

***The National Biomarker Development Alliance  
(NBDA) \****

***\*(Founding Alliance Partners: Arizona State University, International Genome Consortium and the Critical Path Institute)***

***Collaborating Partners: Mayo Clinic – Several Additional Partners in Discussions***

**A CONVERSATIONAL, RESULTS- ORIENTED  
WORKSHOP**

***December 12, 2012 (Arrival), 13 and 14 (Departure)***

***“DESIGNING, CONSTRUCTING AND IMPLEMENTING A  
STANDARDS-BASED END-TO-END SYSTEM FOR  
BIOMARKER DEVELOPMENT”***

***Start-Up Funding: Flinn Foundation and ASU Foundation***

**December 13, 2012**

(All events will be held in the Peace Pipe Ballroom unless otherwise specified).

**7:30 a.m. - 8:00 a.m.            Breakfast**

***OVERALL MEETING CHAIR: ANN BARKER (ANN) (FIRST NAMES ONLY MEETING)***

**8:00 a.m. - 8:30a.m.            *NBDA Background, Goals for the Workshop and Agenda***

**Anna D. Barker, Ph.D., ASU; Carolyn Compton, M.D., Ph.D.,  
C-Path; Robert Penny, M.D., Ph.D., IGC**

**8:30 a.m. – 9:15 a.m.            State Setting Keynote Presentation (45 minutes – Discussion to  
Follow)**

***A Status Report on Biomarkers:  
biomarkers that are not; standards that are forgot;  
and the need to transform the system we've got!***

**George Poste DVM, Ph.D., ASU**

In this opening presentation George Poste (George) will lay out the myriad challenges, problems and issues that make the successful development of biomarkers a challenge not to be undertaken by the faint of heart. We are awash in biomarkers – yet the FDA has approved less than 1.5 per year since the mid 1990's (Anderson, et.al. Genome Technology, April 2010) despite over 1500 submissions. There are a dozen biomarker meetings a week – hundreds of millions of dollars being spent – and yet most biomarker driven phase III clinical trials fail – especially in an area like oncology. Precision medicine will limp along, but never proceed at scale or at a rate that will really benefit the patients who need targeted interventions. George will also offer some perspectives on what has to be done – and provide some direction for re-thinking this entire system which isn't really a system.

**9:15 a.m. – 10:00 a.m.            Discussion: The One Thing that Could Make the Difference  
(Your Best Idea)**

**10:00 a.m. – 10:20 a.m.            Break**

**10:20 a.m. – 11:30 a.m.**

**Panel/Discussion**

**Early and Late (Translatable Biomarker Discovery)** – It’s a eureka moment – you have discovered a biomarker. What exactly does that mean? There is no real guidebook to tell you that yes, it’s a biomarker – what evidence would you need to decide to go forward. What is the “chain of custody” for the discovery? Is documentation of process and procedures, etc. really there? Really this slows down discovery - is all of that really necessary? How should it be determine to move forward into late or translatable discovery – e.g., assay development (not inexpensive)? These first two critical phases of biomarker development are the root of most biomarker failures. Why - and what needs to be done to move this beyond a black box? Hopefully we have given the panelists a place to start!

**(Panel Moderator, Carolyn Compton)**

- **The really critical stuff – what makes the biomarker discovery process robust? When in the process does it have to become robust (i.e., reproducible? Why should we care? George Vasmatazis, Ph.D., Mayo Clinic**
- **Finding biomarkers in really really big multi-generational data sets – is this going to work – and how many genes (and or the RNA, proteome, epigenome) make a biomarker? Or is it a signature? Are we discovering or digging larger deeper holes? Joe Vockley, Ph.D., Inova Translational Medicine Institute**
- **Not So Fast – Show me the biomarker – View from the industry – Anahita Bhathena, Ph.D., Abbot Laboratories**

**11:30 a.m. – 12:15 p.m.**

**Discussion:** In an end –to-end model of biomarker development, what are the major questions (read level of evidence) that must be answered in early discovery to make an informed decision to proceed to translatable (late) discovery? Are the standards and decision points going to be very specific for every biomarker class? Free –think some recommendations for “fixing” these modules – we need ideas – open forum.

**12:15 p.m. - 1:15 p.m.**

**Lunch**

**1:15 p.m. – 2:15 p.m.**

**Panel Discussion**

**Assay Development and Assay Performance**

**(Panel Moderator, Robert Penny, IGC)**

Assay development – when and how do you know you have a winner? Have you ever seen a biomarker you didn't like – when do you say no? Is assay development too important to leave in the hands of novices? The world of Laboratory Developed Tests is exploding – if some of my FDA colleagues were here they would tell you that they just don't really care – they don't recognize LDTs. What is the role of these tests vs. 510Ks or PMAs. Why is analytical validation important if you want to use the test in patients -or is it? Head spinning stuff - can a diagnostic be a biomarker – can a biomarker be a diagnostic?

- **The HER-2 assay story (FISH – IHC) - are there major lessons to learn about assay development and use here? Patrick Roche, Ph.D., Ventana Medical Systems**
- **We are all beginning to think (and no doubt worry) about complex assay development (e.g., gene/other “signatures”, multiplexed assays). Will this mean new levels of evidence requirements? Kevin Halling, M.D. , Ph.D., Mayo Clinic**
- **Developing assays in the translational medicine space – – could biomarker qualification serve in this space? If a biomarker doesn't “qualify” in FDA-ease – is it done? Jannick Anderson, Ph.D., MD Anderson**

**2:15 p.m. – 2:40 p.m.**

**Discussion**

**2:40 p.m. – 3:00 p.m.**

**Break**

**3:00 p.m. – 4:15 p.m.**

**The Biomarker Complexity Conundrum**

Just when we think we know something about biomarkers, they are biomolecular entities – right? Wrong! If you can dream it, discover it, measure it, demonstrate that it is clinically relevant it can be called, and may even be, a biomarker. In fact if it is “fit for the purpose” it may be used: to predict of clinical response; monitor therapy; stratify patients for trials, etc. – it can become a biomarker. How many classes of biomarkers are there? Is it infinite? As we move into the mystical world of molecularly based medicine we face new challenges – complex signatures – nanotechnologies – advanced imaging. Let’s discuss what this means – especially in terms of levels of evidence requirements.

**Panel Moderator, Ken Buetow, Ph.D., ASU**

- **Is imaging the ultimate contemporary biomarker? Given the looming “epidemic” in Alzheimer’s disease – will biomarkers be critical? Are there lessons to learn from AD? Eric Reiman, M.D., Banner Health**
- **We are all focused on the genome, proteome, etc. – are there potentially better more quantifiable biomarkers – waiting to take their place? Ariel Anbar, Ph.D., ASU**
- **Algorithms as biomarkers –precision medicine almost demands that we be able to make sense of multi-dimensional “big data”. Is this the future of biomarkers? Andy Hospodor, Ph.D., U.C., Santa Cruz**

**4:15 p.m. – 4:45 p.m.**

*Qualifying vs. validating a biomarker – can this work so that it isn’t a “Where’s Waldo Experience”*

**Laura Vant Veer, Ph.D., UCSF**

**4:45 p.m. – 5:15 p.m.**

**Summing Up and Tomorrow**

**6:00 p.m.**

**Reception and Dinner, Camelback Patio**

*December 14, 2012*

**7:30 a.m. - 8:00 a.m.**

**Breakfast**

**8:00 a.m. - 8:30 a.m.**

***Mind-Bending Presentation***

***Designing and Implementing Biomarker Driven Clinical Trial:  
Reflections on the ISPY-2 and other Experiences – Can this be  
Generalized?***

**Donald Berry, Ph.D., University of Texas - MD Anderson  
Cancer Center**

**8:30 a.m. - 9:00 a.m.**

**Discussion**

**9:00 a.m. – 10:15 a.m.**

**Panel Discussion**

**Panel Moderator, Karen Anderson, M.D., Ph.D., ASU**

**Biomarker Driven Clinical Trials – The Last Stop on the Way  
to Regulatory Submission:**

If you've gotten this far -and it's all good – you may be ready to design and undertake a biomarker driven clinical trial. If so, extract your wallet and prepare to fail! Coming back to a familiar theme – biomarker trials have to work – otherwise very little personalized medicine will materialize, and the statistics currently don't look that good. If level of evidence standards got you this far – should you expect to succeed?

This panel has an assignment – 3 questions (1) As you look at the biomarker field today what is the single biggest barrier to use these advances to enable smaller, better trials? (2) If you had total control how would you develop a system for biomarker-enabled clinical trials that was faster/cheaper - and obviously produced better drugs? (It goes without saying that you can't remove FDA) and (3) Will biomarkers make the randomized clinical trial irrelevant?

**Ray Dubois, M.D., Ph.D, ASU (Colon Cancer)**

**Rafael Fonseca, M.D., Mayo Clinic (Multiple Myeloma)**

**Michael Berens, Ph.D., TGEN (GBM)**

**Randy Nelson, Ph.D., ASU (Diabetes)**

**10:15 a.m. - 10:30 a.m.**

**Break**

**10:30 a.m. – 11:30 a.m.**

**Individual Group Discussions – The end-to-end pipeline – recommendations for level of evidence standards (be as specific and detailed as you feel appropriate)**

**11:30 a.m. - 12:15 p.m.**

**Recommendations for the NBDA and the field – A convergent discussion – (goal of publishing our recommendations)**

**12:30 p.m.**

**Lunch and/or Depart**