The committees will discuss safety considerations of ultrasound contrast agents (materials intended to improve the clarity of ultrasound imaging), particularly related to new information and developments since the prior Advisory Committee meeting on the same topic on June 24, 2008. The discussion will include the results of required postmarketing safety studies and data from postmarketing surveillance. Specific drugs to be discussed include: (1) New drug application (NDA) 21-064, perflutren lipid microsphere injectable suspension, Lantheus Medical Imaging, Inc.; (2) NDA 20-899, perflutren protein-type A microspheres injectable suspension, GE Healthcare; and (3) the investigational new drug (IND) application for sulfur hexafluoride microbubble injection, Bracco Diagnostics, Inc. Perflutren lipid microsphere injectable suspension and perflutren protein-type A microspheres injectable suspension are indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border (improve the clarity of imaging of specific areas of the left lower side of the heart).

8:00 a.m. Call to Order
Introduction of Committee
Conflict of Interest Statement
Milton Packer, M.D.
Acting Chair, CRDAC
Nicole Vesely, Pharm.D.
Designated Federal Officer, CRDAC

8:10 a.m. FDA Presentation
Regulatory History of Ultrasound Contrast Agents
Ira Krefting, M.D.
Deputy Director for Safety, Division of Medical Imaging Products, Office of Drug Evaluation IV, CDER

8:30 a.m. Speaker Presentation
Current Cardiological Applications of Contrast Echocardiography
Sanjiv Kaul, M.D. (Guest Speaker)
Professor of Medicine and Radiology Head, Division of Cardiovascular Medicine Oregon Health & Science University

9:00 a.m. Industry Presentation
DEFINITY® Post Marketing Studies Results
Mark Hibberd, M.D.
Senior Medical Director, Medical Affairs Lantheus Medical Imaging, Inc.
DEFINITY® Pharmacovigilance Safety Data Review
Dana Washburn, M.D.
Vice President, Clinical Development & Medical Affairs Lantheus Medical Imaging, Inc.
DEFINITY® Risk/Benefit Profile
Michael Main, M.D.
Cardiologist St. Luke’s Mid-America Heart Institute Kansas City, MO

9:30 a.m. Break

9:35 a.m. Industry Presentation GE Healthcare - perflutren protein-type A microspheres injectable suspension (Optison)
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Presenter(s)</th>
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<tr>
<td>10:05 a.m.</td>
<td><strong>Break</strong></td>
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<tr>
<td>10:20 a.m.</td>
<td><strong>Industry Presentation</strong></td>
<td><strong>Bracco Diagnostics, Inc - sulfur hexafluoride microbubble injection (SonoVue)</strong></td>
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|           |  **Safety Profile of SonoVue® (Sulfur Hexafluoride Microbubbles)** | Alberto Spinazzi, M.D.  
Senior Vice President,  
Group Medical and Regulatory Affairs,  
Bracco Diagnostics, Inc. |
| 10:50 a.m. | **Questions to Industry Presenters**      |                                                                              |
| 11:10 a.m. | **FDA Presentation**                     | **Janelle Charles, Ph.D**  
Mathematical Statistician, Division of Biometrics VII,  
Office of Biostatistics, CDER |
|           |  **Retrospective Observational Database Analyses for Definity and Optison** |                                                                              |
|           |  **FDA Presentation (cont.)**             | **Ross Filice, M.D.**  
Medical Officer, Division of Medical Imaging Products,  
Office of Drug Evaluation IV, CDER |
| 11:50 a.m. | **Questions to FDA Presenters**           |                                                                              |
| 12:10 p.m. | **Lunch**                                |                                                                              |
1:10 p.m.     Open Public Hearing

2:10 p.m.     Questions to the Committees

3:00 pm.      Break

3:15 p.m.     Questions to the Committees (continued)

4:00 p.m.     Adjourn