Interact with Senior FDA Members to Explore Emerging Issues in Cardiovascular Safety and Diabetic Drug Development.

The development of Type 2 diabetic (T2DM) medications has been significantly impacted by recent data suggesting possible increases in cardiovascular (CV) risk associated with the use of aggressive glucose control with insulin or certain oral medications to treat T2DM.

In 2008, the Division of Metabolism and Endocrinology Products of the US Food and Drug Administration (FDA) adopted a new regulatory guidance stating that all new T2DM drugs must demonstrate CV safety in appropriately designed and powered outcome studies. The European Medicines Agency (EMA) released a similar draft guidance in 2010. These new guidances have resulted in the evolution of a variety of different approaches to the development of medications to treat Type 2 Diabetes Mellitus.

This two-day conference will examine:

- Diabetic Drugs and CV Risk: Optimal Clinical Trial Designs
- Diabetes Mellitus Regulatory Guidances: Current Experience
- Post-marketing Assessment
- Preclinical Testing to Evaluate CV Risk and Mechanistic Considerations
- Biomarkers, Pharmacogenomics and Collaborative Efforts
- Efficient Drug Development – Is the Future Outcome Trials for All CV/Metabolic Medications?

WHO SHOULD ATTEND

- Pharmaceutical executives
- Pharmaceutical cardiac safety experts
- Clinical diabetology experts
- Clinical epidemiology experts
- Pharmaceutical physicians
- Regulatory affairs specialists
- Pharmacovigilance specialists
- Clinical drug safety specialists
- Biostatisticians and data managers
- Project teams working in endocrine/metabolic areas
- Clinical investigators working in endocrine/metabolic areas
- Preclinical safety experts
- Biomarker professionals

Conference Contact Information
Benjamin Zaitz, Program Manager, Phone: +1.215.293.5803 / Fax +1.215.442.6199 / email: Benjamin.Zaitz@diahome.org
CONTINUING EDUCATION CREDITS

Accreditation Council for Continuing Medical Education

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Postgraduate Institute for Medicine (PIM) and the Drug Information Association. PIM is accredited by the ACCME to provide continuing medical education for physicians.

PIM designates this educational activity for a maximum of 14.75 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Drug Information Association is accredited by the Accreditation Council for Pharmacy Education as a Provider of continuing pharmacy education. This program is designated for 14.75 contact hours or 1.475 continuing education units (CEUs). 286-000-10-036-L04-P

Type of Activity: Knowledge

Drug Information Association has been approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 8405 Greensboro Drive, Suite 800, McLean, VA 22102; (703) 506-3275.

Drug Information Association is authorized by IACET to offer 1.5 CEUs for this program.

PLEASE NOTE: Continuing education credits are not available for the presentation, “Quantitative 3-dimensional Electrocardiography Substantially Improves Diagnosis of Acute Coronary Syndromes in Type II Diabetic Patients,” in Session 4 on Tuesday, October 5.

Disclosure of Conflicts of Interest

PIM and the Drug Information Association require instructors, planners, managers and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by PIM for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. If you would like to receive a statement of credit, you must attend the program, scan your name badge at the DIA registration desk each day of the program, and complete the on-line credit request process through My Transcript at www.diahome.org. Participants will be able to download a statement of credit upon successful submission of the credit request.

LEARNING OBJECTIVES: At the conclusion of this conference, participants should be able to:

• Summarize the evidence for cardiovascular risk with new and existing T2DM drugs
• Recognize the current and evolving regulatory initiatives for CV safety of T2DM drugs
• Discuss how new regulations will impact clinical development of new T2DM drugs
• Evaluate scientific data including preclinical and clinical sources, pre- and post- marketing strategies, and other sources to drive future efforts to develop efficient approaches to the development of T2DM drugs.
• Identify approaches to assure definition of CV safety in development of T2DM drugs.

Unless otherwise disclosed, DIA acknowledges that the statements made by speakers are their own opinion and not necessarily that of the organization they represent, or that of the Drug Information Association. Speakers and agenda are subject to change without notice. Recording of any DIA tutorial/workshop information in any type of media, is prohibited without prior written consent from DIA.

DAY 1 | MONDAY, OCTOBER 4, 2010

4:00-6:00 PM REGISTRATION

DAY 2 | TUESDAY, OCTOBER 5, 2010

7:00-8:00 AM REGISTRATION AND CONTINENTAL BREAKFAST

8:00-8:15 AM WELCOME AND OPENING REMARKS

Philip T. Sager, MD, FACC, FAHA
Pharmaceutical Consultant, USA
Chair, Scientific Oversight Committee
Cardiac Safety Research Consortium

8:15-8:45 AM SESSION 1

Plenary Lecture: CV Safety and Drug Development

SESSION CHAIRPERSON

Philip T. Sager, MD, FACC, FAHA

Douglas C. Throckmorton, MD
Deputy Director, Regulatory Programs
Office of the Center Director
CDER, FDA

8:45-9:45 AM SESSION 2

Preclinical Testing to Evaluate CV Risk and Mechanistic Considerations

SESSION CHAIRPERSON

Borje Darpo, MD, PhD
Associate Professor of Cardiology, Pharmaceutical Consultant, Sweden

Preclinical Safety Testing for CV Risk - What Safety Issues Are and Are Not Identified by S7A/S7B Studies (20 min)

Peter Hoffmann, MD, PhD
Executive Director Preclinical Safety
Translational Cardiovascular Advisory Team
Novartis Pharmaceuticals Corporation
Nonclinical Cardiovascular Safety of Novel Diabetes Therapies: Assessing CV Safety Through Improvements in CV Endpoints (20 min)
Nick Edmunds, PhD
Cardiovascular Discipline Leader, Global Safety Pharmacology Pfizer Global Research and Development, UK

Potential Mechanisms of CV Risk Associated with Diabetic Medications and Treatment (20 min)
Jeri El Hage, PhD
Regulatory Toxicology Consultant Aclairo Pharmaceutical Development Group

9:45-10:15 AM REFRESHMENT BREAK

10:15 AM-12:15 PM SESSION 3
Diabetic Drugs and CV Risk
SESSION CHAIRPERSON
Norman Stockbridge, MD, PhD
Director, Division of Cardiovascular and Renal Products Office of Drug Evaluation I, Office of New Drugs CDER, FDA

- Diabetic Medications and Microvascular Benefits of Glycemic Control (20 min)
  Stephen Clement, MD
  Associate Professor, Department of Medicine
  Interim Chief of the Division of Endocrinology and Metabolism
  Director of the Georgetown Diabetes Center
  Georgetown University Medical Center

- Increased CV Clinical Risk Associated with Diabetic Medications - Implications of Large Trials Including Accord, Advance and Approach (20 min)
  Yves D. Rosenberg, MD, MPH
  Program Director, Acting Branch Chief Atherothrombosis and Coronary Artery Disease Branch Division of Cardiovascular Sciences National Heart, Lung and Blood Institute

- Diabetic Medications - CV Safety and Benefit Risk Considerations (20 min)
  Allison B. Goldfine, MD
  Head, Section of Clinical Research Joslin Diabetes Center

- Panel Discussion (60 min)

Should Future Diabetic Drug Development Focus on Reducing CV Outcomes and Not Just Glycemic Control?
All Session Speakers and
Philip T. Sager, MD, FACC, FAHA
Mary Parks, MD
Borje Darpo, MD, PhD

12:15-12:45 PM SESSION 4
Abstract Presentations
SESSION CHAIRPERSON
Norman Stockbridge, MD, PhD

Adaptive Decision Making for CV Outcomes in Diabetic Drug Development
Deborah Shapiro, DrPH
Senior Director, Late Development Statistics Biostatistics and Research Decision Sciences Merck Research Laboratories

Quantitative 3-dimensional Electrocardiography Substantially Improves Diagnosis of Acute Coronary Syndromes in Type II Diabetic Patients
Ihor Gussak, MD, PhD, FACC
Vice President and Chief Medical Officer NewCardio, Inc.

12:45-1:45 PM LUNCHEON

1:45-3:00 PM SESSION 5
Diabetes Mellitus Regulatory Guidances: Current Experience
SESSION CHAIRPERSON
Mary Parks, MD
Director
Division of Metabolism and Endocrinology Products Office of Drug Evaluation II, Office of New Drugs CDER, FDA

- Commentary on FDA Diabetes Mellitus Regulatory Guidance (5 min)
  Mary Parks, MD

- HbA1c as an Endpoint for T2DM Approval and Key Aspects of the FDA Diabetes Mellitus Regulatory Guidance (25 min)
  Hylton V. Joffe, MD, MMSc
  Lead Medical Officer, Diabetes Drug Group I Division of Metabolism and Endocrinology Products Office of New Drugs CDER, FDA

- Responses/Reactions to the FDA Guidance and Preliminary Lessons Learned (25 min)
  Ilan Irony, MD
  Clinical Team Leader Division of Metabolism and Endocrinology Products Office of New Drugs CDER, FDA

- EMEA Draft Guidance (20 min)
  Kristina Dunder, MD, PhD
  Clinical Assessor, Senior Expert Alternate CHMP Member Medical Products Agency, Sweden
3:30-5:00 PM SESSION 5 CONTINUED

Diabetes Mellitus Regulatory Guidances: Current Experience

SESSION CHAIRPERSON
Mary Parks, MD

Regional Variations in Regulatory Guidances for CV Safety of T2DM Drugs and Their Implications for Drug Development (20 min)
Boaz Mendzelevski, MD
Vice President, Cardiology
CoreLabs Partners, Inc

Sponsors Viewpoint – The T2DM Regulatory Guidances and Implications for Drug Development (30 min)
Anders Svensson, MD, PhD
Head of Global Clinical Development – Metabolism
F. Hoffmann-La Roche Ltd., Switzerland

Panel Discussion (40 min)
All Session Speakers and
Robert J. Temple, MD

5:00-5:30 PM SESSION 6

Efficient Drug Development – Is the Future Outcome Trials for All CV/Metabolic Medications?

SESSION CHAIRPERSON
Norman Stockbridge, MD, PhD

Robert J. Temple, MD
Deputy Center Director for Clinical Science
CDER, FDA

5:30 PM END OF DAY 1

5:30-6:30 PM NETWORKING RECEPTION

DAY 3 | WEDNESDAY, OCTOBER 6, 2010

7:00-7:45 AM REGISTRATION AND CONTINENTAL BREAKFAST

7:45-11:00 AM SESSION 7

Clinical Trials

SESSION CHAIRPERSON
Philip T. Sager, MD, FACC, FAHA

MACE Definitions for Clinical Diabetes Trials (20 min)
Kenneth William Mahaffey, MD
Associate Professor, Medicine
Co-Director, Cardiovascular Research
Medical Director, Clinical Events Classification (CEC) Group
Duke Clinical Research Institute

State of the Art Outcome Adjudication Processes (20 min)
Jonathan Goldman, MD, FACC
Executive Vice President Strategic Programs
ICON Clinical Research

Strengths/Limitations of Different Clinical Sources of Evidence for Drug Safety in Pharmacologic Treatments of Type 2 DM – Controlled Clinical Trials, Observational Data, Meta-Analysis (25 min)
Dean Follmann, PhD
Assistant Director for Biostatistics, NIAID
Chief Biostatistics Research Branch
National Institute of Allergy and Infectious Diseases

Statistical Considerations, Including Using Composites, “Early Looks,” Meta Analyses, and Novel Approaches for Diabetes Trials (30 min)
Georgina Bermann, PhD
Senior Expert Statistician, Metabolic Science Unit
Novartis Pharma AG

Case Examples from Sponsors of Novel Trial Designs and Novel Future Possible Approaches (30 min)
J. Todd Sahliroot, PhD
Deputy Director and Team Leader
Office of Translational Sciences, Office of Biostatistics
CDER, FDA

Design of Phase 3 Clinical Trials (20 min)
Shamik J. Parikh, MD
Executive Director, Clinical Development, CV/GI
AstraZeneca

How Can We Improve CV Risk Assessment in Clinical Trials with Anti-diabetics Drugs (20 min)
Mary Jane Geiger, MD, PhD, FACP
Senior Medical Advisor, Diabetes Business Unit
Eli Lilly & Company

Panel Discussion (30 min)
All Session Speakers
Clinical Trials
SESSION CHAIRPERSON
Norman Stockbridge, MD, PhD

Going Beyond Glycemic Control: How to Make Good Choices for My Patients (30 min)
Abraham Thomas, MD, MPH
Division of Endocrinology
Henry Ford Hospital System

Debate: There is Clear and Convincing Evidence for Increased Cardiovascular Risk Associated with Rosiglitazone (40 min)

PRO Argument
Steven Nissen, MD, MACC
Chairman, Department of Cardiovascular Medicine
Professor of Medicine, Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Cleveland Clinic

CON Argument
Sanjay Kaul, MD, FACC, FAHA
Director, Cardiovascular Diseases Fellowship Training Program
Cedars-Sinai Heart Institute
Professor of Medicine, Cedars-Sinai Medical Center and Geffen School of Medicine at UCLA

FDA Commentary (10 min)
Mary Parks, MD

Panel Discussion (40 min)
All Session Speakers

Post-marketing Assessment
SESSION CHAIRPERSON
Mary Parks, MD

Advances in Post-marketing Risk Assessment - The Sentinel Effort and Other Novel Strategies (20 min)
Judith Racoosin, MD, MPH
Sentinel Initiative Scientific Lead
Office of the Commissioner
FDA

Cardiovascular Risk Assessment of the Liraglutide Clinical Program and the Design of the LEADER Trial (20 min)
Marcin Jan Zychma, MD, PhD
International Medical Director
Medical and Science, GLP-1 Development
Global Development
Novo Nordisk, Poland

Abstract Presentations
SESSION CHAIRPERSON
Borje Darpo, MD, PhD

Implementing the Large Simple Trial and Appropriate Technologies to Efficiently Evaluate Cardiovascular Safety of Chronic Therapies
Alexander Fleming, MD
President and CEO
Kinexum, LLC

How Using Online Endpoint Adjudication System (EAS) Technology Optimizes the Entire CV Endpoint Assessment Process
Zaher El-Assi
Vice President, Global Sales & Strategic Partnerships
KIKI Clinical Solutions

Collaborative Efforts
SESSION CHAIRPERSON
Borje Darpo, MD, PhD

CSRC Collaborative Efforts and Diabetes Efforts (20 min)
Mitchell W. Krucoff, MD, FACC, FAHA
Professor, Medicine/Cardiology
Director, Cardiovascular Devices Unit
Director, eECC Core Laboratory
Duke University Medical Center/Duke Clinical Research Institute

Panel Discussion (30 min)
All Speakers from Sessions 8 and 10

3:20-3:30 PM CLOSING REMARKS
Philip T. Sager, MD, FACC, FAHA
Borje Darpo, MD, PhD
Mary Parks, MD
Norman Stockbridge, MD, PhD

3:30 PM CONFERENCE ADJOURNED
**REGISTRATION FORM**

Register online or fax this page to +1.215.442.6199

---

**Development of Type 2 Diabetes Mellitus Drugs: State of the Art Cardiovascular Safety Assessments**

Event #10035 • October 5-6, 2010
L’Enfant Plaza Hotel, Washington, DC 20024, USA

---

**Event Information**
Contact Benjamin Zaitz, Program Manager, Phone +1.215.293.5803
Fax +1.215.442.6199, email Benjamin.Zaitz@diahome.org

---

**Registration Fees**
Registration fee includes refreshment breaks, luncheons, and reception (if applicable), and will be accepted by mail, fax, or online.

- **Industry Fee**
  - US $1295

- **Join DIA now to save on future events and to receive all the benefits of membership**
  - Membership US $140

- **Discount Fees**
  - Government (Full-time) US $390
  - Charitable Nonprofit/Academia (Full-time) US $650

---

**Payment Options:**
Register online at www.diahome.org or check payment method.

- **CREDIT CARD**
  - number may be faxed to: +1.215.442.6199. You may prefer to pay by check or bank transfer since non-U.S. credit card payment will be subject to the currency conversion rate at the time of the charge.

- **CHECK**
  - drawn on a U.S. bank payable to and mailed along with this form to: Drug Information Association Inc. P.O. Box 95000-1240, Philadelphia, PA 19195-1240, USA. Please include a copy of this registration form to facilitate identification of attendee.

- **BANK TRANSFER**
  - When DIA completes your registration, an email will be sent to the address on the registration form with instructions on how to complete the Bank Transfer. Payment should be made in US dollars. Your name and company, as well as the Event I.D. # must be included on the transfer document to ensure payment to your account.

---

**Participants with Disabilities:** DIA event facilities and overnight accommodations are accessible to persons with disabilities. Services will be made available to sensory-impaired persons attending the event if requested at least 15 days prior to event. Contact the DIA office to indicate your needs.

---

**TRAVEL AND HOTEL**
The most convenient airport is Reagan National Airport or Washington Dulles International Airport and attendees should make airline reservations as early as possible. The L’Enfant Plaza Hotel is holding a block of rooms at the reduced rate below until September 10, 2010, for the DIA event attendees. Room availability at this rate is guaranteed only until this date or until the block is filled.

- **Single $229**
- **Double $229**

Attendees must make their own hotel reservations. Contact the L’Enfant Plaza Hotel by telephone at +1.800.635.5065 and mention the DIA event. The hotel is located at 480 L’Enfant Plaza, SW, Washington, DC 20024, USA.

**CANCELLATION POLICY:**
On or before **SEPTEMBER 28, 2010**
Administrative fee that will be withheld from refund amount:
- Member or Nonmember = $200
- Government or Academy or Nonprofit (Member or Nonmember) = $100
- Tutorial (if applicable) = $50

Cancellations must be in writing and be received by the cancellation date above. Registrants who do not cancel by that date and do not attend will be responsible for the full registration fee paid. Registrants are responsible for canceling their own hotel and airline reservations. You may transfer your registration to a colleague at any time but membership is not transferable. Please notify DIA of any such substitutions as soon as possible. Substitute registrants will be responsible for nonmember fee, if applicable.

DIA reserves the right to alter the venue, if necessary. If an event is cancelled, DIA is not responsible for any airfare, hotel or other costs incurred by registrants.

---

**Please check the applicable category:**

- **Academia**
- **Government**
- **Industry**
- **CSO**
- **Student**
  - (Call for registration information)

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>M.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degrees</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dr.</td>
<td>Mr.</td>
</tr>
<tr>
<td></td>
<td>Ms.</td>
<td></td>
</tr>
<tr>
<td>Job Title</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Company</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address</th>
<th>(As required for postal delivery to your location)</th>
<th>Mail Stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>City</td>
<td>State</td>
<td>Zip/Postal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Email</th>
<th>Required for confirmation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phone Number</td>
<td>Fax Number</td>
<td>Required for confirmation</td>
</tr>
</tbody>
</table>