



Welcome to the 2005
Cardiovascular Biomarkers and
Surrogate Endpoints Symposium

September 23-24, 2005
Bethesda, MD

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GE Healthcare
Merck Research Laboratories
Pfizer Inc.
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Novartis
GlaxoSmithKline
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[Program Objectives]

- Examine the pathogenesis of CV disease
- Identify current issues in CV biomarker application
- Review examples of effective biomarker use in drug development
- Consider use of biomarkers to bridge early clinical development and drug approval
- Provide opportunity to debate biomarker utility
- Outline international approaches to using biomarkers for regulatory decision making

[Friday, September 23rd]

- AM Presentations/Q &A/panel discussions
- 12:30 Lunch and 4 concurrent breakout sessions
- PM Presentations/Q &A/panel discussions
- 4:30 Adjourn

[Saturday, September 24th]

- AM Presentations/Q &A/panel discussions
- 12:00 Lunch and 3 concurrent breakout sessions
- PM Breakout session feedback and discussions
- 3:30 Adjourn

Breakout Session Leaders

Friday, September 23rd concurrent sessions:

- A. How should pharmacogenomics be used prospectively in clinical studies of drug safety and efficacy?
 - John Thompson – Pfizer
 - Michael Phillips – Genome Quebec
- B. The future of diagnostics – who are the drivers?
 - Donald Black – GE Healthcare
 - Jim Udelson - Tufts
- D. How should biomarkers be used in pre-clinical modeling and early dose selection?
 - Martin Ogletree – Bristol-Myers Squibb
 - Jay Heineke – U of Washington
- E. Rational approach to biomarker validation
 - Paul Ridker – Brigham and Women's Hospital
 - Philip Barter – Heart Research Institute

Saturday, September 24th concurrent sessions:

- C. How can we maximize the application and utility of safety biomarkers?
 - Michele Mercuri – Novartis
 - Eric Brass – UCLA Medical Center
- F. How do you develop a drug that does not target an accepted surrogate endpoint?
 - Don Black – GE Healthcare
 - Bill Sasiela - Pfizer
- G. Vascular imaging technologies – technical and clinical considerations
 - Jean-Claude Tardif – MHI
 - Steve Nissen – CCF

[Administrative Notes]

- CME provided by the University of Montreal
- Please complete assessment forms
- No recording devices allowed in presentation or breakout rooms

NIH Biomarkers Definition Working Group (1998)

- Biological marker (biomarker)
 - a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention
- Clinical endpoint
 - a characteristic or variable that reflects how a patient feels, functions or survives.
- Surrogate endpoint
 - a biomarker intended to substitute for a clinical endpoint. A surrogate endpoint is expected to predict clinical benefit (or harm, or lack of benefit or harm) based on epidemiologic, therapeutic, pathophysiologic or other scientific evidence.

Benefits of Appropriate Biomarker Application



Selecting biomarker based on MOA and pathogenesis

Formative stage

Endothelial function
FMD

Adaptive stage

Myocardial perfusion
PET

Plaque volume
IMT, IVUS

Clinical stage

Perfusion
PET

Function
exercise testing

Morphology
IVUS, MRI, CT

CV endpoints



Lesion prone area of artery

Precursor lesion

Fibro-fatty plaque + inflammation (sub-clinical)

Plaque remodeling

Wall remodeling

Sub-clinical plaque

Plaque enlargement + inflammation

Complicated plaque/instability

Stenosis/rupture/occlusion

