies on genetic susceptibility to drug-induced liver injury including the discovery of strong association of HLA genotypes with idiosyncratic hepatotoxicity has enhanced the understanding of the key role adaptive immunity plays in the pathogenesis. Guru Aithal has been the co-chair of international drug-induce liver injury consortium leading genome wide association studies enrolling patients in Europe, Canada, China and India. His other research interests are in ‘non-alcoholic fatty liver disease’ (mechanisms, biomarkers of liver injury and effective interventions), ‘epidemiology of liver and biliary disease’ (cause and consequences) and ‘hepatobiliary imaging’ (assessment of degree of liver injury and endoscopic imaging techniques). Guru Aithal has over 100 publications including those in Nature Genetics, Nature Review, Lancet, British Medical Journal, Gastroenterology and Hepatology.

**Presentation:**
RUCAM or Expert Opinions --- a Debate
Viewpoint
Rebuttal
Shashi Amur, Ph.D.
Office of Translational Sciences
Center for Drug Evaluation and Research
Food and Drug Administration

Shashi Amur, Ph.D. is the Biomarker Qualification Scientific Coordinator in the Office of Translational Sciences at the Center for Drug Evaluation and Research, FDA.

Dr. Amur received her Ph.D. in biochemistry from Indian Institute of Science, India and completed post-doctoral fellowship at Temple University and at UCLA researching regulation of myelination using in vitro model systems. She then joined Specialty Laboratories in Santa Monica, CA as a Molecular Biologist in the R&D division. Dr. Amur moved to Applied Biosystems in Foster City, CA, and applied DNA sequencing and PCR technologies to transplantation and toxicogenomics research. Prior to joining FDA, she worked as the Associate Director of Assay Development at Immune Tolerance Network and Neotropix, Inc.

Dr. Amur joined FDA as a Senior Genomics reviewer in the Office of Clinical Pharmacology in 2005 and reviewed genomics- and biomarker-relevant sections of regulatory submissions in several therapeutic areas. She joined the Office of Translational Sciences as Biomarker Qualification Science Coordinator in 2011.

Dr. Amur is currently the Chair of the Pharmacogenomics Interest Group at OCP/FDA and is a steering committee member of the Pharmacogenomics Focus Group at the American Association of Pharmaceutical Scientists (AAPS). Her current research interests include pharmacogenomics, HLA-associated adverse events and biomarkers in Autoimmune Diseases and in Alzheimer’s disease.

Presentation:
Application of translational science to drug safety
Dr Dan Antoine is currently a Wellcome Trust research fellow at the MRC Centre for Drug Safety Science (CDSS) and lecturer in Pharmacology at the University of Liverpool, UK. Dan completed his PhD in 2009 in Pharmacology. Prior to his PhD, Dr Antoine completed his B.Sc (Hons) in Biochemistry and worked in Molecular Toxicology at AstraZeneca. He undertook postdoctoral training at the CDSS in Prof BK Park’s laboratory as well as Royal Society International Travelling Fellowships at the Harvard Medical School, USA, with Prof JV Bonventre. Dr Antoine’s research is mainly focused on the development of translational biomarkers of drug-induced liver and kidney injury and has authored publications on these topics in journals such as Nature, PNAS and The Lancet. He is a member of the DILI project team for the SAFE-T (safer and evidence based translation) IMI consortium to develop and qualify safety biomarkers. He sits on the British Toxicology Society’s (BTS) Education, Training and Early Career Toxicologists Sub-Committee and received the 2013 British Toxicology Society’s early career investigator award. He is also an active member of the Society of Toxicology, The British Pharmacological Society and the International Society for Xenobiotics as well as an editorial board member for Pharmacology Research & Perspectives. Dr Antoine’s academic research is currently funded by grants awarded from the European Commission, Medical Research Council, Wellcome Trust and Royal Society.

Presentation:
Translational mechanistic biomarkers
DILI Conference XIV
Predicting Serious Drug-Induced Liver Injury in Patients
Who Gets It? Who Doesn't? Why?

Speaker BIO & Presentation Links
In alphabetical order

Irwin M. Arias, MD
Triple Emeritus: Professor of Medicine (Albert Einstein College of Medicine); Professor of Physiology and Medicine (Tufts University School of Medicine and Senior Scientist (National Institute of Health)

Following graduation from medical school and residency training in Boston, Irwin Arias ("Win") specialized in medicine and hepatology in Boston after which he spent 29 years at the Albert Einstein College of Medicine as Professor of Medicine, Vice- Chairman of Medicine, Founder of the first NIH supported Liver Research and Director of the GI-Liver Training Program. In 1982, he became Chairman and Professor of Physiology and Professor of Medicine at Tufts Medical School In 2000, Win and Lyuba moved to NIH where he is Senior Scientist in the Cell Biology and Metabolism Program of the NICHD and Assistant to the Director of the Intramural Program at NIH. Win has received Distinguished Achievement Awards from the AASLD, AGA, ACG, ALF and other liver-related organizations around the world, served as President of AASLD, Vice-President of the ASCI, and Founding Editor of Hepatology. Since inception of the ALF, Win has been an active leader in promoting "the cause" and served for many years on the Board of the New England Chapter and the National Organization. In 1991, the New England Chapter honored him by naming an annual Symposium in Boston on "Bridging Basic Science and Liver Disease". This highly successful event brings leading biomedical scientists and physicians who share interest in liver biology and disease to meet with students, fellows and scientists. Win has published over 450 research papers, reviews, book chapters and position papers. His wide-ranging research focuses on bringing advances in basic science to better understanding of liver function and disease, both acquired and inheritable.

Presentation:
Mitochondrial-autophagy drive hepatocyte polarization
Mark Avigan obtained his B.Sc. (1972) and M.D. C.M. degrees (1977) from McGill University in Montreal, Canada. He completed residency training in Internal Medicine at the VA Medical Center/Georgetown University in Washington DC. Subsequently, he completed a clinical GI/Hepatology/Nutrition fellowship. Dr. Avigan served as a staff fellow in the Liver Unit of the National Institute of Arthritis Diabetes, and Digestive and Kidney Diseases where he participated in studies of viral hepatitis and in the evaluation of new therapeutics for the treatment of these conditions. He later moved to NCI where he pursued studies in molecular and cellular mechanisms governing the dysfunctional expression of oncogenes during carcinogenesis.

In 1990 Dr. Avigan joined the faculty at the School of Medicine at Georgetown University. As an assistant and later associate professor he attended patients on the GI/Liver service at the Georgetown University Medical Center and served as a mentor of graduate students in the Department of Pathology and clinical fellows in the GI clinical program. He was the principal investigator of NIH funded R-29 and R0-1 grants to elucidate basic mechanisms in the transcriptional and post-transcriptional regulation of pathways critical for cellular growth and differentiation.

After joining the Center for Drug Evaluation and Research (CDER) of the Food and Drug Administration in 1999 as a Medical Officer in the Division of Gastrointestinal and Coagulation Drug Products, he developed a strong interest in drug-induced liver injury and the impact of pharmacogenomic analysis on evaluation of risk associated with drug treatment. Between 2003 and 2011 he served as Director of the Division of Drug Risk Evaluation, and Division of Pharmacovigilance in the Office of Surveillance and Epidemiology (OSE). With an interest to develop mechanistic as well as population-based perspectives in drug safety, Dr. Avigan is currently Associate Director of OSE for Critical Path Initiatives. He is a member of CDER’s Drug Safety Oversight Board and has served as an ex officio advisor for the NIH Drug-induced Liver Injury Network (DILIN). He has co-authored over 100 publications, bookchapters and professional meeting abstracts in the fields of cellular regulation, GI/hepatology and drug safety.

**Moderator:**
What new and useful biomarkers (and predictors) are out there?

**Session Transcript**

**Presentation:**
DILI biomarkers – what is really needed?
DILI Conference XIV
Predicting Serious Drug-Induced Liver Injury in Patients
Who Gets It? Who Doesn’t? Why?

Speaker BIO & Presentation Links
In alphabetical order

Herbert L. Bonkovsky, MD
Professor of Medicine Senior Advisor for Research, Carolinas HealthCare System Director of Liver, Digestive, and Metabolic Disorders Laboratory Department of Internal Medicine
Professor, University of Connecticut
Professor, University of North Carolina at Charlotte
Professor, University of North Carolina at Chapel Hill

Throughout a medical career now spanning more than 40 years, Dr. Bonkovsky has been committed to Clinical and Translational Research. His research career began in medical school when he performed studies on interactions of iron with mitochondria in the laboratories of L.T. Webster, Jr. and J.W. Harris at Case Western Reserve University School of Medicine. This began a continuing interest in the study of iron metabolism and disorders of iron metabolism, especially various forms of hemochromatosis. During this time, Dr. Bonkovsky also worked closely with G. Gabuzda and L. Shear. This work led to a landmark paper that described clearly the occurrence of renal tubular acidosis in a subset in patients with hepatic cirrhosis and its importance as a risk factor for development of hepatic encephalopathy [NEJM 1969; 280: 1-7].

Dr. Bonkovsky spent two years as a clinical associate in the Metabolism Branch in the National Cancer Institute, where his mentors were N.I. Berlin and D.P. Tschudy. During this time, he carried out groundbreaking studies in the laboratory and in the general clinical research center on the nature of the enzymatic defects that underlie the porphyrias. He was among the first to show that hepatic porphyrin and heme synthesis is under the negative feedback regulatory control of heme itself, acting chiefly to down-regulate delta-aminolevulinic acid (ALA) synthase-1 the rate controlling enzyme for heme synthesis. This led Dr. Bonkovsky to develop parenterally-administered heme as therapy of acute attacks of porphyria, which is still today the treatment of choice for these life-threatening attacks.

Dr. Bonkovsky has performed both basic and clinical studies on alcoholic liver disease and its management and on drug-induced liver injury (DILI). He is one of the principal investigators of the NIH–supported national Drug Induced Liver Injury Network (DILIN). This ongoing active network has developed a registry of patients with clinically important DILI and repositories of serum, DNA, urine and other samples from such patients. Other ongoing activities of the network include several important ancillary studies examining the genetic underpinnings of toxicity caused by drugs and chemicals, genome wide association studies looking for new genetic variations that increase the risk of development of DILI, the characterization of infiltrating lymphocytes in liver biopsies of patients with DILI and the development of improved laboratory methods for lymphocyte stimulation tests as an aide to the diagnosis of DILI and the assignation of causative agents in DILI.

Presentation:
DILIN experience with biomarkers
Ann Daly is Professor of Pharmacogenetics at the Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK. She received a PhD from the University of Dublin (Trinity College), performing biochemical studies on aldo-keto reductases and glutathione S-transferases. She subsequently worked on nuclear structure at the University of Geneva and then moved to Newcastle University. At Newcastle she worked initially on the molecular biology of retinoic acid action, and was a founder member of the Newcastle Pharmacogenetics Research Group. Her current research is focused on the pharmacogenetics of the human cytochromes P450, genetic susceptibility to idiosyncratic adverse drug reactions and the genetics of complex diseases, particularly liver disease. She has published over 190 peer reviewed articles and is an editorial board member on a number of journals.

Presentation:
It’s the genome -
Gerald J. Dal Pan, MD, MHS
Director Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Gerald J. Dal Pan, MD, MHS became the Director of the Office of Surveillance and Epidemiology (known then as the Office of Drug Safety) in FDA’s Center for Drug Evaluation and Research in November 2005. Prior to that, he was the Director of the Division of Surveillance, Research, and Communication Support in CDER’s Office of Drug Safety, a position he held since December 2003. He received his medical degree from Columbia University, and his Master's degree in clinical epidemiology from Johns Hopkins University. He trained in Internal Medicine at the Hospital of the University of Pennsylvania, and in Neurology at Johns Hopkins Hospital. He is board certified in Internal Medicine and Neurology. He was an instructor in the Neurology Department at Johns Hopkins. He next worked for Guilford Pharmaceuticals in Baltimore, and then for HHI Clinical Research and Statistical Services in Hunt Valley, MD. He joined the FDA in July 2000 as a medical officer in the Division of Anesthetic, Critical Care, and Addiction Drug Products.

Presentation:
Surveillance for liver toxicity after marketing
Dr. Fontana is a translational investigator with research interests in drug induced liver injury and acute liver failure. Dr. Fontana completed his gastroenterology/hepatology training at the University of Michigan and has been on the faculty since 1995. He is currently a Professor of Medicine and Medical Director of Liver Transplantation. He is a principal investigator at one of the 6 Drug Induced Liver Injury Network (DILIN) clinical sites and also serves as Co-chair of the DILIN Steering committee. He has helped lead efforts to carefully phenotype patients with DILI as well as determine the likelihood of early adverse outcomes and chronicity with prolonged follow-up in the DILIN prospective study. Dr. Fontana is also the current Chair of the AASLD Hepatotoxicity Special Interest Group. He has also been an active member of the US Acute Liver Failure Study Group as a site principal investigator and lead investigator on the long-term outcomes protocol since 1998.

Moderator:
Can we really predict? Or just detect?
Session Transcript

Presenter:
RUCAM or Expert Opinions?
Viewpoint
Rebuttal
Brett Howell is a Co-Project Lead for the DILI-sim modeling team and a Lead Scientist and Manager at the Hamner Institutes. Dr. Howell’s research experience has focused on the use of mathematical modeling techniques to solve interesting biological problems. He has published in a variety of areas including the use of physiological modeling to optimize drug overdose treatment, the use of liposomes to test chemicals for ocular toxicity without animals, basic principles associated with lipid-membrane interactions, and most recently, modeling of drug-induced liver injury. Dr. Howell, along with Dr. Scott Siler, leads the modeling effort for the DILI-sim Initiative and acts as a technical contributor. The DILI-sim Initiative is a pre-competitive partnership between The Hamner and a diverse set of stakeholders to develop a computational model that will predict whether new drug candidates will cause drug-induced liver injury (DILI) in patients. The goals of the Initiative are to improve patient safety, reduce the need for animal testing, and reduce the costs and time necessary to develop new drugs. Dr. Howell holds Bachelors of Science degrees in chemical engineering and textile engineering from North Carolina State University and a Ph.D. in chemical engineering from the University of Florida.

**Presentation:**
*In silico insights*
Dr. Hoofnagle is the director of Liver Disease Research Branch at NIDDK and is responsible for administration and award of research grants on liver and biliary diseases for the Institute. He also is a senior investigator in the Liver Diseases Branch in the Intramural Division of NIDDK and conducts clinical research on liver diseases, including viral hepatitis, nonalcoholic steatohepatitis, drug-induced liver injury and autoimmune liver diseases at the NIH Clinical Center.

Dr. Hoofnagle has a Bachelor of Arts degree from the University of Virginia and a Medical Degree from Yale Medical School. He did post-graduate training in internal medicine at the University of Virginia Hospital and the Washington DC VA Hospital where he also did a gastroenterology-hepatology fellowship. From 1972 to 1974, he was a research staff fellow in the Hepatitis Branch of the FDA, and was the acting director of the Branch in 1975. In 1978, Dr. Hoofnagle was appointed a senior investigator in the Liver Diseases Section, NIH where he did clinical research on viral hepatitis and liver diseases. From 1986 to 1988, Dr. Hoofnagle served as the Clinical Director of NIDDK, responsible for oversight of the intramural clinical research of the Institute. In 1988, Dr. Hoofnagle was appointed the director of the Division of Digestive Diseases and Nutrition, NIDDK, an extramural position responsible for administration and funding of grants, fellowships, awards and contracts in nutrition, gastroenterology and liver disease. In June 2003, Dr. Hoofnagle was appointed the Director of the newly formulated Liver Disease Research Branch where he continues to serve having oversight over extramural liver disease-related research for NIDDK. Dr Hoofnagle has published more than 300 original journal articles and more than 100 reviews and book chapters on hepatitis and liver disease and is the recipient of several honors for his contributions to liver disease research including the Distinguished Achievement Award from the American Association for the Study of Liver Diseases, the Gold Medal for Liver Disease Research from the Canadian Liver Foundation, Scientific Achievement awards from the American Liver Foundation, the Hepatitis Foundation International and the Hepatitis B Foundation and the Sheila Sherlock Award for contributions to clinical hepatology from the Herbert Falk Foundation.

Presentation:
LiverTox - an update
Christine M. Hunt, MD, FACP, AGAF is board-certified in Internal Medicine and Gastroenterology/Hepatology. She pursued basic and clinical hepatology research on the faculty of Virginia Commonwealth University (1987-1988) and Duke University (1988-1996), examining the effects of aging on drug metabolism and pursuing viral hepatitis research. In 1996, she was recruited to GSK to develop new hepatitis and GI drug therapies; these efforts yielded successful new drug approvals. Dr. Hunt created and chaired the GSK Hepatotoxicity Board, which analyzed liver safety data, risk factors and predictors of drug toxicity, developed and executed proactive safety systems for global clinical studies, and led the development of computer algorithms to identify drug-induced liver injury in electronic health records. In 2007, Dr. Hunt was appointed Vice President, GSK Clinical Safety Systems. Dr. Hunt retired from GSK in 2012 to collaborate on clinical care systems at the VA and public health globally, while pursuing her Masters in Public Heath at the University of North Carolina. She also serves as an Adjunct Associate Professor of Medicine at Duke University.

Moderator:
Can we really predict? Or just detect?

Session Transcript
Mwango Kashoki, MD MPH  
Associate Director for Safety  
Office of New Drugs  
CDER/FDA

Dr. Kashoki is the Associate Director for Safety in the Office of New Drugs (OND), in the Center for Drug Evaluation and Research (CDER) at FDA. Dr. Kashoki’s responsibilities include ensuring OND’s implementation of the policies and processes related to CDER's various safety initiatives, including the Safety First and Sentinel Initiatives. She also leads OND's implementation of FDA's new authorities to require safety labeling changes, postmarketing investigations, and risk evaluation and mitigation strategies, as provided under the FDA Amendments Act (FDAAA).

Dr. Kashoki joined OND in 2002 as a primary medical officer in the former Division of Anesthetic, Critical Care and Addiction Drug Products, and then served as a clinical team leader in that division for several years. As a team leader, she supervised primary medical officers in reviewing investigational and new drug applications, as well as in providing guidance to individual researchers and pharmaceutical companies regarding addiction and analgesic drug development programs. Prior to her current position, Dr. Kashoki served as Associate Director for Special Projects in the former Division of Anesthesia, Analgesia and Rheumatology Products, leading the development and conduct of research projects under FDA's Critical Path Initiative and in collaboration with external groups. Dr. Kashoki received her medical degree from the Johns Hopkins University School of Medicine, and her public health degree from the Columbia University School of Public Health. She is board certified in Preventive Medicine and Public Health.

Presentation:  
Review of new drug applications for liver safety
Jeff Lawrence is the Director of Biochemical Toxicology in the Department of Toxicological Sciences at Amgen in Thousand Oaks, CA. Jeff’s research interests include mitochondrial biology, energy metabolism, mechanisms of hepatotoxicity, and identification of novel safety biomarkers and their qualification. Jeff Lawrence holds a B.Sc. degree in Toxicology from the Philadelphia College of Pharmacy and Science, and a Ph.D in Pharmacology from the University of Florida. He started his scientific career in hepatotoxicity as a postdoctoral scientist at Eli Lilly and Co, where he worked in the Hepatotoxicity laboratory and later in the Cardiovascular Discovery Research group. Following his postdoctoral training, Jeff worked in the Department of Safety Assessment at Merck and Co., Inc. for 10 years, then, in 2006, joined Amgen, Inc. Jeff is co-chair of the Hepatotoxicity Safety Advisory Committee at Amgen. Jeff is currently the co-chair of the PSTC Hepatotoxicity Working Group.

Presentation:

Predictive Safety Testing Consortium Initiatives
Dr. Lee graduated from Amherst College cum laude and from the College of Physicians and Surgeons of Columbia University AOA, completing his internal medicine residency at the Presbyterian Hospital in New York City where he served as Chief Resident. After additional studies at Kings College Hospital, London, he has served on the faculties of Columbia University, the Medical University of South Carolina and, since 1990, the University of Texas Southwestern Medical Center at Dallas where he is Professor of Internal Medicine and holds the Meredith Mosle Chair in Liver Diseases in his honor. He is also currently serving as a Clinical Professor at The Ohio State University.

He founded the Acute Liver Failure Study Group (ALFSG), a national network to study this orphan disease, which has been funded by the National Institutes of Health since 1997. The ALFSG under Dr. Lee’s guidance has performed important studies on the causes and treatment of this rare condition in more than 50 peer-reviewed papers. He focused attention on the severe and frequent liver injury and liver failure due to acetaminophen in seminal studies from Parkland Hospital in the 1990’s and through the ALF Study Group, provided important data to the 2002 and 2009 FDA Advisory Committee meetings on acetaminophen toxicity. In addition, Dr. Lee has served as a site investigator for the HALT-C Trial, the Drug-Induced Liver Injury Network (DILIN) and the Hepatitis B Research Network—all sponsored by the National Institutes of Health. In 2011 he was given the Award for Excellence in Community Service for Medicine by the Dallas Historical Society.

Presentation:

Reckless behavior causes acute liver failure
Willis C. Maddrey, MD
Professor of Internal Medicine
UT Southwestern Medical Center

Willis C. Maddrey, MD, is Professor of Internal Medicine and Assistant to the President at The University of Texas Southwestern Medical Center at Dallas. Dr. Maddrey received his medical degree from The Johns Hopkins University School of Medicine in Baltimore, Maryland, and completed his residency on the Osler Medical Service of The Johns Hopkins Hospital. He was Chief Medical Resident in 1969. Additional postgraduate work includes a fellowship in liver disease with Dr. Gerald Klatskin at Yale University School of Medicine. From 1970 to 1981 Dr. Maddrey directed the liver unit at The Johns Hopkins University School of Medicine where he was Professor of Medicine and Associate Physician in Chief. From 1982 to 1990 he was Magee Professor and Chairman of the Department of Medicine at Jefferson Medical College. Dr. Maddrey has authored numerous scientific publications. He has published extensively in the areas of chronic viral hepatitis, drug-induced liver disease, alcohol-induced liver disease, liver transplantation, and primary biliary cirrhosis. He has authored numerous publications focusing on hepatitis and liver disease. He has edited or co-edited nine books including Transplantation of the Liver which is now in its third edition, and Schiff’s Diseases of the Liver, now in its ninth edition. Dr. Maddrey is a member of several societies including the American Society for Clinical Investigation and the American Gastroenterological Association. He was President of the American Association for the Study of Liver Diseases in 1981. He is a Master of the American College of Physicians and served as President of the American College of Physicians in 1992-93. He is also a Fellow of the Royal College of Physicians of London, the Royal College of Physicians of Glasgow, and the Royal Australasian College of Physicians and Surgeons. Dr. Maddrey was named the Adelyn and Edmund M. Hoffman Distinguished Chair in Medical Science in 1998. Dr. Maddrey was awarded the George Stuart Outstanding Teacher Award at The Johns Hopkins University School of Medicine and the Christian R. and Mary F. Lindback Award for distinguished teaching in the clinical sciences at Jefferson Medical College in 1986. He received the Distinguished Service Citation from Wake Forest University in 1991, and was awarded the Distinguished Educator Award by the American Gastroenterological Association in 1998. He was awarded the Distinguished Service Award of the American Association for the Study of Liver Diseases in 2000.

Presentation:
A view from an academic consultant to industry
Mitchell R. McGill, Ph.D.
Postdoctoral Fellow
Dept. of Pharmacology, Toxicology & Therapeutics
University of Kansas Medical Center

Mitch is currently a postdoctoral fellow in the laboratory of Dr. Hartmut Jaeschke. He earned his PhD at the University of Kansas Medical Center, where the purpose of his dissertation work was to translate the pathophysiology of acetaminophen (APAP) hepatotoxicity from rodent models to humans using mechanistic serum biomarkers, as well as in vitro human systems. He has authored or co-authored twenty-six papers and four book chapters.

Presentation:
Mitochondrial dysfunction biomarkers
Dr. Michael Merz is a clinical pharmacologist by training, with a main focus on drug safety during the past ten years. He worked as phase 1 investigator and Head of Phase 1 clinic for Quintiles in Freiburg, Germany, and joined Novartis Pharma in Basel, Switzerland, as Clinical Pharmacology Expert in 1998. At Novartis, he assumed responsibility as Head, Modeling and Simulation in Clinical Pharmacology, worked as Senior Medical Safety Expert in Clinical Safety and Epidemiology. He led the Systems Toxicology Section in Preclinical Safety. He has set up the company’s liver expert team in 2008 and has been leading the group since then. In addition, Dr. Merz is the project coordinator for the European Union’s IMI SAFE-T consortium, focusing on clinical qualification of liver, kidney, and vascular safety biomarkers.

Presentations:
Industry initiatives: what's new?

RUCAM or Expert Opinions --- a Debate
  Viewpoint
  Rebuttal

European IMI SAFE-T consortium: progress and challenges
Dr Sif Ormarsdottir
Chair, Hepatotoxicity Safety Knowledge Group
AstraZeneca

Dr Ormarsdottir graduated with a MD from the University of Iceland. She did her training at the University hospital in Uppsala, Sweden in Internal Medicine and Gastroenterology and Hepatology, where she then held position as a consultant. She did her PhD in medicine on research related to bone metabolism in chronic liver disease. In 2001 Sif was employed by the Medical Products Agency in Sweden as a clinical assessor/senior expert. In 2003, she moved to the Icelandic Medicines Agency and at the same time started her own private practice, which she maintained until 2010. Her regulatory work has mainly been concerned with EU centralized procedures, co-ordinated by the European Medicines Agency, EMA. Between 2004-2010 she was a member of the CHMP and the SAWP. She was the co-rapporteur for several centralized drug applications and a coordinator for a large number of scientific advices. As a member of the EWP, she was the coordinator for three regulatory guidelines in the field of gastroenterology and in 2010 she became the chair of the Gastroenterology Drafting Group at the EMA. In 2011 Sif joined AstraZeneca as a Senior Hepatotoxicity Expert and a Safety Physician. She currently chairs and is the clinical lead of the Hepatotoxicity Safety Knowledge Group at AstraZeneca.

Presentation:
A view from the pharmaceutical industry
Lana L. Pauls, MPH  
Associate Director, Executive Operations and Strategic Planning  
Office of Surveillance and Epidemiology  
U.S. Food and Drug Administration

Lana Pauls joined the Office of Surveillance and Epidemiology (OSE) as the Associate Director for Strategic Planning and Quality Management in August 2009. Her staff is responsible for long-range strategic planning, quality development and best-practice implementation as well as training within the Office.

Prior to this position in OSE, Lana was the Director of the Quality Management Staff (QMS) in the Center for Drug Evaluation and Research (CDER). Lana joined QMS in November 2000. The QMS was responsible for conducting quality assurance audits, as well as developing a quality system for the Center. She served as Acting Director from March 2002 until her selection as Director in February 2003.

Lana received her Masters degree in Public Health from the Uniformed Services University of the Health Sciences in 1993 (through an FDA-sponsored program). In 1998 she completed a year-long Excellence in Government Fellows Program with the Council for Excellence in Government (CEG).

In 2006, Lana was selected as a National Examiner for the Malcolm Baldrige National Quality Program administered by the National Institute of Standards and Technology, and completed three years as an examiner for the program. This opportunity afforded her the ability to bring additional insight about best practice in performance excellence back to the Agency.

Lana started her career with the FDA in September 1990. She served as a Project Manager for 6 years in the Division of Metabolic and Endocrine Products (DMEP) prior to being named as the Chief, Project Management Staff in the Division of Reproductive Products (DRUP). She was then named the Associate Director in DRUP, in which she served as a policy expert regarding FDAMA and PDUFA.

**Moderator:**
The Real World: Should trial subjects reflect patients to be treated?  
Session Transcript

**Presentations:**
Welcome

Results of RUCAM vs Expert Opinion Poll and discussion
Arie Regev M.D.
Chair, Liver and GI Safety Committee
Global Patient Safety
Eli Lilly & Company

Dr. Regev received his B.Sc. and M.D. degrees from the Hebrew University in Jerusalem, Israel. He completed residency in Medicine and fellowship in Gastroenterology at Rabin Medical Center and Tel Aviv University, where he continued working as attending physician and Associate Chief of Medicine. He subsequently completed clinical fellowship in Hepatology and Transplant Hepatology at the Division of Hepatology of the University of Miami, and Jackson Memorial Hospital in Miami, Florida. After his fellowship he continued working in the Division of Hepatology as full time faculty and subsequently Associate Professor of Medicine and Director of the Hepatology Fellowship Program until 2007. Dr. Regev has conducted numerous clinical trials in the field of viral hepatitis and liver transplantation. He was the principal investigator of a number of NIH funded clinical trials and has served as principal investigator on several investigator initiated and industry supported clinical trials in the area of viral hepatitis and liver transplantation. He is the author of numerous publications in major medical Journals including American Journal of Gastroenterology, Clinical Gastroenterology and Hepatology, Journal of Hepatology, Liver Transplantation, Gut, Transplantation, Proceedings in Transplantation, and Digestive Diseases and Sciences. He authored several chapters in major medical textbooks including Schiff’s Diseases of the Liver, The Clinician’s Guide to Liver Disease, Viral Hepatitis, Requisites in Gastroenterology and Advances in Internal Medicine. Dr. Regev received Teaching and Research Awards at the University of Miami as well as Tel Aviv University. He served as an active member of the Training and Clinical Policy Committee of the American Association for the Study of Liver Diseases. In January 2007 Dr. Regev joined Eli-Lilly in a Hepatology Consulting position and as Chair of the Liver and GI Safety Committee in the Global Patients Safety organization. He is currently an adjunct Associate Professor of Medicine at the Division of Gastroenterology and Hepatology of Indiana University, and he heads the Safety Advisory Hub at Eli Lilly and Company.

Moderator:
RUCAM or Expert Opinions --- a Debate
Session Transcript

Presentation:
Drug-induced hepatic steatosis/itis
Don C. Rockey, M.D., is currently a Professor of Medicine and Chairman of the Department of Medicine at the Medical University of South Carolina. His medical training (internship, residency, chief resident, fellowship) was at the University of California, San Francisco. He was Director of the Liver Center, and Hepatology at Duke University Medical Center before moving to the University of Texas Southwestern to serve as Chief of the Division of Digestive and Liver Diseases. His training has been in clinical, translational, and basic research. He maintains focused efforts in these areas, including in primary and mentoring roles.

Dr. Rockey has been involved in clinical, translational, and basic Gastroenterology and Hepatology research throughout his career. Specific research interests in the clinical arena include topics related to management strategies for common GI problems, including GI bleeding and colorectal cancer screening as well as multiple aspects of liver disease. He has performed significant basic research resulting in translating specific therapeutics from the laboratory to patients. Drug induced liver injury has become a specific research focus over the last 10 years, and Dr. Rockey has been actively involved with the ongoing DILIN network, serving as co-chair for the Causality Committee. He has further ongoing primary and collaborative projects in liver related topics ranging from management of portal hypertension and novel anti-fibrotic compounds to drug induced liver injury. In these roles he has had and maintains significant leadership positions in aspects of study conception, study design, study execution, protocol development, site coordination, data management, statistical evaluation, manuscript preparation, and communication of results.

Presentation:
RUCAM or Expert Opinions --- a Debate
Viewpoint
Rebuttal
Dr. John Michael Sauer is a toxicologist by training with over 15 years of experience in drug discovery and development. He has been responsible for leading multiple functional areas across several pharmaceutical companies. He is dedicated to bringing quantitative translational science approaches to safety assessment, as well as transforming the way we use nonclinical safety data to drive clinical study design and data interpretation.

John Michael has over 100 scientific publications in the areas of toxicology, drug metabolism, clinical pharmacology, pharmacokinetics, and pharmacology. Prior to joining C-Path in 2013, John Michael had the opportunity to play an individual contributor role at Eli Lilly where he participated in the development, registration, and commercialization of Strattera for the treatment of ADHD in children and adults, as well as supported many other discovery and development teams. He also played a pivotal leadership role in the transformation of Elan Pharmaceutical’s discovery and development strategies including the incorporation of several quantitative translational science approaches. John Michael also gained operational and management experience in the Contract Research Organization (CRO) environment as the Site Scientific Head for the Covance Chandler site in Arizona.

John Michael received his undergraduate and Master’s degree in Biomedical Sciences at Western Michigan University and his Doctorate degree in Pharmacology and Toxicology from The University of Arizona.

Presentation:
Critical Path’s Predictive Safety Testing Consortium - 10 years of progress
DILI Conference XIV
Predicting Serious Drug-Induced Liver Injury in Patients
Who Gets It? Who Doesn't? Why?

Speaker BIO & Presentation Links
In alphabetical order

John R. Senior, M.D.
Associate Director for Science
Office of Pharmacovigilance and Epidemiology
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration

John Senior is a native of Philadelphia, educated in chemical engineering at Drexel University and in physics at the Pennsylvania State University (B.S. in Physics, summa cum laude). He graduated from the School of Medicine of the University of Pennsylvania (1954), completed an internal medicine residency and clinical fellowship in gastroenterology at the Hospital of the University of Pennsylvania. He then held a National Institutes of Health Special Research Fellowship at the Massachusetts General Hospital (1959-62), where he worked out the mechanisms of intestinal absorption of fats across the small intestinal epithelial cells, and taught at the medical school of Harvard University.

He returned to Penn in 1962 to set up a Gastrointestinal Research Laboratory at the Philadelphia General Hospital, and there worked on detecting viral hepatitis after transfusion of blood, and was among the first to screen donor blood for “Australia antigen,” a marker of hepatitis B, to reduce sharply the incidence of post-transfusion hepatitis, working closely with Baruch Blumberg, awarded the Nobel Prize in Medicine in 1976 for its discovery. Senior was elected in 1969 to the Council, American Association for the Study of Liver Diseases, and became its 24th President in 1973-4. He opened a Special Treatment Unit for Alcohol-Related Disorders that provided advanced levels of medical care for 3500 patients with life-threatening medical complications of alcoholism from 1974-9.

He worked in pharmaceutical research and development, at Squibb as Director of Regulatory Projects (1979-81), then at Sterling-Winthrop Research Institute as Vice President for Worldwide Clinical Affairs (1981-4). Subsequently (1984-95), he was a consultant to pharmaceutical companies in Japan, Europe, and North America for the design, analysis, and reporting of clinical trial data for New Drug Applications.

In June 1995 he joined the Center for Drug Evaluation and Research, Food and Drug Administration as a medical reviewer for gastrointestinal drug products. In January 2000 he became Senior Scientific Advisor to the Director of the Office of Drug Safety, with special focus on the problems of detecting and attributing causality for idiosyncratic drug-induced liver injury, and is serving as Associate Director for Science, Office of Pharmacovigilance and Epidemiology in the Center for Drug Evaluation and Research.

He is an Adjunct Professor of Medicine at the School of Medicine of the University of Pennsylvania and is retired from the Navy as a Rear Admiral, Medical Corps, United States Naval Reserve, after 39 years of service (1945-84).

Presentations:
Welcome
The DILI Conferences 1999-2014
How can we reconcile inherent conflicts?
Leonard B. Seeff, MD
Hepatology Consultant, Retired

A graduate in 1961 of the University of the Witwatersrand Medical School, Johannesburg, South Africa, Dr. Seeff came to the United States in 1964 to work with Dr. Hyman J Zimmerman, then Chief of Medicine at Mt Sinai Hospital, Chicago, Ill. A year later, he moved with Dr. Zimmerman to the VA Medical Center in Washington DC to complete training in general medicine and a fellowship in GI/Hepatology. Thereafter, he initiated and coordinated 4 large-scale VA cooperative studies on post-transfusion hepatitis B and C funded by the VA, NIAID, NHLBI, and NCI. He moved to the VA Medical Center in Boston in 1968, returning to the Washington VA Medical Center in 1971 as Assistant Chief of Medicine for 8 years. He was appointed Chief of Gastroenterology and Hepatology in 1979 and Co-Director of the VA Medical Center-Georgetown University-NIH Gastroenterology & Hepatology Training Program. He continued research in viral hepatitis B and C, focusing on the natural history of the two viral diseases. In 1984, he was appointed Professor of Medicine at Georgetown University School of Medicine. In 1998, he joined NIDDK, NIH as Senior Scientist for Hepatitis Research where he helped develop and oversee several NIDDK-funded multicenter studies such as the HALT-C Trial and the Drug-Induced Liver Injury Network (DILIN), as well as organize a number of meetings and Workshops (Consensus Development Conferences on Hepatitis C, Drug-Induced Liver Injury, Complementary and Alternative Medicine and Liver Disease, Liver Cancer, HCV and the Kidney, HCV in Prisons, etc.). In 2009, he retired from the NIH but then joined the Food & Drug Administration (FDA) as a consultant in Hepatology. He is a long-time member of the American Association for the Study of Liver Disease (AASLD) where he served as Councilor-at-Large from 1997-2000 and where he has served on several committees. He is the senior author of the AASLD guidelines for the treatment of hepatitis C as well as other guidelines. His primary research interests are viral hepatitis and drug-induced liver injury. He has received a number of awards and has published over 160 articles and over 50 chapters.

Moderator:
RUCAM or Expert Opinions --- a Debate

Session Transcript

Presentation:
Subjects with active liver disease need special observation
Gyongyi Szabo, MD, PhD
Professor of Medicine, Associate Dean for Clinical & Translational Sciences
Director, Hepatology and Liver Center; Director, MD/PhD Program
University of Massachusetts, Worcester MA

I am a physician scientist with expertise in liver immunity and signal transduction. My basic and translational research focuses on the cellular and molecular mechanisms of inflammation in the liver as it relates to viral hepatitis, alcoholic can non-alcoholic steatohepatitis and progressive liver damage and repair. We study the role of endogenous and exogenous danger signals in inflammation as it relates the pathogenesis of alcoholic liver disease, HCV hepatitis and non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) using human specimens and animal models. My clinical trials are conducted in HCV, HBV infection and non-alcoholic liver disease. My expertise in innate immunity, signaling and alcoholic liver disease has been recognized nationally and internationally as reflected by numerous invitations to conferences and prestigious institutions as invited speaker and/or advisory board member. I had the honor to give the State of the-Art lecture at DDW 2009 and the Zimmerman lecture at AASLD in 2010 on innate immunity in liver disease and the keynote lecture at the Shanghai Transplantation Immunology meeting on miRNA regulation in liver disease. I served as Associate Editor of Hepatology and currently as Field Editor of Alcoholism, Clinical & Experimental Research. I am privileged to be active in the liver scientific community by participating on the NIAAA Council, organizing satellite meetings on alcohol-mediated tissue injury and by serving on the Governing Board of the AASLD as Councilor and future president.

Presentations:
Do the hepatologists (AASLD) have any answers?
Sting-IRF# pathway for apoptosis in early alcoholic injury
Dr. Robert Temple was recently appointed Deputy Center Director for Clinical Science of FDA’s Center for Drug Evaluation and Research and is also Acting Director of the Office of Drug Evaluation I (ODE-I). He has served in this capacity since the office’s establishment in 1995. Dr. Temple received his medical degree from the New York University School of Medicine in 1967. In 1972 he joined CDER as a review Medical Officer in the Division of Metabolic and Endocrine Drug Products. He later moved into the position of Director of the Division of Cardio-Renal Drug Products. In his current position, Dr. Temple oversees ODE-1 which is responsible for the regulation of cardio-renal, neuropharmacologic, and psychopharmacologic drug products. Dr. Temple has a long-standing interest in the design and conduct of clinical trials and has written extensively on this subject, especially on choice of control group in clinical trials, evaluation of active control trials, trials to evaluate dose-response, and trials using “enrichment” designs.

**Moderator:**
The Real World: Should trial subjects reflect patients to be treated?

[Session Transcript](#)

**Presentation:**
[A view from the medical regulatory side](#)
DILI Conference XIV
Predicting Serious Drug-Induced Liver Injury in Patients
Who Gets It? Who Doesn't? Why?

Speaker BIO & Presentation Links
In alphabetical order

Jack Uetrecht, M.D., Ph.D.
Canada Research Chair in Adverse Drug Reactions
University of Toronto

Dr. Uetrecht is Professor of Pharmacy and Medicine and the Canada Research Chair in Adverse Drug Reactions. He received his Ph.D. in organic chemistry at Cornell University in 1972, M.D. at Ohio State University in 1975 and did his internal medical residency at the University of Kansas Medical Center from 1975-1978. He completed his clinical pharmacology fellowship in 1981 at Vanderbilt University and then joined the faculty. He moved to the University of Toronto in 1985 and was the associate dean of pharmacy from 1994 to 1998. His research is focused on the mechanisms of idiosyncratic drug reactions.

Presentation:
It’s the immune system -
Paul B. Watkins, M.D.
Director, Hamner – UNC Institute for Drug Safety

Dr. Paul B. Watkins is the Verne S. Caviness Distinguished Professor of Medicine, and also Professor of Pharmacology and Experimental Therapeutics, and Professor of Toxicology at the University of North Carolina in Chapel Hill (UNC-CH). He attended medical school at Cornell and completed his residency in internal medicine at New York Hospital-Cornell Medical Center. He received subspecialty training in hepatology at the Medical College of Virginia. He was on faculty at the University of Michigan from 1986-1999 when he moved to North Carolina. There he became the Director of the General Clinical Research center and more recently director of the UNC Translational and Clinical Sciences (TraCS) Institute. In June of 2009, he became the director of a new Institute for Drug Safety Sciences which represents a collaboration between UNC-CH and The Hamner Institutes. The Hamner Institutes is a not-for-profit organization based in Research Triangle Park. It was formerly called the Chemical Institute for Industrial Toxicology [CIIT] and has a three decade history of leading research into the health effects of environmental chemicals. Dr. Watkins is an accomplished basic and translational investigator in the fields of drug metabolism and hepatotoxicity. He is one of the most frequently cited authors in the field of pharmacology according to www.ISIhighlycited.com. He serves as the chair of both the Steering and Genetics Committees for the national Drug Induced Liver Injury Network (DILIN) (U01DK065201).

Moderator:
What new and useful biomarkers (and predictors) are out there?
Session Transcript

Presentations:
Academic research breakthroughs – will biomarkers do it?
Lessons from healthy volunteers
Presentation of eDISH Plaque to John R. Senior
Janet Woodcock, MD  
Director of the Center for Drug Evaluation and Research  
Food and Drug Administration

Janet Woodcock is Director of the Center for Drug Evaluation and Research (CDER), at the Food and Drug Administration (FDA). Dr. Woodcock first joined CDER in 1994. For three years, from 2005 until 2008, she served FDA’s Commissioner, holding several positions, including as Deputy Commissioner and Chief Medical Officer, Deputy Commissioner for Operations, and Chief Operating Officer. Her responsibilities involved oversight of various aspects of scientific and medical regulatory operations. Before joining CDER, Dr. Woodcock served as Director, Office of Therapeutics Research and Review, and Acting Deputy Director in FDA’s Center for Biologics Evaluation and Research. Dr. Woodcock received her M.D. from Northwestern Medical School and completed further training and held teaching appointments at the Pennsylvania State University and the University of California in San Francisco. She joined FDA in 1986.

Presentations:

CDER Outstanding Service Award presented to John R. Senior

Launching the Critical Path Initiative: intents, consequences
Kyunhee Yang, M.S., is a Ph.D. student in the Division of Pharmacotherapy and Experimental Therapeutics of the UNC Eshelman School of Pharmacy. She received her B.S. in pharmacy and M.S. in pharmacokinetics from Seoul National University, South Korea. She then worked as a research specialist at UIC College of Pharmacy for two years, and joined the Pharmaceutical Sciences program at the University of North Carolina at Chapel Hill in 2010. Her research focuses on investigating the mechanisms of drug-induced liver injury that involves transporter-mediated drug-bile acid interactions and developing a mechanistic model to predict DILI liability of drugs under the guidance of Dr. Kim Brouwer. She joined the DILI-sim modeling team in 2011, and works on the computational modeling of drug-induced liver injury regarding interference of bile acid transport by the hepatotoxic drugs. In 2013, she was awarded Amgen Predoctoral Fellowship. As a result of her doctoral research, she earned travel awards and gave podium presentations for the 2011 AAPS Workshop on Drug Transporters in ADME: From the Bench to the Bedside and 2013 RTP DMDG Winter Symposium. Her abstract on mechanistic modeling of troglitazone-mediated hepatotoxicity was selected for a podium presentation at ASCPT 2014 Annual Meeting.

**Presentation:**

*Modeling for susceptibility factors*