SRMs are Critical to Continued Innovation in Healthcare

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Outline

- Who we are
- NIST questions
- SRMs for molecular diagnostics
  - Needs in oncology
  - Needs in virology
  - Needs in genetics
  - Prioritization

About Association for Molecular Pathology

- ~2,000 members - diverse
- Subdivisions:
  - Genetics (inherited conditions)
  - Hematopathology (leukemias & lymphomas)
  - Infectious Diseases
  - Solid Tumors
- Scientific Interest Group:
  - Pharmacogenetics

Member Interests Addressed by Committees

- Clinical Practice
- Professional Relations
- Economic Affairs
- Membership & Professional Development
- Nominating
- Program
- Publications
- Strategic Planning
- Training & Education

SRMs a Focus of AMP CPC

- Clinical Practice Committee (CPC)
- Addresses challenges facing clinical molecular diagnostic laboratories, and, therefore, improve patient care
- Standards are an integral part of high quality diagnostics.

Questions to Address

- What NIST measurement services does your organization or industry sector rely upon?
- What are the impact of these services?
- Are there any issues related to NIST measurement services (e.g.,timeliness, gaps, priorities)?

Gaps in SRMs

- Molecular diagnostics is standard of care in many aspects of health care
  - Oncology
  - Virology
  - Genetics
  - HLA
- We are currently performing the vast majority of these tests without access to SRMs

Lack of SRMs Hinders Effective Medical Care

- SRMs ensure sensitivity, specificity, reproducibility
- Lack of SRMs
  - Hinders best patient care
  - Barrier to introduction & adoption of advanced diagnostic tests
- Future
  - Whole genome sequencing
  - Personalized medicine

AMP.org Association for Molecular Pathology

Targeted Therapeutics & Tumor Markers

- Disease: Chronic Myelogenous Leukemia (CML)
  - Tumor Marker: *BCR-ABL1*
  - Targeted Therapeutic: tyrosine kinase inhibitors (TKIs)
- Approximately 5050 new case/year
- Quantitative testing performed q 3 months

Targeted Therapeutics & Tumor Markers

- Therapy for CML is guided by amount of disease burden
- The lack of SRMs limits the reproducibility of assays, limiting patient's care options
- CML model may become the standard for other genes with molecularly targetable mutations or mutations suitable for minimal residual disease monitoring

Companion Diagnostics in Oncology

- KRAS Mutation Analysis
  - Colorectal cancer
    - 106,100 new cases/year (cancer.org 2009)
  - Predicts response to Erbitux & Vectibix
- EGFR Mutation Analysis
  - Non-small cell lung cancer
    - 219,440 new cases lung cancer/year
  - Predicts response to TKIs
- Standardized reagents are urgently needed to allow comparative analysis between clinical protocols

Transplant Follow-up Care

- >170,000 in U.S. living with a solid organ transplant (2006)
- Immune-suppressive therapy induces susceptibility to viral and fungal diseases
- Quantitative viral load testing is standard of care
- Tests show marked variability among commonly used methods because there are no established quantitative virus standards.
  - Repeat testing is often required when a patient switches health insurance or travels to a different hospital or city.

(Example) Need in Medical Genetics

- Cystic fibrosis
  - FDA approved tests must have controls for all mutations
  - Patient samples not available for rare mutations

Reference Gene Sequence Database

- IT a critical tool for test interpretation & reporting
- Genotypic bacterial identification
  - Id & resistance testing (TB)
- Human genes
  - Reproducibility
  - Accuracy
  - Interpretation

Priorities – Immediate (Needed “Yesterday”)

- Cytomegalovirus (CMV)
- BCR-ABL Adelaide standard
- KRAS mutation standards
- EGFR mutation standards

Priorities – Medium (Needed within 1 year)

- BK virus (BKV)
- Epstein Barr Virus (EBV)

Priorities - Longer Term (Needed in 1-3 years)

- Adenovirus, quantitative assay standard
- Enterovirus, qualitative assay standard
- Hepatitis B virus
- Herpes simplex (HSV), types 1 and 2, qualitative assay standard
- HHV-6, HHV-7, and HHV-8
- HTLV 1 and 2, qualitative assay standard
- Human metapneumovirus (HMPV), qualitative assay std

Priorities - Longer Term (Needed in 1-3 years)

- Influenza virus, qualitative assay standard
- JC virus, quantitative assay standard
- Parainfluenza virus, qualitative assay standard
- Parvovirus B19, quantitative assay standard
- Respiratory syncytial virus (RSV), both qual & quant stds
- Varicella zoster virus (VZV)

Priorities - Longer Term (Needed in 1-3 years)

- Certified Gene Sequence Databases (CGSDs)
  - Gene mutation sequence database, suitable for clinical test reference
  - Infectious agent (bacteria, viruses) sequence database, suitable for clinical test reference
- Scientific advisory committee to identify and prioritize areas of needed references materials

The Growing Gap

- Current available standards do not meet our needs
- The gap is widening rapidly
- Goal:
  - Rapid development of new SRMs
  - SRMs available for purchase by test manufacturing companies and/or clinical laboratories

Presentation to the Visiting Committee on Advanced Technology (VCAT)

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