

ERCC Workshop

FDA Perspectives

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FDA PERSPECTIVE

NEED:

Control materials for performance evaluation of reproducibility, sensitivity and robustness in gene expression analysis

GOAL:

IMPROVE MEDICAL PRODUCT SAFETY AND QUALITY

WHY STANDARDS?

*Understand and control
variability within and
comparability between
different arrays and
methods*

*Define and reduce data
submission requirements*

EFFORTS SUPPORTING STANDARDIZATION

- **Nucleic acid standards**
- **Platform standards**
- **Methodological standards**

ERCC: SPIKE-IN RNA CONTROLS

- **Microarray and RT-PCR performance**
 - **Reproducibility**
 - **Sensitivity**
 - **Specificity**
 - **Robustness**
- **Within and between platforms**

CUSTOMERS

- *Array Users*
- *Array Manufacturers*
- *Regulatory Agencies*

VARIABILITY

- **Different laboratories, platforms, sample types, extraction methods**
 - **Quality of starting, processed (labeled/amplified) sample**
 - **Stringency of hybridization**
 - **Deposition: printing, in-situ**
 - **Probes: (oligo and cDNA)**
 - **Primer: oligo (d)T, random hexamers**

VARIABILITY (2)

- Image scanning
- Instrument settings
- Data transformation/normalization
- Data fidelity decisions (false positive/ negative)

Biologically Significant Measurement

IMPACT on FDA OVERSIGHT

- **Clinical diagnostics**
 - **Diseased tissues, tumors, pathogens**
 - **Drug response analysis (pharmacogenomics)**
- **Product development/characterization**
 - **Preclinical studies**
 - **Potency**
 - **Lot release**

**Gene expression response data to support
claims for safety and efficacy**

Enhanced QC in the production of biologics

PERFORMANCE REQUIREMENTS

- **RISK BASED ANALYSIS!**
 - **Different requirements for different uses**
 - **Population**
 - **Age**
 - **Disease or Indication**
 - **Childhood Vaccine vs Adult Cancer Therapy**
- **IND or NDA**
- **Device PMA or 510(k)**
- **License for Drug or Biologic Product**

NEXT STEPS

- **Standard material availability**
- **Application to address the challenges**

Thanks ERCC and NIST!