

**FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)  
Joint Meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Drug Safety and  
Risk Management Advisory Committee  
Gaithersburg Holiday Inn, Two Montgomery Village Avenue, Gaithersburg, Maryland**

**AGENDA**

**July 30, 2007**

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*The Committees will discuss the cardiovascular ischemic/thrombotic risks of the thiazolidinediones, with focus on rosiglitazone, as presented by the FDA and GlaxoSmithKline.*

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8:00 a.m.	Call to Order and Introductions	<b>Clifford J. Rosen, M.D.</b> (Acting) Committee Chair
8:05 a.m.	Conflict of Interest Statement	<b>LCDR Cathy A. Miller, M.P.H.</b> Designated Federal Official Endocrinologic and Metabolic Drugs Advisory Committee
8:10 a.m.	Introduction/Background	<b>Mary H. Parks, M.D.</b> Director, FDA/CDER Division of Metabolism and Endocrine Products

**PRESENTATIONS:**

**Guest Speaker Presentation:**

8:15 a.m.	Achieving Diabetes Targets: Where Are We and How Can We Do Better?	<b>Robert E. Ratner, M.D.</b> Vice-President of Scientific Affairs MedStar Research Institute Washington, DC
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**GlaxoSmithKline Presentations:**

8:35 a.m.	Introduction	<b>Ronald L. Krall, M.D.</b> Senior Vice President and Chief Medical Officer GlaxoSmithKline
	Review of Data	<b>Murray W. Stewart, D.M., FRCP</b> Vice President, Clinical Development GlaxoSmithKline
	Conclusions	<b>Ronald L. Krall, M.D.</b>

9:50 a.m. **Clarifying Questions from the Committee**

10:05 a.m. **Break**

**FDA Presentations:**

10:15	FDA Meta-Analysis	<b>Joy D. Mele, M.S.</b> Statistician, FDA/CDER Office of Biostatistics, Division of Biometrics II
	Overview of Large, Long-Term, Prospective Trials of Thiazolidinediones	<b>Karen M. Mahoney, M.D.</b> Medical Officer, FDA/CDER Division of Metabolism Endocrine Products

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**Page 2**

**NIH Speaker Presentation:**

Use of Rosiglitazone in the  
Bypass Angioplasty Revascularization  
Investigation (BARI) 2 Diabetes Trial

**David J. Gordon, M.D., Ph.D.**  
Division of Cardiovascular Diseases  
National Institute of Health (NIH)  
National Heart, Lung and Blood Institute

**FDA Presentations (Continued):**

Observational Studies: Effect of  
Anti-Diabetic Agent Choice on  
Cardiovascular Morbidity and  
Mortality in Type II Diabetes Mellitus

**Kate Gelperin, M.D., M.P.H.**  
Medical Officer, FDA/CDER Office of Surveillance and  
Epidemiology, Division of Drug Risk Evaluation

Assessment of Cardiovascular Risks  
And Health Benefits of  
Rosiglitazone

**David Graham, M.D., M.P.H.**  
FDA/CDER Associate Director for Science and Medicine  
Office Surveillance and Epidemiology

Conclusions and Summary

**Robert Meyer, M.D.**  
Director, FDA/CDER Office of New Drug Evaluation II

**Gerald Dal Pan, M.D., M.H.S.**  
Director, FDA/CDER Office of Surveillance and Epidemiology

12:00 p.m.

**Lunch**

1:00 - 2:30 p.m.

**Open Public Hearing**

2:30 p.m.

**Questions to the FDA/Discussion**

3:15 p.m.

**Break**

3:30 p.m.

**Questions to the Committee**

5:00 p.m.

**Adjourn**

# PUBLIC CONDUCT DURING FDA ADVISORY COMMITTEE MEETINGS SUMMARY SHEET

The FDA would like to ensure that advisory committee meetings proceed in an orderly fashion, are conducted in a safe and secure environment, that the right of free speech is protected, and that the ability of FDA Advisory Committees and Panels to accomplish their objectives is not disrupted. Therefore, the following procedures will be followed:

- An interested person who wishes to be assured of the right to make an oral presentation during the Open Public Hearing portion of an advisory committee meeting should register with FDA before the meeting. See 21 CFR 14.29(b). Those who have not registered before the meeting will only be invited to speak at the discretion of the Chair, and should submit their request to FDA officials at the registration desk on the day of the meeting.
- Open Public Hearing participants who are designated to speak may be questioned only by the Chair or other members of the Committee.
- Audience members may not present comments or questions to the Committee unless recognized by the Chair.
- Attendees may be subject to security screening, such as presenting identification, passing through metal detectors, and inspection of briefcases, packages, etc.
- Attendees at the meeting are asked to maintain order and not display behavior that is disruptive to the meeting (i.e., shouting from the audience, loud outbursts).
- The committee Chair or Designated Federal Official will note on the record any disruptive behavior and will ask the person to cease the behavior or else leave the meeting room.
- We ask that attendees not approach the advisory committee table area before, during, or after the meeting without permission from a Designated Federal Official/Executive Secretary.

**Endocrinologic and Metabolic Drugs Advisory Committee and the  
Drug Safety and Risk Management Advisory Committee**

**July 30, 2007**

**Holiday Inn Gaithersburg  
Gaithersburg, Maryland**

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Meeting Roster

**ENDOCRINOLOGIC AND METABOLIC DRUGS ADVISORY COMMITTEE MEMBERS  
(Voting)**

Kenneth D. Burman, M.D.  
Chief, Endocrine Section  
Washington Hospital Center  
Washington, District of Columbia

Katherine M. Flegal, Ph.D.  
Senior Research Scientist  
Distinguished Consultant  
National Center for Health Statistics  
Centers for Disease Control and Prevention  
Hyattsville, Maryland

Jessica W. Henderson, Ph.D.  
Associate Professor, Division of Health and  
Physical Education  
Western Oregon University  
Monmouth, Oregon

Clifford J. Rosen, M.D. [Acting Chair]  
Senior Staff Scientist  
Maine Center for Osteoporosis  
St. Joseph Hospital  
Bangor, Maine

**DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE MEMBERS  
(Voting)**

Sean Hennessy, Pharm.D., Ph.D.  
Assistant Professor of Epidemiology  
University of Pennsylvania School of  
Medicine  
Philadelphia, Pennsylvania

Judith M. Kramer, M.D., M.S.  
Associate Professor of Medicine  
Division of General Internal Medicine and  
Clinical Pharmacology  
Duke University Medical Center  
Durham, North Carolina

Timothy S. Lesar, Pharm.D.  
Director of Pharmacy  
Albany Medical Center  
Albany, New York

**TEMPORARY MEMBERS (Voting)**

Ruth S. Day, Ph.D.  
Director, Medical Cognition Laboratory  
Duke University  
Durham, North Carolina

Judith Fradkin, M.D.  
Director, Division of Diabetes, Endocrinology  
& Metabolic Diseases  
NIDDK, National Institutes of Health  
Bethesda, Maryland

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**Meeting Roster**

**TEMPORARY MEMBERS (Voting)  
(Continued)**

Nancy L. Geller, Ph.D.  
Director, Office of Biostatistics Research  
NHLBI, National Institutes of Health  
Bethesda, Maryland

Allison Goldfine, M.D.  
Investigator and Assistant Director of Clinical  
Research Section  
Joslin Diabetes Center  
Boston, Massachusetts

Eric S. Holmboe, M.D., F.A.C.P.  
Vice President for Evaluation Research  
Director, Clinical Performance Services  
American Board of Internal Medicine  
Philadelphia, Pennsylvania

Rebecca W. Killion  
Patient Representative  
Bowie, Maryland

Arthur A. Levin, M.P.H.  
Director, Center for Medical Consumers  
New York, New York

Arthur J. Moss, M.D.  
Professor of Medicine  
Director, Heart Research Follow-up Program  
University of Rochester Medical Center  
Rochester, New York

Lewis S. Nelson, M.D., F.A.C.E.P.  
Associate Professor, Department of  
Emergency Medicine  
Director, Medical Toxicology Fellowship  
Training Program  
New York University School of Medicine and  
NYU Hospital Center  
New York, New York

David Oakes, Ph.D.  
Professor of Biostatistics and Statistics  
University of Rochester  
Department of Biostatistics and Computational  
Biology  
Rochester, New York

Thomas G. Pickering, M.D., D.Phil.  
Assistant Professor of Medicine  
Director, Behavioral Cardiovascular Health  
and Hypertension Program  
Columbia University Medical Center  
New York, New York

Peter J. Savage, M.D.  
Division of Epidemiology and clinical  
Applications  
NHLBI, National Institutes of Health  
Bethesda, Maryland

David S. Schade, M.D.  
Professor Medicine  
Director, Core Laboratory, Vice Chairman for  
Research  
University of New Mexico School of Medicine  
Albuquerque, New Mexico

**Endocrinologic and Metabolic Drugs Advisory Committee and the  
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**Meeting Roster**

**TEMPORARY MEMBERS (Voting)  
(Continued)**

Morris Schambelan, M.D.  
Chief, Division of Endocrinology  
San Francisco General Hospital  
San Francisco, California

John R. Teerlink, M.D.  
Director, Heart Failure Clinic  
Director, Clinical Echocardiography  
Cardiology  
University of California, San Francisco  
San Francisco VA Medical Center  
San Francisco, California

Gerald Van Belle, Ph.D.  
Professor of Environmental/Occupational  
Health Sciences and Biostatistics  
University of Washington School of Public  
Health & Community Medicine  
Department of Environmental and  
Occupational Health Sciences  
Seattle, Washington

**TEMPORARY MEMBERS (Non-Voting)**

Curt D. Furberg, M.D., Ph.D.  
Professor, Department of Public Health Services  
Wake Forest University School of Medicine  
Winston-Salem, North Carolina

**INDUSTRY REPRESENTATIVES (Non-Voting)**

Steven W. Ryder, M.D.  
Senior Vice President, Pfizer Global Research  
& Development  
New London, Connecticut

Annette Stemhagen, Dr.PH.  
Vice President, United BioSource Corporation  
321 Norristown Road  
Ambler, Pennsylvania

**GUEST SPEAKER (Non-Voting)**

David Gordon, M.D., Ph.D., M.P.H.  
Special Assistant for Clinical Studies  
Division of Heart & Vascular Diseases  
NHLBI, National Institutes of Health  
Bethesda, Maryland

Robert E. Ratner, M.D.  
Vice-President of Scientific Affairs  
MedStar Research Institute  
6495 New Hampshire Avenue, Suite 201  
Hyattsville, Maryland

**Endocrinologic and Metabolic Drugs Advisory Committee and the  
Drug Safety and Risk Management Advisory Committee**

**July 30, 2007**

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Gaithersburg, Maryland**

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Meeting Roster

**CONSULTANT (Non-Voting)**

Steven Nissen, M.D.  
Medical Director, Cleveland Clinic  
Cardiovascular Coordinating Center  
Department of Cardiovascular Medicine  
9500 Euclid Ave.  
Cleveland, Ohio

**FDA PARTICIPANTS (Non-Voting)**

Mark I. Avigan, M.D., C.M.  
Director, Division of Drug Risk Evaluation  
Office of Surveillance and Epidemiology  
CDER, FDA

Gerald Dal Pan, M.D., M.H.S.  
Director, Office of Surveillance and  
Epidemiology  
CDER, FDA

Sandra L. Kweder, M.D.  
Deputy Director, Office of New Drugs  
CDER, FDA

Douglas C. Throckmorton, M.D.  
Deputy Director, CDER, FDA

Robert J. Meyer, M.D.  
Director, Office of Drug Evaluation II  
CDER, FDA

Robert T. O'Neill, Ph.D.  
Director, Office of Biostatistics  
CDER, FDA

Mary H. Parks, M.D.  
Director, Division of Metabolism and  
Endocrine Products  
CDER, FDA

**ENDOCRINOLOGIC AND METABOLIC DRUGS ADVISORY COMMITTEE  
2007 Member Roster**

**Chair**

**Nelson B. Watts, M.D.**

Expertise: Endocrinology

Term: 02/13/03 - 06/30/08

Internal Medicine

Professor, Clinical Endocrinology

Director, UC Bone Health

Medical Arts Building, Suite 4300

222 Piedmont Avenue

Cincinnati, Ohio 45219

**Kenneth D. Burman, M.D.**

Expertise: Endocrinology/Thyroid Disease

Term: 7/10/06 – 6/30/10

Chief, Endocrine Section

Washington Hospital Center

110 Irving Street, N.W.

2A72

Washington, DC 20010

**Sonia Caprio, M.D.**

Expertise: Pediatric Endocrinology

Term: 10/24/04 – 06/30/08

Professor of Pediatrics

Division of Endocrinology, Pediatrics

Yale University

School of Medicine

333 Cedar Street

New Haven, Connecticut 06510-8064

**Katherine M. Flegal, Ph.D.**

Expertise: Obesity/Epidemiology

Term: 7/10/06 – 6/30/10

Senior Research Scientist

Distinguished Consultant

National Center for Health Statistics

Centers for Disease Control and Prevention

3311 Toledo Road, Room 4311

Hyattsville, Maryland 20782

**Designated Federal Official**

**Cathy A. Miller, M.P.H., R.N.**

Advisors and Consultants Staff HFD-21

Center for Drug Evaluation and Research

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5600 Fishers Lane

Rockville, Maryland 20857

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(301) 827-7001, FAX (301) 827-6776

Expertise: Public Health Education

Term: 7/10/06 – 6/30/09

Associate Professor

Division of Health and Physical Education

Western Oregon University

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Monmouth, Oregon 97361

**Michael A. Proschan, Ph.D.**

Expertise: Biostatistics

Term: 7/10/06 – 6/30/10

Biostatistician

Biostatistics Research Branch

National Institute of Allergy and Infectious Diseases

National Institutes of Health

6700A Rockledge Drive, Room 5140

Bethesda, MD 20892-7609

**Clifford J. Rosen, M.D.**

Expertise: Metabolic Bone Disease/Osteoporosis

Term: 7/10/06 – 6/30/10

Senior Staff Scientist

Maine Center for Osteoporosis

St. Joseph Hospital

900 Broadway, Building #2, Suite A

Bangor, Maine 04401

**\*\*Steven W. Ryder, M.D.**

Expertise: Endocrinology

Term: 02/02/04 - 10/31/07

Senior Vice President

Pfizer Global Research & Development

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New London, Connecticut 06443

\*Jessica W. Henderson, Ph.D.

\*Consumer Representative

\*\*Industry Representative

Updated July 1, 2007

**Food and Drug Administration**  
**Center for Drug Evaluation and Research**  
**DRUG SAFETY AND RISK MANAGEMENT ADVISORY COMMITTEE**

**CHAIR**

**Richard Platt, M.D., M.Sc.**

Term: 07/13/04-05/31/08

Expertise: Epidemiology & Biometrics  
Professor, Harvard Medical School  
133 Brookline Ave, 6<sup>th</sup> floor  
Boston, Massachusetts 02215

**EXECUTIVE SECRETARY**

**Victoria Ferretti-Aceto, Pharm.D.**

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**MEMBERS**

**Terry C. Davis, Ph.D.**

Term: 02/02/06 – 5/31/09

Expertise: Risk Communication  
Professor, Department of Medicine and Pediatrics  
Louisiana State University Health Sciences Center  
1501 Kings Highway, Rm. 6-212  
Shreveport, Louisiana 71130

**Judith M. Kramer, M.D., M.S.**

Term: 10/24/06 – 05/31/10

Expertise: Internal Medicine  
Associate Professor of Medicine  
Division of General Internal Medicine and Clinical  
Pharmacology  
Duke University Medical Center  
2400 Pratt Street, Room 0311 Terrace Level  
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Durham, North Carolina 27705

**Sander Greenland, Dr. P.H.**

Term: 06/01/06 – 5/31/10

Expertise: Statistics/Epidemiology  
Professor of Epidemiology  
UCLA School of Public Health  
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**Timothy S. Lesar, Pharm.D.**

Term: 10/24/06 – 05/31/09

Expertise: Pharmacy  
Director of Pharmacy  
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Albany, New York 12208

**Susan R. Heckbert, M.D., Ph.D.**

Term: 10/24/06 – 05/31/10

Expertise: Epidemiology  
Professor of Epidemiology  
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Health Research Unit  
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**\*\*Annette Stenhagen, Dr.PH**

Term: 02/02/04-10/31/07

Expertise: Pharmacoepidemiology  
Vice President, Epidemiology & Risk Management  
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**Sean P. Hennessy, Pharm.D., Ph.D.**

Term: 10/24/06 – 05/31/09

Expertise: Epidemiology  
Assistant Professor of Epidemiology  
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423 Guardian Drive, 803 Blockley Hall  
Philadelphia, Pennsylvania 19104-6021

**\*Consumer Representative**

**\*\* Industry Representative**

**Questions for Advisory Committee Members  
Endocrinologic and Metabolic Drugs Advisory Committee and Drug Safety and  
Risk Management Advisory Committee Meeting  
July 30, 2007**

1. Please comment on the contribution of the meta-analysis of the 42 controlled clinical trials (e.g., strengths and limitations) to the understanding of cardiac ischemic risk for Avandia.
2. Please comment on the contribution of the observational cohort studies (e.g., strengths and limitations) to the understanding of cardiac ischemic risk for Avandia.
3. Please comment on the contribution of large randomized controlled trials of rosiglitazone (e.g., strengths and limitations of DREAM, ADOPT, and RECORD) to the understanding of cardiac ischemic risk for Avandia.
4. Do the available data support a conclusion that Avandia increases cardiac ischemic risk in type 2 diabetes mellitus (**VOTE requested**)?
  - If yes, is there evidence that this risk is greater than other available therapies for the treatment of type 2 diabetes mellitus?
5. Does the overall risk-benefit profile of Avandia support its continued marketing in the US (**VOTE requested**)?
  - If yes, please comment on what FDA should do to maximize the risk-benefit considerations (e.g., limit to certain patients, incorporate a boxed warning....)