

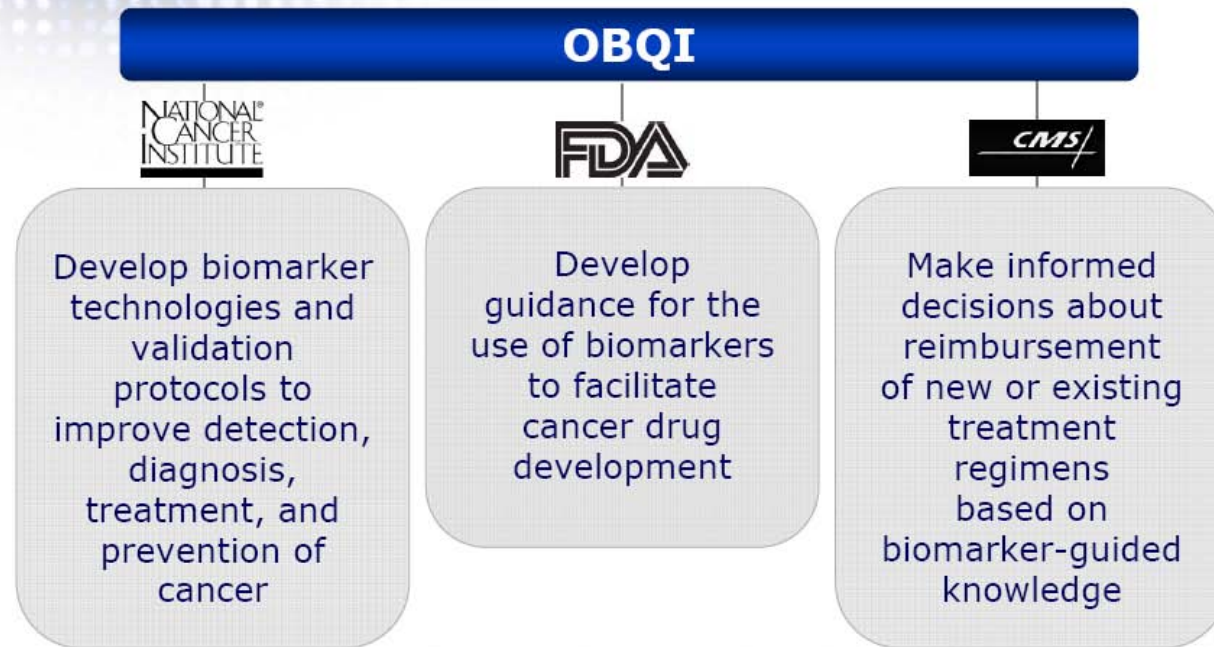
OBQI: Unique HHS Partnership

**The Oncology Biomarkers Qualification Initiative (OBQI)
is a new and innovative collaboration among
NCI, FDA, and CMS designed to qualify biomarkers for
use in clinical trials – and ultimately speed
better agents to cancer patients***



*Tri-partite MOU signed 01/23/2006

OBQI Coordinates Cross-HHS Goals for Biomarker Validation and Clinical Use

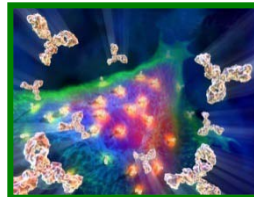


The Biomarkers Consortium is led by an Executive Committee and organized around four Steering Committees

Cancer



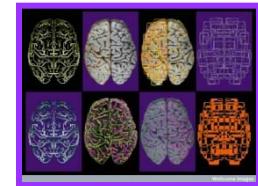
Inflammation & Immunity



Metabolic Disorders



Neuroscience



Gary J. Kelloff, MD,
NCI/NIH (Co-Chair)
David R. Parkinson, MD,
Nodality, Inc. (Co-Chair)

Caroline C. Sigman, PhD, CCS
Associates, Project Manager
Sonia Pearson-White, PhD
Scientific Program Manager, FNIH

- *Accelerate Drug Development in all Cancers*
- *Circulating Tumor Cells (CTCs) as a Biomarker*
- *Improve and Standardize Imaging*

Brian Kotzin, MD, Amgen Corporation (Co-chair)
Dan Rotrosen, MD, NIAID/NIH (Co-Chair)

TBN
Scientific Program Manager,
FNIH

- *Rheumatoid Arthritis*
- *Transplantation*

Myrlene Staten, MD, NIDDK/NIH (Co-Chair)
David Kelley, MD, Merck & Co., Inc. (Co-Chair)

Maria Vassileva, PhD
Scientific Program Manager,
FNIH

- *Atherosclerosis*
- *Beta Cell Function*
- *Microvascular Complications in Diabetes*
- *Functional Changes in Aging*

Huda Akil, PhD, MA, University of Michigan (Co-Chair)
Husseini K. Manji, MD, FRCP, Johnson & Johnson Pharmaceutical R&D (Co-Chair)

Judy Siuciak, PhD
Scientific Program Manager

- *Imaging in Alzheimer's Disease*
- *Markers of Depression and Anti-Depressant Response*

Biomarkers:

Analytical & Clinical Validation

Biomarker validation is the process of assessing the assay and its measurement performance characteristics, and determining the range of conditions (including clinical settings) under which the assay will give reproducible and accurate data

Wagner et al., Clin Pharm Therap 2007; 81: 104–107

Biomarker Qualification

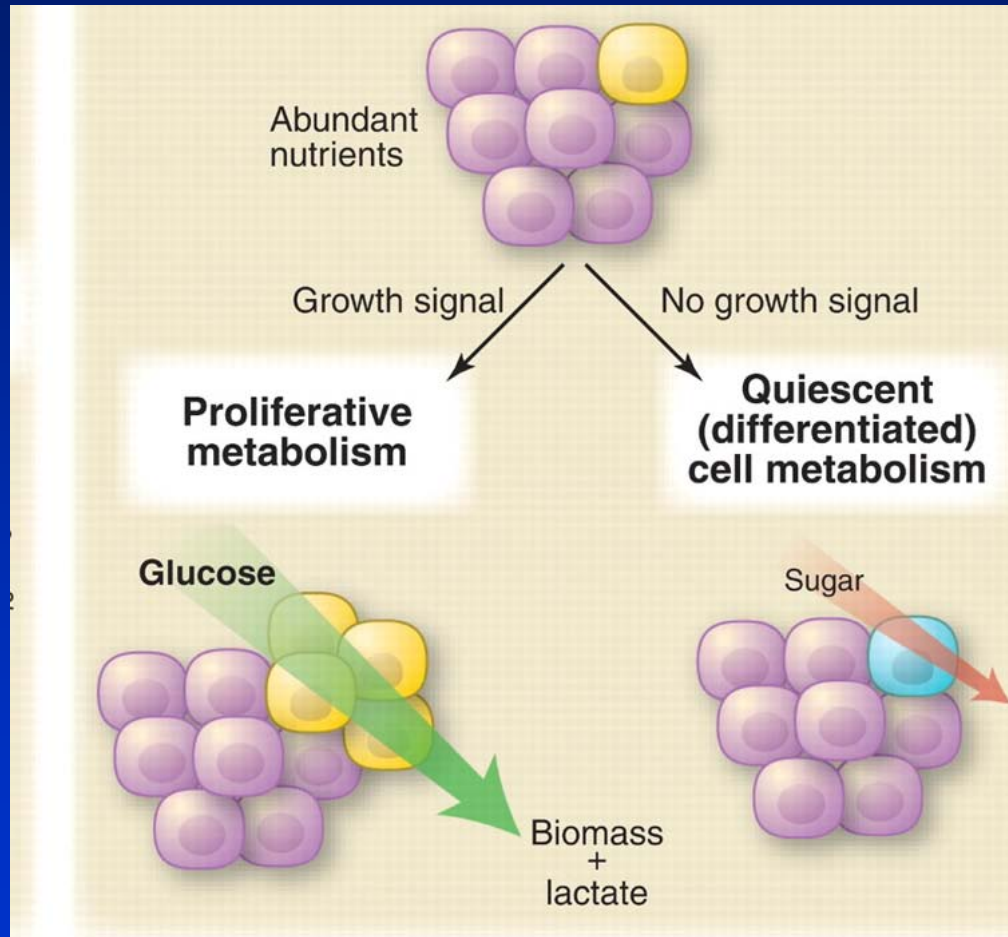
- Biomarker qualification is the evidentiary process of linking a biomarker with biological processes and clinical endpoints.
- Qualification is verification that the biomarker is “fit-for-purpose”

Wagner *et al.*, *Clin Pharm Therap* 2007; 81: 104–107

Why FDG-PET

- FDG-PET exploits the reliance of tumor cells on glucose and glycolytic metabolism to image cancers (Warburg Effect, strong mechanistic rationale)
- FDG-PET data can be assessed visually, or analyzed semiquantitatively or quantitatively
- FDG-PET is approved for use in the diagnosis, staging, and restaging of a variety of cancer types, and in these applications can significantly impact the clinical management of disease
- In a number of clinical settings (*e.g.*, NSCLC, esophageal cancer, lymphoma), FDG-PET can provide an early measure of response to treatment with approved therapies
- With a few additional studies, FDG-PET could facilitate drug development and patient care by resulting in:
 - Shorter duration of Phase II studies to evaluate new drug/regimen
 - Accelerated approval in Phase III trials, with full approval contingent on evidence of clinical benefit (*e.g.*, PFS, OS) after longer term follow-up
 - Better patient care by ceasing ineffective therapies earlier

Understanding the Warburg Effect: Metabolic Requirements of Cell Proliferation



Adapted from Vander Heiden et al., *Science* 324, 1029 -1033 (2009)

Published by AAAS

Initial Qualification of FDG-PET as a Surrogate Endpoint for Clinical Benefit

Baseline FDG-PET



Treat with Approved Chemotherapeutic Drug (Standard Therapy)



FDG-PET: Metabolic Response (Predetermined Response Level)



Continue Treatment to Clinical Endpoint(s)—*e.g.*, OS, DFS, PFS, OR by Conventional Measurement

Further Qualification (e.g., 2 Different Drugs with Different Mechanisms in a Specific Target Organ) of FDG-PET as a Surrogate Endpoint for Clinical Benefit for Evaluation of New Therapies

Baseline FDG-PET



Treat with New Therapy vs. Standard Therapy



FDG-PET: Metabolic Response
(Predetermined Response Level)

If Response Is Met for Predetermined % of Patients, May Support Claim of Clinical Benefit and Accelerated Approval for New Therapy



Continue Treatment to Clinical Endpoint(s) OR Carry Out Confirmatory Trial with Clinical Endpoint(s)