



Biospecimens for Genomic and Proteomic Analyses

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1



A Science-based Approach to Biospecimen Quality in Regulatory Decision-making

2

Biospecimen Quality

- Biospecimen quality: minimal or controlled non-biological variability
- Evidence-based criteria for quality
 - Patient preparation
 - Sample
 - Collection
 - Handling
 - Storage
 - Extraction/purification
 - Rich clinical annotation
 - Demography
 - Clinical characteristics/outcome

3

Current State

- Biospecimen quality as a regulatory issue
 - New sensitive technologies: RNA, plasma proteome, etc
 - Known lability/variability of analytes
 - 20% of HER2 testing inaccurate (ASCO guidelines, Wolff et al, JCO 2007)
 - Minimal evidence base for establishing quality criteria
 - Few requirements for sponsor control of quality

4

Potential Consequences

- **Premarket**
 - Poor quality biospecimens in development
 - Miss real associations
 - Identify spurious/false associations
 - Waste \$\$, time, opportunity
- **Postmarket**
 - Poor quality biospecimens in clinical practice
 - Decreased confidence in diagnostic performance
 - Patient consequences
 - Misdiagnosis
 - Wrong or suboptimal therapy

5

FDA Science-based Approach to Biospecimen Quality

Current activities:

- **FDA/NCI collaboration**
 - Develop and carry out evidence-generating science
 - Develop best practices
 - Advise on study design where requested to optimize quality
- **FDA/College of American Pathologists (CAP) collaboration**
 - CAP
 - Identify key parameters of biospecimen quality
 - Provide recommendations to FDA
 - FDA/CAP to promote biospecimen quality as a laboratory priority
- **PGx Data Submissions companion guidance (draft) and other IVD guidances**

6

Science Board Role

- Subcommittee to review biospecimens recommendations
 - Recommendations solicited from CAP
 - SB subcommittee meeting
 - Review CAP recommendations
 - CAP and others (e.g., AACC, ACS, NCI) to provide public comment
 - SB to provide additional perspective and advice on FDA biospecimen initiatives
 - Proposed 2009 meeting

7

The Future

Future activities

- Guidance
 - Provide specific regulatory advice to sponsors regarding biospecimen quality
- Phase in recommendations for biospecimen quality reporting in regulatory submissions
 - Provide biospecimen quality parameter reporting capability in regulatory submissions
 - CDER, CBER, CDRH
- Gather additional information on biospecimen quality
 - IT structures to data-mine existing data for evidence criteria
 - caTissue Core example: path/clin annotation function
- FDA research program
 - develop biospecimen quality parameters using scientific evidence

8