



Determining and Monitoring Needs for QC Materials for Genetic Testing: The US Experience

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QC Materials Meetings 2003-2004

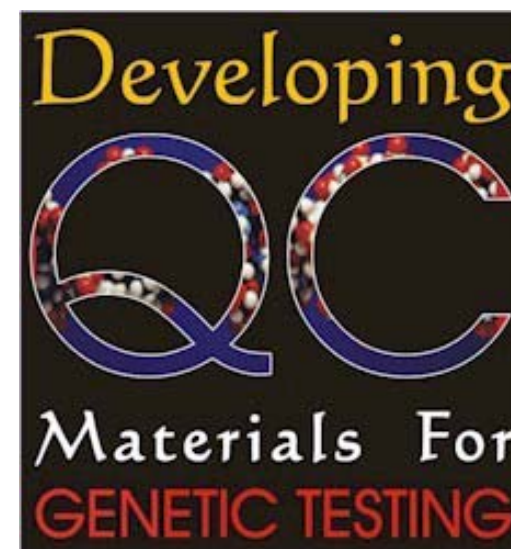


❖ Areas of need addressed and recommendations

- QC Material Priorities
- Professional Guidance
- Oversight of QC Products
- Research
- Use of Cell Banks
- Material Contributors
- Validation of QC Materials
- Funding Coordination

❖ Next steps and future directions

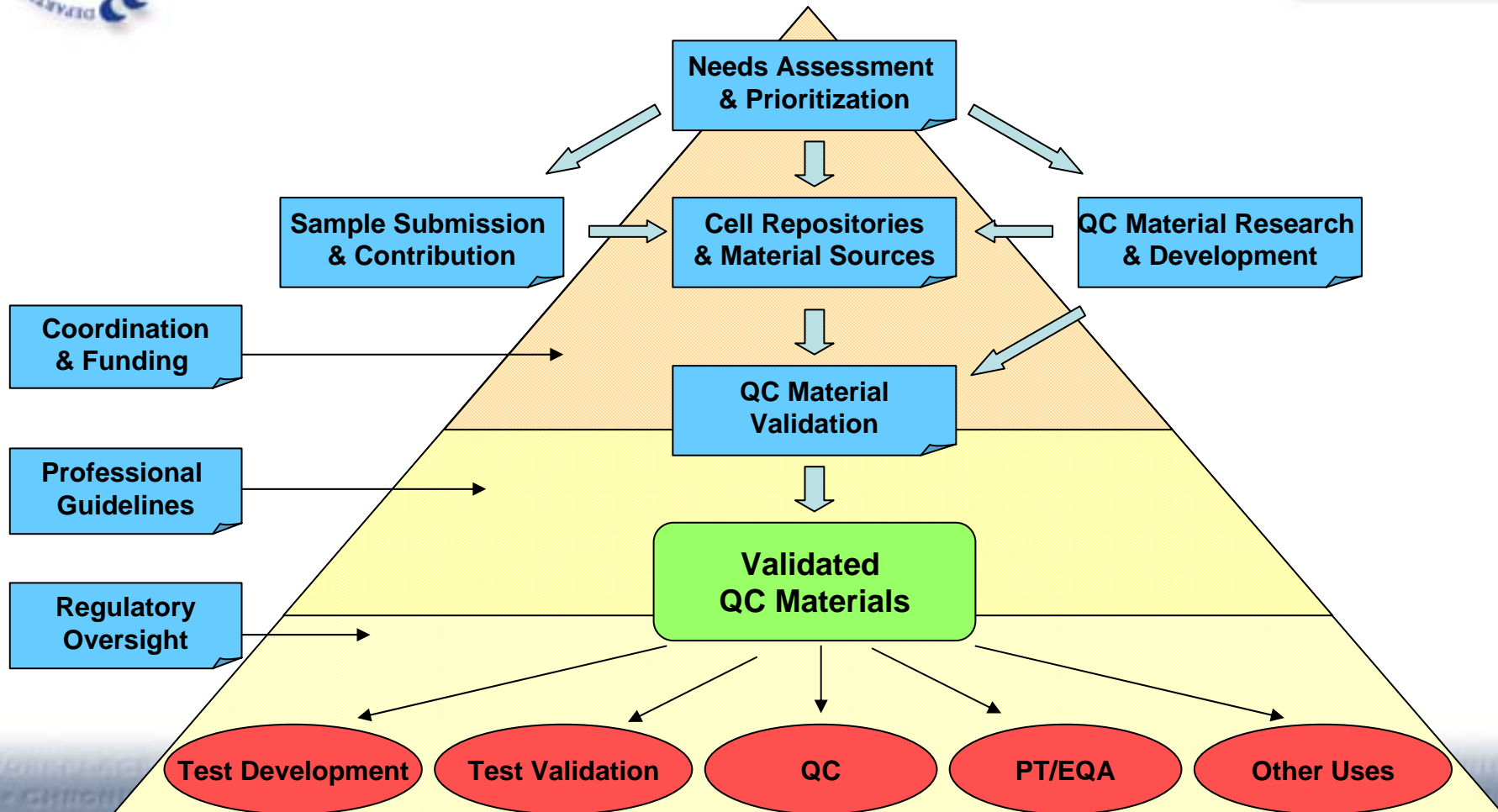
- Coordination
- Continuous needs monitoring
- Information dissemination



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QC Materials Workgroups and Process





QC Material Needs for Genetic Testing – Factors Considered



- ❖ Multi-facet discussion and consideration
- ❖ Some drivers of QC material needs considered
 - Volume and commonality of testing
 - Professional/practice recommendations regarding test utilization
 - Voluntary laboratory standards and professional recommendations
 - Regulatory oversight
 - FDA requirements
 - CLIA regulations
 - State requirements
 - Need for testing standardization
 - Test development (commercial and in-house)

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CLIA Requirements



- ❖ Federal standards for laboratories performing patient testing to ensure the quality of laboratory testing in U.S.
- ❖ Current regulations contain requirements for a clinical cytogenetics specialty but no specific requirements for molecular or biochemical genetic testing
- ❖ Laboratories performing molecular and/or biochemical genetic testing are subject to applicable general requirements
- ❖ Proposed rule for a genetics specialty under development





CLIA Requirements (cont.)



- ❖ General requirements for control materials applicable to genetic testing
 - Control procedures must monitor the test system over time and detect immediate errors
 - At least two control materials for each molecular amplification procedure
 - A control material capable of detecting reaction inhibition if this is a significant source of false negative results in a molecular amplification procedure
 - A negative and positive control material for each qualitative procedure
 - Two control materials of different concentrations for each quantitative procedure
 - Two control materials, including one capable of detecting errors in the extraction process, for each test system having an extraction phase

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CLIA Requirements (cont.)



- ❖ General requirements for control materials applicable to genetic testing (cont.)
 - Establish or verify the criteria for acceptability of all control materials. Results of control materials must meet the criteria for acceptability before patient test results can be reported
 - For in-house-developed tests (including most genetic tests), establish the number, type, concentration, and frequency of performance of control materials
 - Test control materials in the same manner as patient specimens
 - Rotate control material testing over time among all operators performing the patient testing
 - Develop an alternative mechanism to detect immediate errors and monitor test system performance over time for test systems that do not have control materials available

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Requirements of State Programs



- ❖ Washington State Laboratory Quality Assurance Program
 - Equivalent to CLIA regarding the use of controls or control materials in the testing process
 - Not specific for genetic testing
- ❖ New York State Clinical Laboratory Evaluation Program
 - Specific QC standards, method validation procedures, and personnel qualifications for genetic testing
 - Require submission of procedure manuals that fully describe control materials used for each assay, both for the method validation procedure and for routine testing process, for each genetic test





Priorities of QC Material Development for Genetic Testing



❖ QC Material Priorities Workgroup

Jean Amos (Leader), Kenneth Friedman, William Highsmith, Elaine Lyon, Walter Noll, Deborah Payne

❖ Charges

- Identify genetic tests in urgent need of QC materials and develop a priority listing
- Develop criteria and key factors for ongoing needs monitoring and evaluation
- Evaluate the identified needs and make recommendations regarding potential approaches to meet the needs





QC Material Needs for Genetic Testing (con.t)



- ❖ Areas of need identified
 - Intra-laboratory testing process (method validation, testing process, lot testing)
 - Test development (in-house and commercial)
 - Performance evaluation: PT/EQA
- ❖ Priority list (next slide)





Priorities based on Genetic Testing in U.S.



- ❖ CFTR mutation analysis
 - ACMG-recommended core panel
 - Other mutations with clinical relevance/significance
 - Genomic (multiple cell lines for each mutation) and synthetic “super-controls”
- ❖ Fragile X testing
 - Additional QC/RMs for both PCR and Southern blot assays to supplement NIST Fragile X SRM
 - Controls for determining methylation status
- ❖ ACOG-recommended AJ carrier testing
 - 8 diseases on the recommended panel (Tay-Sachs disease, Canavan disease, familial dysautonomia, mucopolysaccharidosis IV, Niemann-Pick disease type A, Fanconi anemia group C, Bloom syndrome, and Gaucher disease)
 - QC materials for mutations associated with disease





Priorities based on Genetic Testing in U.S. (cont.)



- ❖ DNA-based diagnostic testing for population/ subpopulation screening
 - Galactosemia
 - Medium-chain acyl-CoA dehydrogenase deficiency
 - Biotinidase deficiency
 - Other newborn screening conditions
- ❖ Pharmacogenetic testing
 - CYP2D6, CYP2C9, CYP2C19, TPMT variants.
 - Control materials need to represent allele specificity in various populations and subpopulations
- ❖ Mitochondrial disorders
- ❖ Sizing standards for other trinucleotide repeat diseases (HD, SCA 1 and 7, DM)
- ❖ Appropriate control materials for sequencing assays





Refining Needs/Priorities and Continuous Monitoring



- ❖ Need for ongoing monitoring and assessment
- ❖ Parameters to be collectively monitored
 - Demand of testing in clinical and public health practice
 - Professional/practice recommendations regarding test utilization
 - Regulatory requirements
 - Need for testing standardization
 - Needs captured by materials repositories
- ❖ Other areas in need of monitoring and improvement
 - Rare disease testing
 - Biochemical genetic testing
 - Emerging testing technology (e.g., microarray-based genomic screening assays)





Mechanisms for Needs Monitoring



- ❖ Periodical surveys among users of QC materials in collaboration with professional organizations
 - Testing laboratories
 - Test developers
 - IVD manufacturers
 - PT/EQA programs
- ❖ Assessment studies
- ❖ Expert meetings
- ❖ Genetic Testing Quality Control Materials Program (GTQC)





First GTQC Expert Panel Meeting Nov. 29, 2005



❖ Goals and discussion topics

- Review progress of the GTQC program since November 2004 -
 - Coordination of QC material verification and submission
 - Information exchange and dissemination
 - Monitoring of community needs
- Discuss issues and obstacles of current activities, suggest strategies for moving forward
- Review and update previously identified QC material needs and priorities
- Discuss opportunities for coordination and collaboration with European groups and/or colleagues
- Discuss evaluation of the success/effectiveness of the GTQC program and suggest improvements needed
- Consider next steps - future activities and next meeting

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First GTQC Expert Panel Meeting Nov. 29, 2005 (cont.)



❖ Recommendations

❖ Next steps

- Activities
- Next meeting





For More Information:

<http://www.phppo.cdc.gov/dls/genetics/default.aspx>

