



Embracing Team Science to Create Drug Development Tools for Clinical Decisions

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Partnerships

Foundation for the NIH

BIOMARKERS
| | | | | CONSORTIUM
IMPROVING HEALTH THROUGH
MEANINGFUL MEASUREMENTS

 **FNIH**
Foundation for the
National Institutes of Health

Outline

- Quick FNIH Background
- The FNIH Biomarkers Consortium place in the field
- Who is involved and how do we work
- Examples of the types of projects we manage

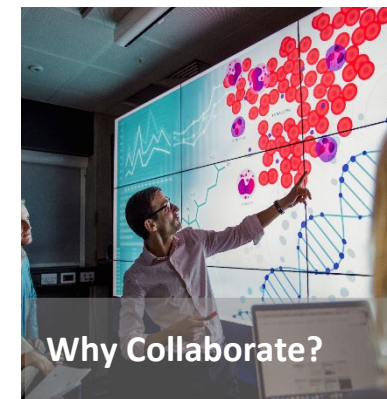
About the FNIH



- The mission of the Foundation for the National Institutes of Health (FNIH) is to **support the mission of the NIH**. The FNIH creates and leads alliances and public-private partnerships that advance breakthrough biomedical discoveries and improve the quality of people's lives.



- The FNIH was **created by Congress** in 1990 as a not-for-profit charitable organization. The Foundation began its work in 1996 to facilitate groundbreaking research at the U.S. National Institutes of Health (NIH) and worldwide.



- Attract and share resources
- Enable insight and innovation
- Establish standards
- Distribute expertise
- Create consensus
- Drive competitiveness in marketplace
- Disseminate knowledge
- Enhance credibility
- Reduce costs
- Support training & education
- Manage complexity

Select Partnerships at the FNIH

Accelerating Medicines Partnership

NIH (OD), NIA, NIAMS, NIDDK, NINDS, 12 companies, 10 not-for-profit organizations

\$302 million

Partnership for Accelerating Cancer Therapies

NCI, PhRMA, 12 pharmaceutical companies

\$220 million

Grand Challenges in Global Health (GCGH)

Bill & Melinda Gates Foundation

\$201 million

Lung-MAP: Master Lung Protocol Trial

NCI (SWOG), FDA, Friends of Cancer Research, 5 companies to date

\$163 million

Alzheimer's Disease Neuroimaging Initiative (ADNI)

NIA, NIBIB, 25+ companies, 3 not-for-profit organizations

\$148 million

The Biomarkers Consortium

FDA, NIH, CMS, PhRMA, BIO, pharmaceutical and nutrition companies, not-for-profit organizations

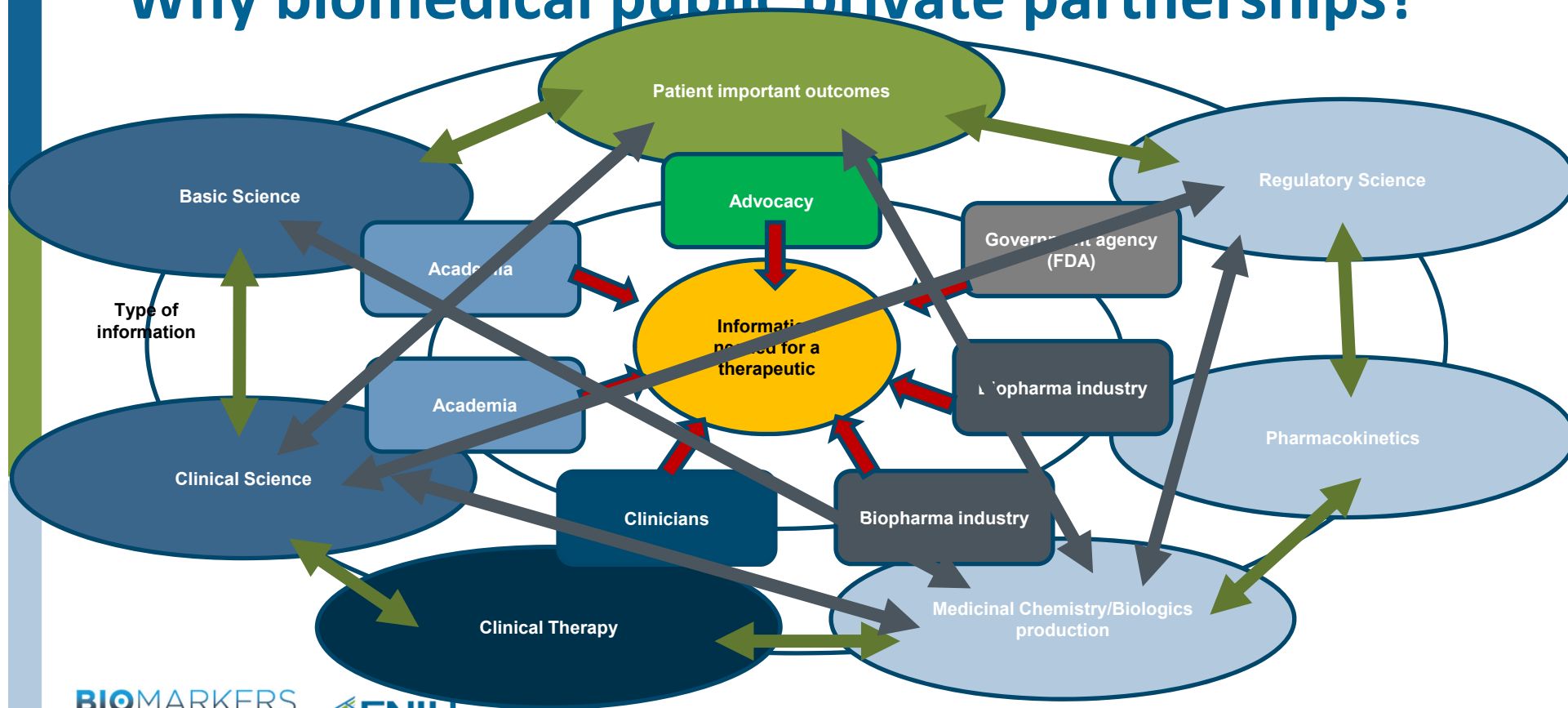
\$95 million

Helping End Addiction Long-Term (HEAL) Partnership Committee

NIH contract

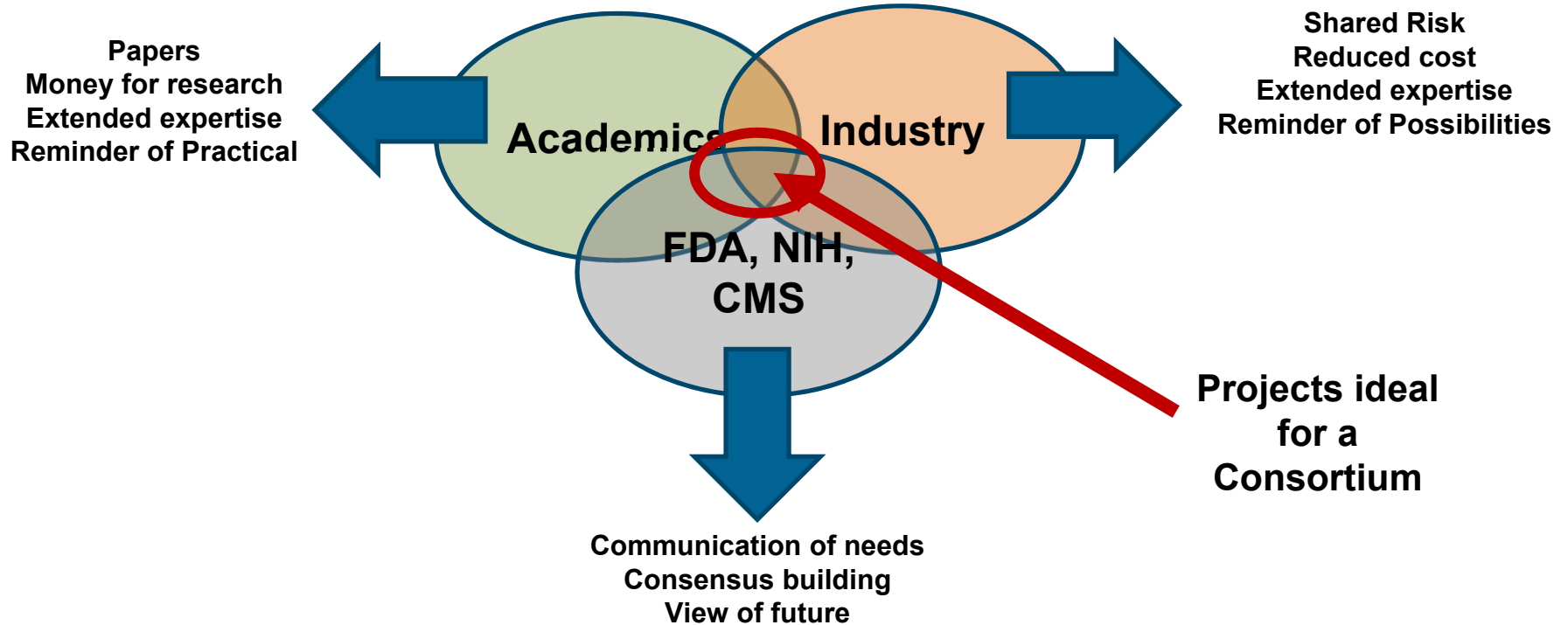
\$0.4 million

Why biomedical public private partnerships?



Why do stakeholders join these projects?

Stakeholders have different needs and interests



Biomarkers Consortium



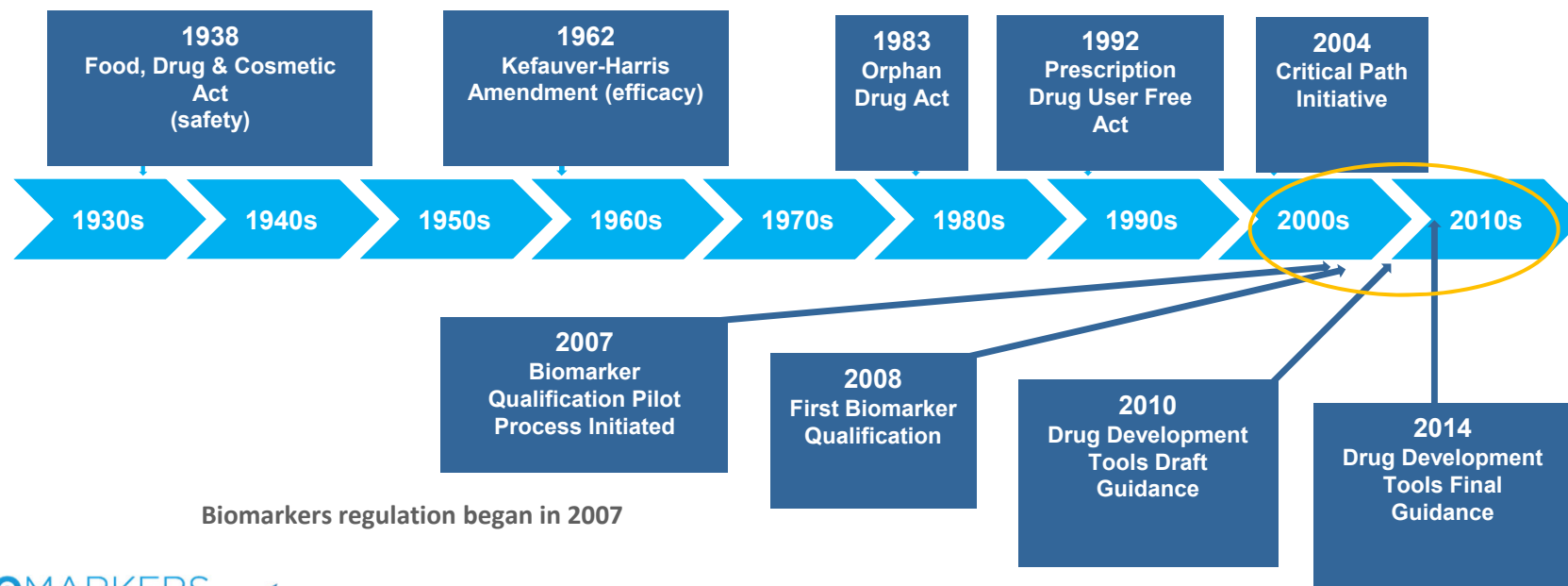
Why do we need a Biomarkers Consortium?

Biomarker qualification is new!

Answer: Precision Medicine

Drug development regulation preceded biomarkers regulation by almost 70 years

Drug development regulation began in 1938



Biomarkers regulation began in 2007

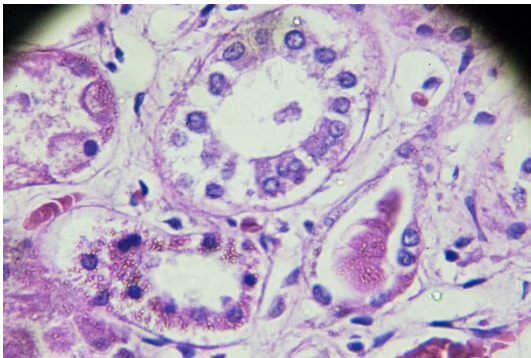
Biomarker Consortium

Vision

- Improving health through meaningful measurements

Mission

- To create and lead cross-sector efforts that validate and qualify biomarkers and other drug development tools to accelerate better decision making for the development of new therapeutics and health technologies.



Goals

- Facilitate the development and the seeking of regulatory approval for biomarkers using new and existing technologies;
- Develop evidence to help qualify biomarkers for specific applications in diagnosing disease, predicting therapeutic response or improving patient outcomes;
- Generate information useful to inform regulatory decision making;
- Make consortium project results broadly available to the entire scientific community.

Biomarkers Consortium

12 years of
collaboration, research
and progress



14 therapeutics advanced based on tools generated

9 clinical tools being used in drug development

5 FDA guidance documents supported by work of the BC



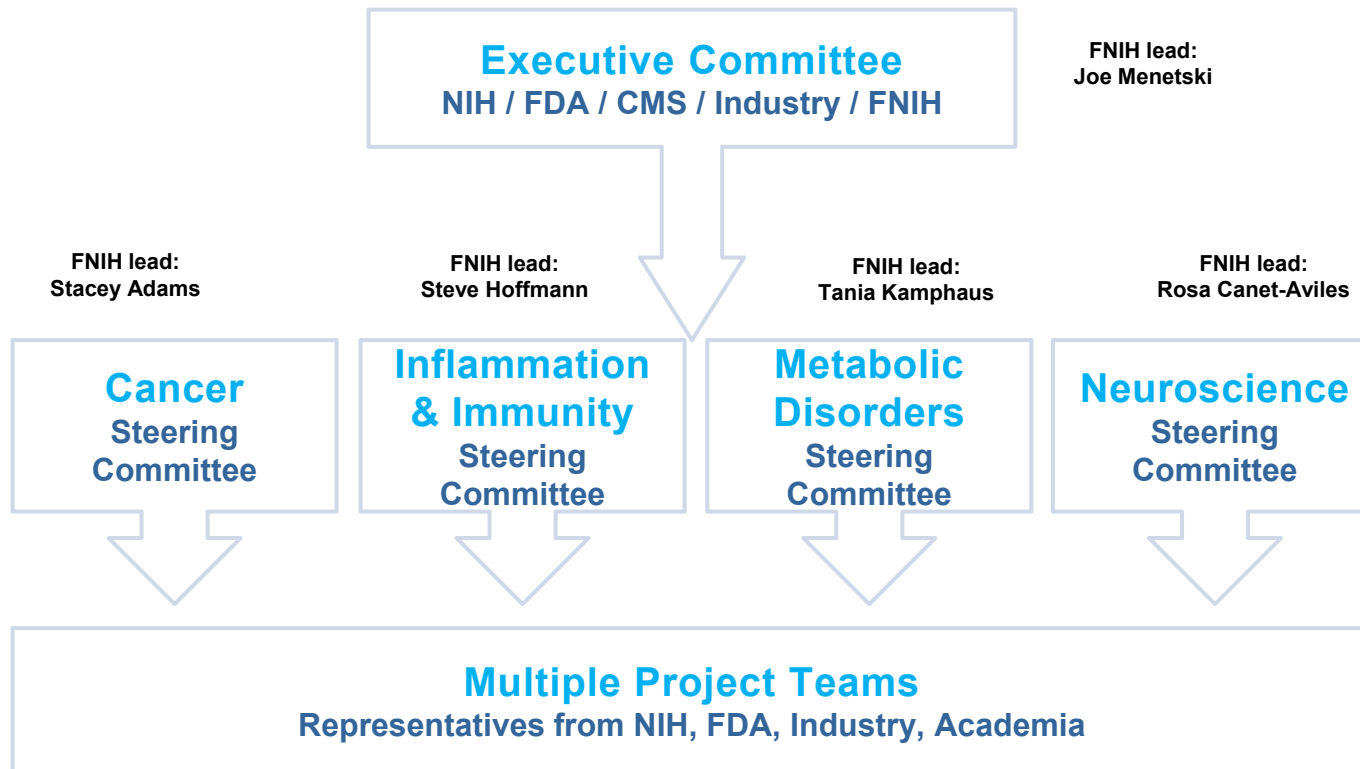
>50 publications

800+ citations



46 member organizations

How is the Biomarkers Consortium governed?



Executive Committee

Provides overall steering committee direction and final project approval

Executive Committee Chair

- Paul Herrling, FNIH Board of Directors

Centers for Medicare and Medicaid Services Executive Committee Chair

- Shari Ling, Center for Clinical Standards and Quality (CCSQ)

FNIH

- Ellen Sigal, Friends of Cancer Research

Food and Drug Administration Research

- Christopher Leptak, Co-director of the Biomarker Qualification Program; OND Biomarker and Companion Diagnostic Lead
- Vasum Peiris, Center for Diseases and Radiological Health (CDRH)
- Janet Woodcock, Center for Drug Evaluation and Research (CDER)

Industry

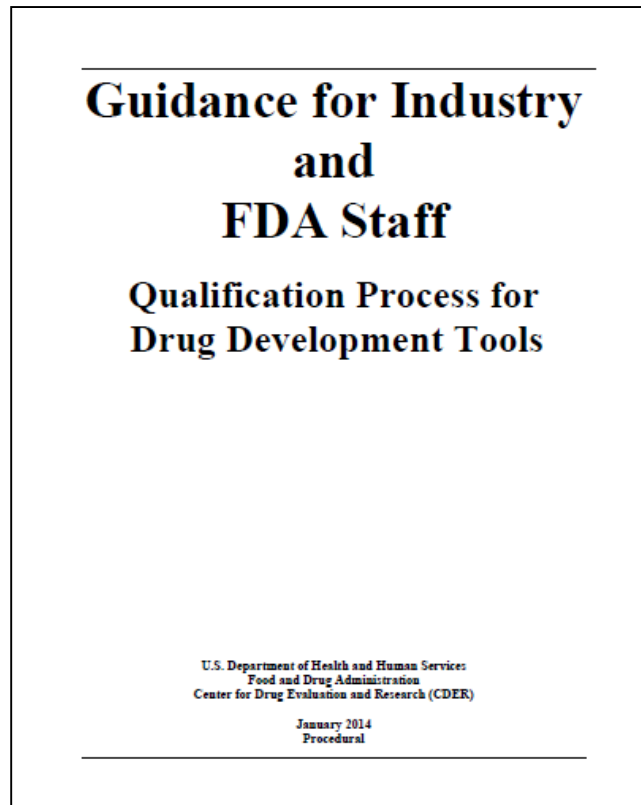
- Peter Honig, Pfizer
- Hussein Manji, Janssen R&D
- Richard Moscicki, PHRMA
- John Wagner, Takeda

National Institutes of Health

- Christopher Austin, National Center for Advancing Translational Sciences (NCATS)
- Douglas Lowy, National Cancer Institute (NCI)
- Linda Birnbaum, National Institute of Environmental Health Sciences (NIEHS)



The consortium approach is encouraged by the FDA



“Because of the substantial work needed to achieve qualification, CDER [Center for Drug Evaluation and Research] encourages the formation of collaborative groups to undertake these tool-development programs... A variety of projects undertaken by consortia have demonstrated the usefulness of this approach.”

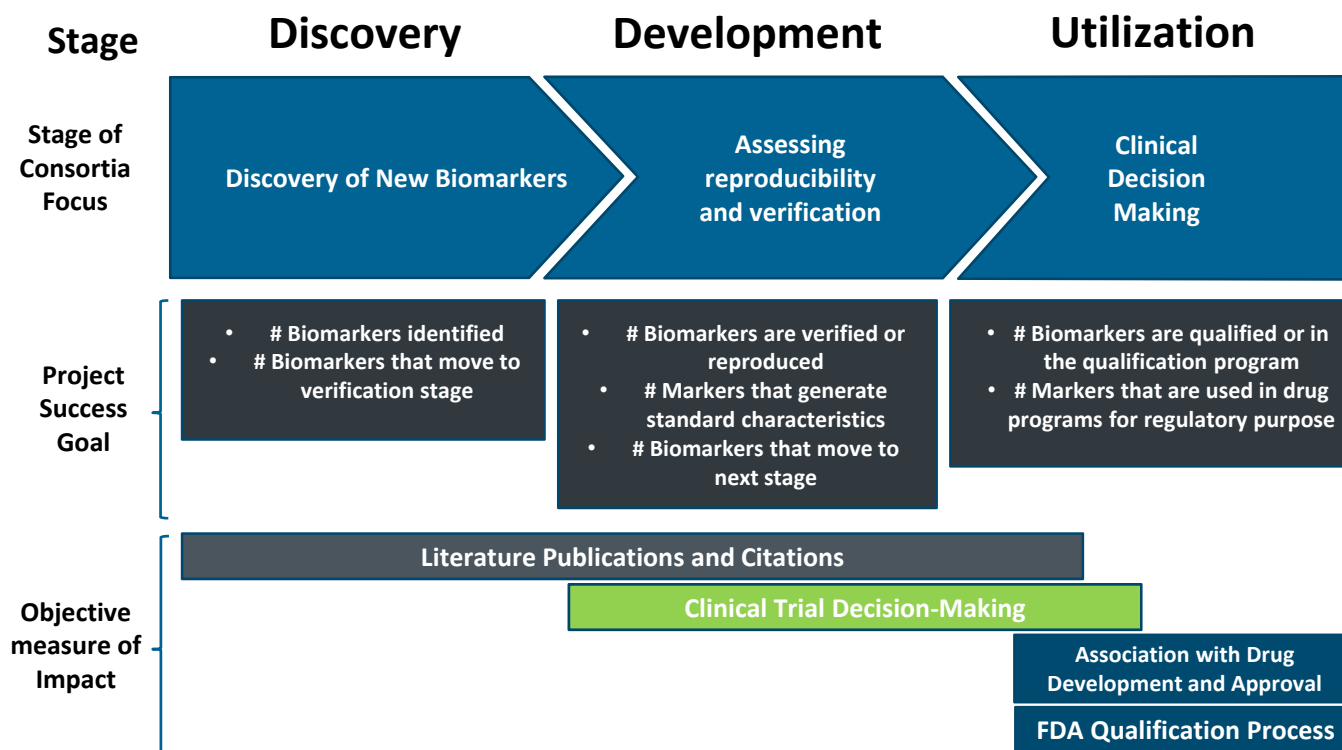
Updated FDA Draft Guidance published
January 2014



Biomarker project characteristics

- Stage of development
- Goals of project
- Type of biomarker

The goals and impact of a project are dependent on the stage of biomarker development.



BEST Resource



- NIH and FDA encourage stakeholders to join them in using BEST terms and definitions so that everyone can “speak the same language” when discussing biomarkers and endpoints.
- Consistent, mutually understood terminology can help accelerate development, validation, and qualification of medical product development tools.
- The BEST Resource will be updated periodically with additional terms, definitions, and examples.
- NIH and FDA welcome feedback, including specific proposed edits with rationales, from all stakeholders.
 - Email biomarkers@ncbi.nlm.nih.gov.

<https://www.ncbi.nlm.nih.gov/books/NBK338448/>

BEST (Biomarkers, EndpointS, and other Tools)

Classification: Range of Biomarker Types

- Susceptibility / risk biomarker
- Diagnostic biomarker
- Prognostic biomarker
- Monitoring biomarker
- Predictive biomarker
- Pharmacodynamic/Response biomarker
- Safety biomarker

Measures of disease presence and status

Measure aspects of response to treatment



BEST (Biomarkers, EndpointS, and other Tools)

Classification: *Disease Focused Biomarkers*

•Susceptibility / risk biomarker:

Examples:

- BMI or 2 hr post-meal glucose for diabetes risk
- Apo E genotype risk for Alzheimer's disease

Key uses:

- Define population for more efficient prevention trials

•Diagnostic biomarker:

Examples:

- Blood pressure in hypertension
 - FEV1 for COPD

Key uses:

- Define disease population for study

•Monitoring biomarker:

Examples:

- HCV-RNA
- PSA in prostate cancer

Key uses:

- Monitor patient status in trials

•Prognostic biomarker:

Examples:

- Gleason score in prostate cancer
- Total kidney volume in AD-PCKD

Key uses:

- Define higher risk disease population, enhancing trial efficiency



BEST (Biomarkers, EndpointS, and other Tools)

Classification: *Treatment-focused biomarkers*



• Predictive biomarker:

Examples:

- Cystic fibrosis genotypes response to ivacaftor
- Microsatellite-high predicts response to pembrolizumab

Key uses:

- Trial enrichment – improves efficiency, reduces sample size, increases response to treatment

• Pharmacodynamic/Response biomarker:

Examples:

- Blood pressure in hypertension
 - FEV1 or 6 minute walk test
 - LDL-C

Key uses:

- Demonstrating drug-target engagement, dose-ranging
- Surrogate endpoints (validated or reasonably-likely)

• Safety biomarker:

Examples:

- ALT, creatinine / eGFR
- Urinary kidney injury biomarkers (KIM-1, etc.)

Key uses:

- Detecting / assessing drug toxicity

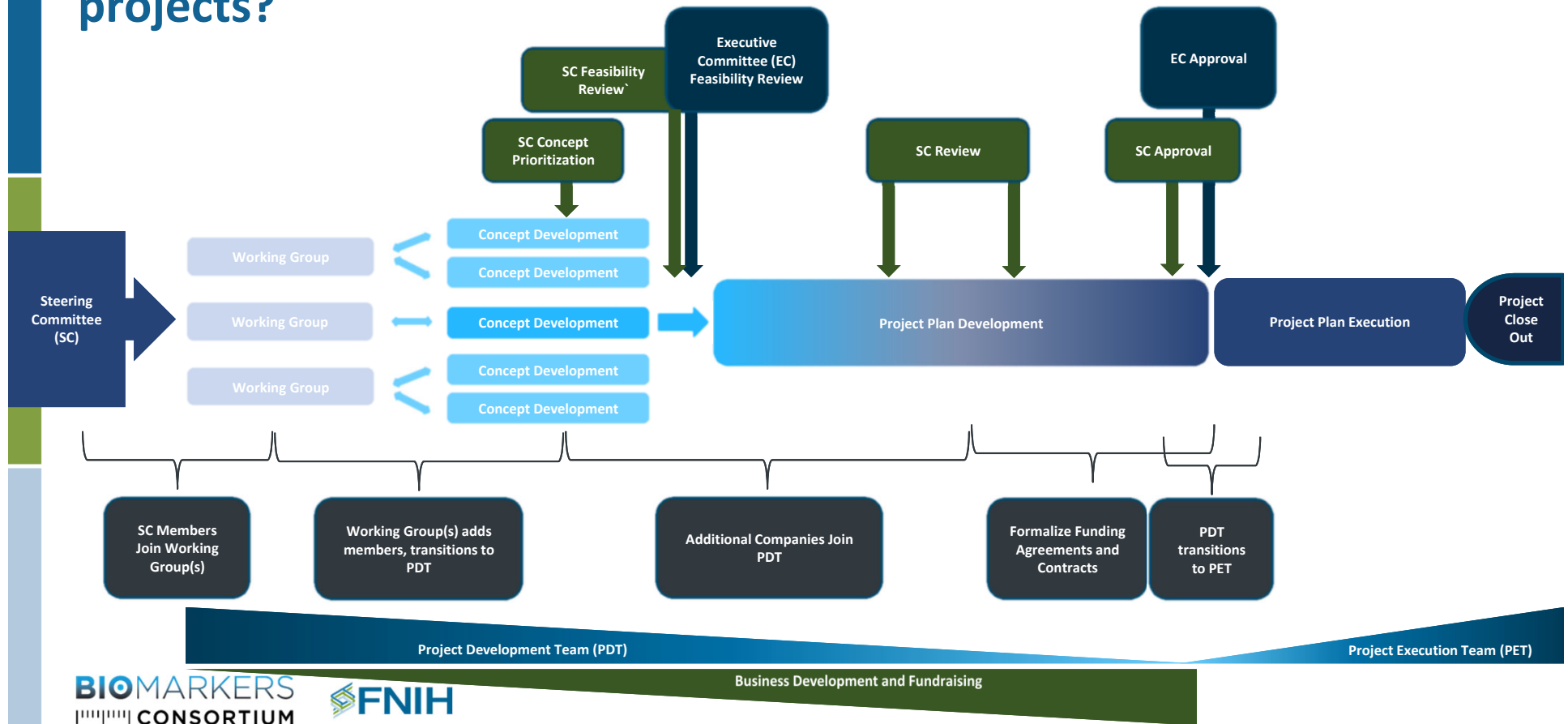
Adapted from:
Peter Stein, M.D.
Deputy Director
OND, CDER,
FDA

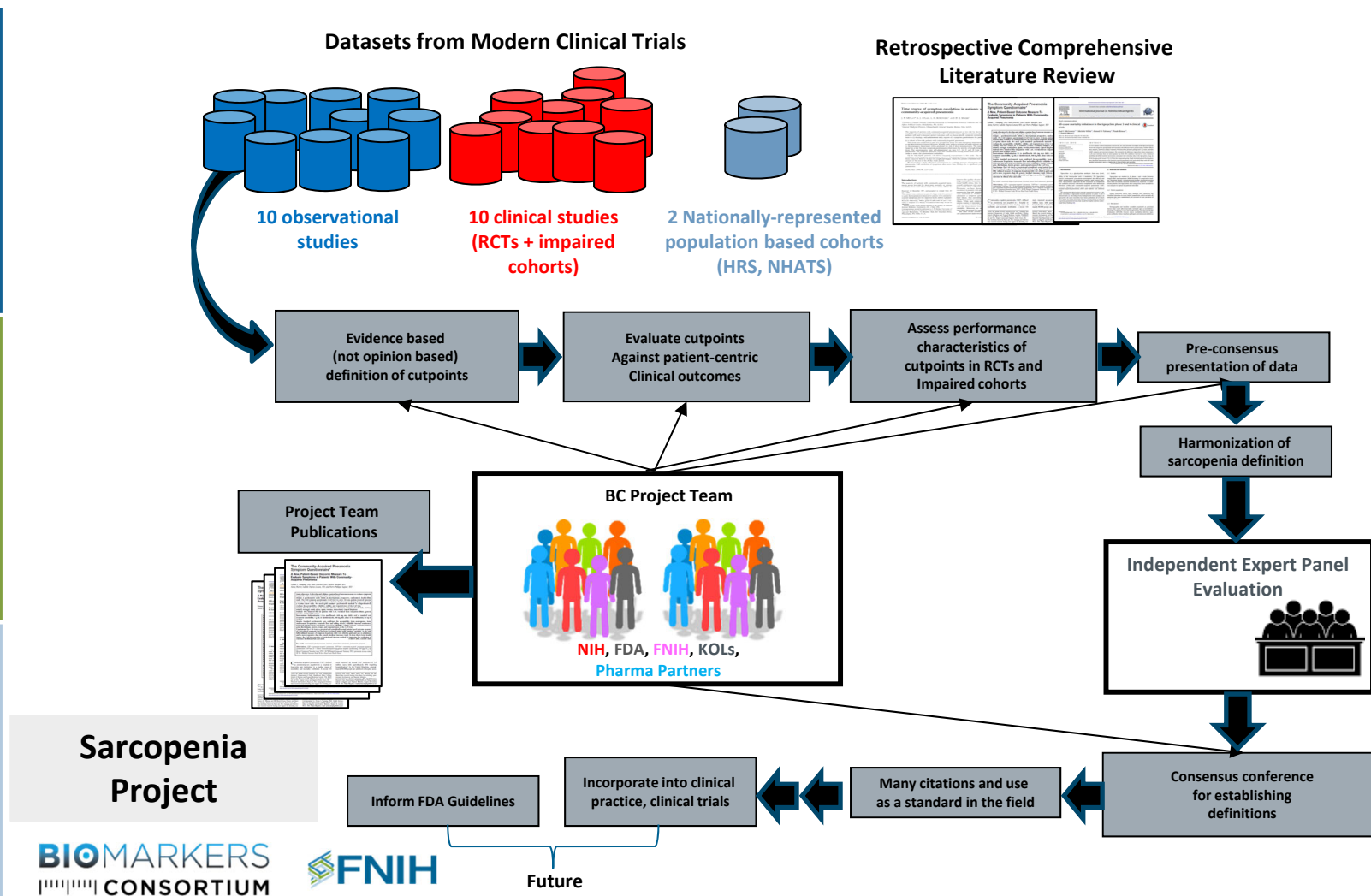
FDA Biomarker Qualification is a goal for some projects

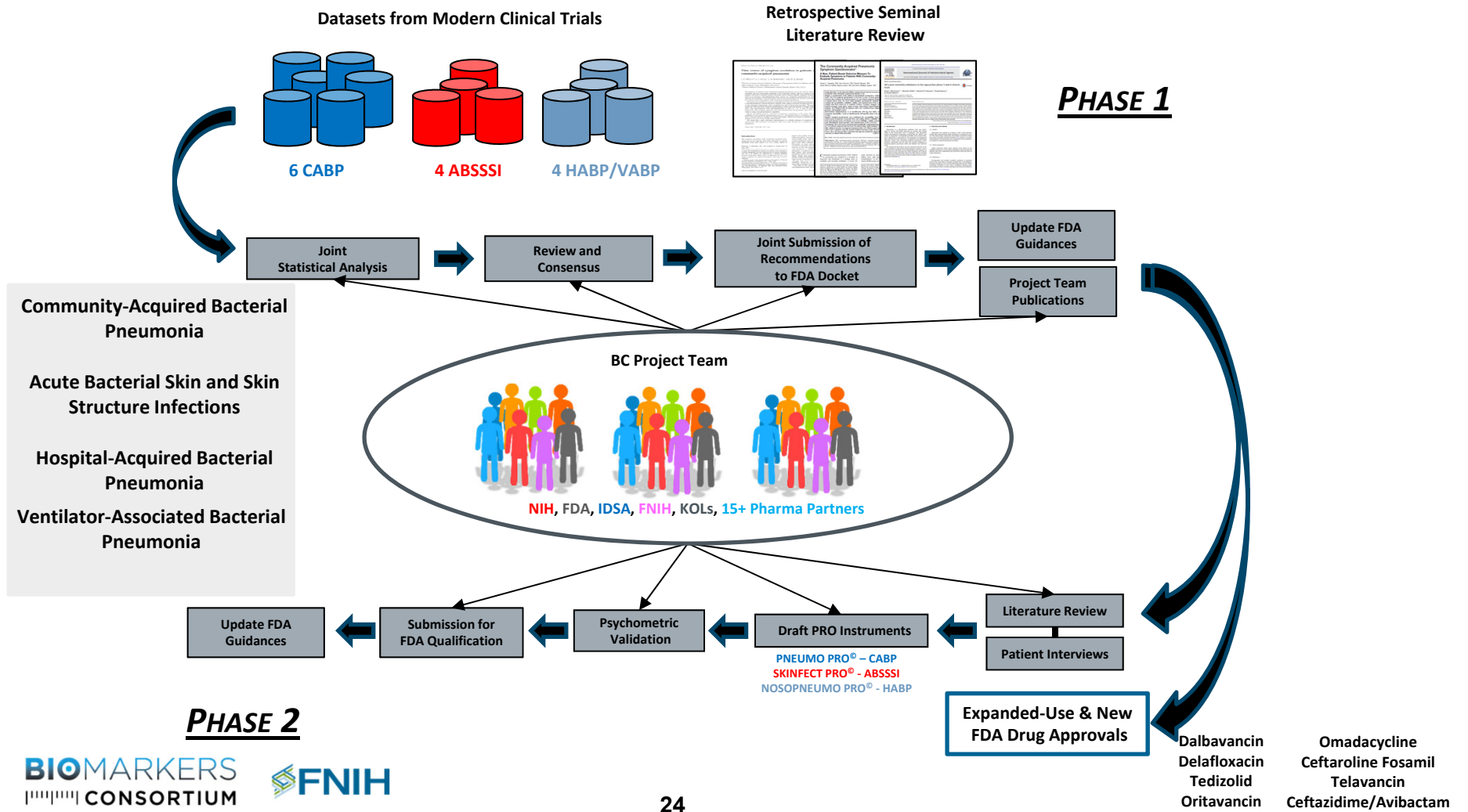
A conclusion, based on a formal regulatory process, that within the stated context of use, a medical product development tool can be relied upon to have a specific interpretation and application in medical product development and regulatory review.

1. **Biomarkers require extensive testing and QUALIFICATION** for practical use. Multiple studies ensure integrity and reproducibility of results
2. **Qualification requires large amounts of DATA** from clinical trials, observational studies and literature, which can be challenging, expensive and time-consuming to gather
3. **Qualification is based on CONSENSUS** among the scientific community, established through understanding of disease risk, natural history and outcomes
4. **Qualification is PRE-COMPETITIVE:** results are broadly available to the entire scientific community
5. **Qualification is DIFFICULT TO ACCOMPLISH IN A SINGLE INSTITUTIONAL SETTING**

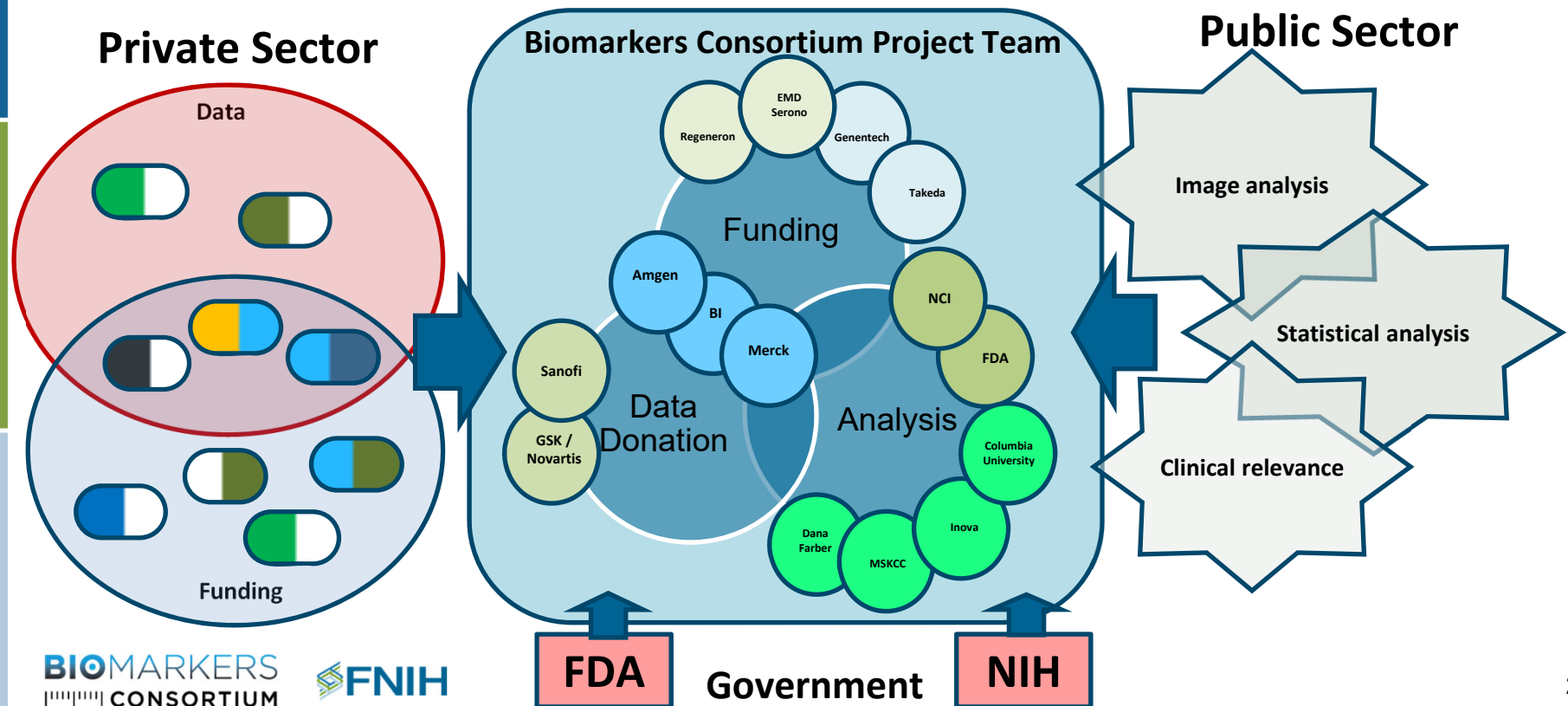
How does the Biomarkers Consortium develop Team-based projects?





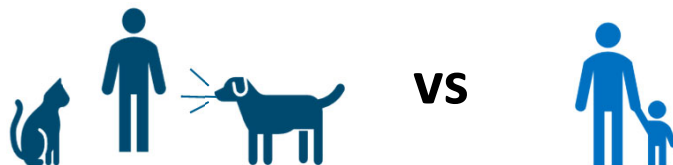


Collaborative projects that would be very hard to do any other way.



What do I do to manage this Consortium?

- Lead the Executive Committee
- Manage the process for project approval, funding and execution
- Ensure and update the overall strategy of the consortium
- Assist with Steering Committee strategy consistency
- Provide additional contacts and context to the stakeholder needs
- Other duties as assigned!



Keys for a Successful Partnership

- A significant unmet medical need
- A robust scientific rationale and design
- A compelling economic premise
- The support of willing, innovative partners (public + private)
- Money
- Leadership (a champion)
- A trusted third party
- Time, dedication, sweat...and flexibility



Attributes of Projects Less Successful at Generating Impact

- Primary focus is development of a technology platform that only benefits a single company
- Development of infrastructure versus hypothesis-driven science
- Single PI leading/Small team/Not true consortium
- No company participation early on in the creation of the project
- No FDA or other regulatory involvement in the design of project
- Does not align with the strategic priorities or needs of the partners

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