Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

Cardiovascular and Renal Drugs Advisory Committee
99th Meeting
May 29, 2003

Holiday Inn, Silver Spring
8777 Georgia Avenue, Silver Spring, MD

AGENDA

8:00	Call to Order and Opening Remarks	Jeffrey Borer, M.D., Chair
	Introduction of Committee	
	Conflict of Interest Statement	Jayne E. Peterson, R.Ph., J.D. Executive Secretary, FDA

QT prolongation issues associated with two new drug applications (NDAs): (1) NDA 21-287, (alfuzosin HCl), Sanofi-Synthelabo Inc., for the proposed indication of treatment of the signs and symptoms of benign prostatic hyperplasia; and (2) NDA 21-400, Levitra (vardenafil HCl), Bayer Corp., proposed for the indication of treatment of erectile dysfunction. The discussion will focus on: (1) Clinical trial designs for the assessment of QT prolongation; (2) approaches to the correction of QT interval for drugs that affect the heart rate; and (3) risks of cardiac arrythmias associated with different degrees of QT prolongation. Premarketing clinical safety data from these applications and postmarketing safety data relevant to cardiac QT prolongation from drugs in the same two drug classes (i.e., alpha adrenergic blockers and phosphodiesterase type 5 inhibitors) will be considered.

8:15	**FDA Presentation**	
	Welcome and Background	Douglas Throckmorton, M.D. Director, Division of Cardiovascular and Renal Drug Products, CDER, FDA
8:30	**Sponsor Presentations**	
	Sanofi-Synthelabo Inc.	
	Background	Jon Villaume, Ph.D. Sanofi-Synthelabo Inc.
	Pharmacokinetics	Jim Oppermann, Ph.D. Sanofi-Synthelabo Inc.
	ECG Studies	Wocjiech Zareba, M.D., Ph.D. University of Rochester
	Conclusions	Jeremy Ruskin, M.D. Massachusetts General Hospital
9:20	Questions from Committee to Sponsor	

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AGENDA (cont.)

9:30	**Bayer Corporation**	
	Introduction	Mary Taylor, M.P.H. Vice President Regulatory Affairs North America Bayer Pharmaceuticals Corporation
	Assessment of the QT/QTc Effect of Vardenafil	Thomas Segerson, M.D. Vice President Medical and Scientific Affairs Bayer Canada
	QT/QTc Study Design, Heart Rate Correction & Risk of Cardiac Arrhythmia	Joel Morganroth, M.D. Clinical Professor of Medicine University of Pennsylvania Chief Scientist eResearch Technology
10:20	Questions from Committee to Sponsor	
10:30	Break	
10:45	**FDA Presentations**	
	Introduction	Donna Griebel, M.D. Deputy Director, Division of Reproductive and Urologic Drug Products, CDER, FDA
	Effect of alfuzosin on QT Interval	Venkat Jarugula, Ph.D. Clinical Pharmacology and Biopharmaceutics Reviewer, FDA
	Effect of vardenafil on QT Interval	Leslie Kenna, Ph.D. Clinical Pharmacology and Biopharmaceutics Reviewer, FDA
	Safety Summary: Adverse events potentially related to QT prolongation or Torsade de Pointes	Marcea Whitaker, M.D. Medical Officer, FDA
	Summary of Review Issues	Donna Griebel, M.D.
11:45	Questions from Committee to FDA	
12:00	Lunch	
1:00	Open Public Hearing	
2:00	Committee Discussion and Response to FDA Questions	
3:00	Break	

3:15 Continuation of Committee Discussion and Response to FDA Questions

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Special Government Employee (SGE) Consultants (voting)

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John Neylan, M.D.
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Open Public Hearing Speakers

- Pfizer Incorporated (two speakers):

  Michael Sweeney, M.D.
  Senior Medical Director
  Pfizer Incorporated

  Rodney Falk, M.D.
  Professor of Medicine
  Director of Clinical Cardiology
  Research and Associate Director of Boston University
  Boston Medical Center
  Boston, Massachusetts

- Culley Carson, M.D.
  Professor and Chief of Urology
  University of North Carolina
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