

**Program, Ides of March 2012**  
**Why DILI Idiosyncrasy? The Immune System and Beyond ...**  
**Why Do Only A Few People Show Serious Liver Dysfunction**  
**From Drugs That Nearly Everybody Else Can Tolerate or Adapt To?**

*DILI is still a major problem for drug development, and a clinical concern after marketing. We need new biomarkers, new understanding, and a path forward to solve the problems. This academic-industry-government international conference will discuss new findings and thinking about drug-induced liver injury (DILI), including presentations by experts in clinical hepatology, toxicology, and other fields, and discussion with all registrants. Come and participate in this conference.*

Organizers: **John R. Senior and Lana Pauls, with advice from**  
**Mark Avigan, Robert Fontana, Christine Hunt, Michael Merz, Arie Regev, Leonard Seeff, Paul Watkins**

National Labor College (NLC), Silver Spring MD, 14-15 March 2012  
10000 New Hampshire Avenue at Powder Mill Road, Silver Spring MD 20903

**Wednesday, 14 March 2012**

7:30 *Continental Breakfast outside the conference room*

8:15 Introductions and Brief Opening Statements

**Stephen Spielberg, FDA**  
**Carolyn Compton, CPI**  
**Paul Watkins, AASLD**

8:35 **Session I: How and why do people respond differently to the same drug?**

Moderators: Paul Watkins and Leonard Seeff

**Session IA: Are there dose-related and idiosyncratic hepatotoxic drugs?**

8:35 What are differences between pre- and post-marketing data?

8:50 What is idiosyncrasy anyway? Is it dose-related?

9:10 Comments by Advisors – 3-4 ' each

9:35 Open discussion

**L. Pauls, CDER**  
**J. Senior, CDER**  
**The Seven Advisors**  
All registrants present

10:00 *Break*

**Session IB: What may explain the different ways people respond?**

10:30 It's the genome -

10:50 Not the inherited genome but epigenetic variations -

11:10 It's the immune system -

11:30 General discussion – panel of speakers above, audience

12:00 *Lunch*

1:00 **Session II: Lessons to learn from**

Moderators: Bob Fontana and Christine Hunt

**Session IIA: Examples to make us think**

1:00 GWAS in DILI: promises and pitfalls

1:15 Lumiracoxib –can it be reborn by HLA typing?

1:30 iPS cells and patient-specific hepatocyte cultures

1:45 A fresh look at isoniazid hepatotoxicity

2:00 General discussion

2:30 *Break*

**Session IIB: Focus on the patients**

3:00 Is it autoimmune hepatitis or DILI?

3:20 Why and how are biologics different than drugs?

3:40 Are children not just little adults in how they respond?

4:00 Plasticity of the transcriptome in autism

4:20 General discussion – panel of speakers above, audience

5:00 *Reception: wine and cheese, mingle and relax ---*

6:00 *dinner on your own, but maybe not too far away, so you may join the debate*

**Matt Nelson, GSK**  
**Igor Koturbash, NCTR/FDA**  
**Gyongyi Szabo, U Mass**  
Panel; All

**Robert Fontana, U MI**  
**Lloyd Klickstein, Novartis**  
**Ed LeCluyse, Hamner-U NC**  
**Jack Uetrecht, U Toronto**  
Speakers and audience

**Keith Lindor, U AZ State**  
**Ross Pierce, CBER**  
**Heide Stirnadel, GSK**  
**Mark Alter, U PA**  
Panel; All

**Session IIC: Revise the guidance on Drug-Induced Liver Injury?**

Moderators: Michael Merz, Christine Hunt, and John Senior

7 – 9 Open discussion of proposals for revision of FDA guidance July 2009

*Main meeting room*

## Thursday, 15 March 2012

7:30 *Continental Breakfast outside the conference room*

### 8:00 **Session III: What new and useful biomarkers (and predictors) are out there?**

Moderators: Mark Avigan and Arie Regev

#### **Session IIIA: New biomarkers for DILI**

8:00 Key features for biomarkers we need

8:20 Animal models of idiosyncratic DILI

8:40 Serum miRNA markers for human DILI

9:00 Another death protein – secretory phospholipase A2

9:20 General discussion – speakers and audience

10:00 *Break*

**Mark Avigan, CDER/FDA**

**Robert Roth, U MI**

**Jonathan Moggs, Novartis**

**Hari Mehendele, U LA Monroe**

All

#### **Session IIIB: What else is new?**

10:20 How can we break the logjam for predictive biomarkers?

10:40 Other side of the coin – cancer chemotherapy resistance

11:00 New liver biomarkers under study in Europe

11:20 Liver test variations in healthy people

11:40 Sharing information, asking questions – liver data warehouse?

12:00 General discussion – speakers and audience

12:30 *Lunch*

**Arie Regev, Lilly**

**Michael Gottesman, OD/NIH**

**Michael Merz, Novartis**

**Xiwu Lin, GSK**

**Paul Watkins, Hamner-U NC**

All

### 1:30 **Session IV: The Real World: Should trial subjects reflect patients to be treated?**

Moderators: Bob Temple and John Senior

1:30 How can we reconcile inherent conflicts?

1:50 Subjects with active liver disease need special observation

2:10 A view from an academic consultant to industry

2:30 A view from the pharmaceutical industry

2:50 A view from the medical regulatory side

3:10 General discussion – speakers and audience

3:30 *Adjourn*

**John Senior, CDER/FDA**

**Leonard Seeff, FDA/SGE**

**Eugene Schiff, U Miami**

**Sif Ormarsdottir, AstraZeneca**

**Robert Temple, CDER/FDA**

All

The program is co-sponsored by the Food and Drug Administration/Center for Drug Evaluation and Research (FDA/CDER), the Critical Path Institute (C-Path), and the Pharmaceutical Research and Manufacturers of America (PhRMA).

The program is endorsed by the National Institutes of Health (NIH) drug-induced liver injury network (DILIN), and the American Association for the Study of Liver Disease (AASLD).

Copies of slides shown, and transcripts of speakers' comments and discussions will be posted on the internet a few weeks after the conference.

*For previous programs go to the following websites:*

[www.fda.gov](http://www.fda.gov) (type **liver toxicity** into search window, click on first entry, and page down)

or to [www.aasld.org](http://www.aasld.org) → Training/Education, Drug-Induced Liver Injury 2011 Program

*Registration by Critical Path Institute: \$550 for industry; \$275 for government or academia  
Make lodging reservations on your own at NLC [www.nlc.edu](http://www.nlc.edu) (click on Conference Services, then ;  
Events/Guests/Registration, then "Book Online")*

