THE SECOND QUALITY CONTROL MATERIALS FOR GENETIC TESTING MEETING

March 8, 2004, Orlando, FL

Executive Summary

The 2nd **Quality Control Materials for Genetic Testing** meeting, organized by the Centers for Disease Control and Prevention (CDC), was held on March 8, 2004, in Orlando, Florida. Participants of this working meeting included more than 50 leaders in genomics and genetic testing from professional organizations, government agencies, industry, laboratories, academic institutions, and proficiency testing (PT)/external Quality Assessment (EQA) programs. The main goals of the meeting were to 1) review activities and progress to date of the eight working subcommittees established at the September 2003 meeting; and 2)develop recommendations and future directions for practical, sustainable mechanisms for making quality control (QC) materials available to the genetic testing community at a reasonable cost.

The meeting began with a brief summary of the first **QC Materials for Genetic Tests** meeting, which was held on September 15-16, 2003, in Atlanta, GA, by Dr. Lawrence M. Silverman, Professor of Pathology in University of Virginia. Dr. Kristy L. Richie, National Institute of Standards and Technology (NIST), presented an update on the development of standard reference materials for determining the trinucleotide expansion of the Fragile X syndrome. Dr. D. Joe Boone, Associate Director for Science, Division of Laboratory Systems, Public Health Practice Program Office, CDC, gave an overview of the charge and tasks of the eight subcommittees, which were formed as a result of the September 2003 meeting to address the following identified areas of needs for developing and providing QC materials for genetic tests:

- Develop a scheme to set priorities for current and future needs
- Develop networks of material contributors to facilitate participation and material collection
- Develop processes to use existing cell banks as material sources
- Identify research activities on QC material development and facilitate collaboration among research efforts
- Develop validation processes for QC materials
- Develop professional guidance on appropriate use of QC materials
- Clarify regulatory oversight for providers and users of QC materials
- Develop better coordination of funding sources and opportunities.

Following the general session, the subcommittees held concurrent breakout discussions to review efforts made to address the respective area of needs and develop further recommendations. In the afternoon, participants returned to a general session to hear the progress reports from each subcommittee. The following major progress and ongoing activities were reported by the subcommittees:

- **The Subcommittee on QC Material Priorities** developed recommendations on the current needs of QC materials at four levels of priority. The subcommittee is working to refine a set of criteria for identifying future priorities, by considering test volume,

recommendations of professional societies, mutations searched for at public repositories, need for standardization, and other factors.

- **The Subcommittee on QC Material Contributors** made the following progress: 1) developed recommendations in conjunction with the Subcommittee on Use of Cell Banks for appropriate submission mechanisms for specimen collection; 2) identified the need for a project coordinator to facilitate collection, development, validation, and distribution of QC materials; 3) developed a draft letter and questionnaire to engage the broader community and identify potential material contributors; and 4) obtained additional input from the American College of Medical Genetics (ACMG) Quality Assurance Committee on these activities.
- **The Subcommittee on Use of Cell Banks** developed additional recommendations on 1) informing the clinical laboratory and research community about the material contribution process; 2) validating and distributing contributed DNA at a nominal cost to investigators and laboratories; 3) exploring ways to permit commercial use of contributed materials; and 4) coordinating with other cell banks or sources to provide information on the availability of QC materials.
- **The Subcommittee on QC Material Research** developed a working report "Maintaining Optimal Quality Control in Molecular Genetic Tests", which summarized the current research efforts to develop artificially constructed control materials and modified cell lines containing targeted mutations or variations. The report also discussed issues and challenges in optimizing and using the materials to maintain accuracy and reliability of the genetic tests.
- **The Subcommittee on QC Material Validation** proposed a two-step approach in developing recommendations for QC material validation, by considering the needs for heritable mutation testing first and the more complex requirements for somatic mutations and quantitative assays as a next step. The Subcommittee has developed a draft report summarizing its considerations for the principle and methods of validation and establishment of traceability for control and reference materials used for molecular genetic tests.
- **The Subcommittee on Professional Guidance** reviewed current US and international practice guidelines and recommendations for use of QC materials in genetic tests, including general and disease-specific guidelines from professional societies and standard-setting organizations, publications by leaders of PT/EQA programs and providers of control or reference materials, and other related documents. The Subcommittee has developed recommendations on the adequacy of existing guidelines and the need to involve industry to make more control materials available.
- **The Subcommittee on Regulatory Oversight** developed a draft document clarifying the current FDA, CLIA, and New York State requirements as they relate to QC materials for genetic tests. The subcommittee is soliciting input on other information to be included to make the document useful for both providers and users of the materials for test development, quality control and proficiency testing.

All subcommittee reports were received with enthusiasm. Further recommendations were made by each subcommittee regarding its continuing efforts, collaborations among subcommittees and with other government agencies and professional groups, future projects, and the need to

establish resources and mechanisms for a sustainable process for developing and providing materials for genetic testing. Among the recommendations for the next steps were the following:

- CDC should continue its leading role in supporting and coordinating activities to ensure and improve availability of appropriate QC materials for genetic tests.
- A National QC Material Coordinator should be established and funded by CDC to facilitate the development, collection, submission, validation, and distribution of materials; monitor the needs of the community on a continuing basis; and improve information exchange among users, repositories and manufacturers of control and reference materials.
- A CDC-sponsored expert panel should be retained to serve as a resource to the National Coordinator.
- Continuing funding and resources are needed to support additional projects to develop and provide the QC materials that have been identified as high priorities.
- It is essential to involve the IVD industry and manufacturers in the process; mechanisms should be explored to establish public/private partnership and make development and provision of QC materials an attractive pursuit.
- Defined protocols need to be developed and provided to laboratories participating in the collection of materials to facilitate contribution of 1) existing blood specimens that have been analyzed and anonymized, 2) specimen re-collections directly from patients with informed consent, and 3) existing cells lines.
- An incentive program should be developed for participants submitting materials, including assurance that final materials will be available to the contributors.
- All controls should be available to the general community without undue patenting or licensing restrictions.
- An interactive web site should be provided by CDC for posting helpful references, such as protocols from completed CDC-funded projects for developing positive QC materials for genetic tests; facilitate use of web-based resources; and serve as a mechanism for communication and discussion among project participants.
- Information dissemination is critical for engaging the broader community and ensuring funding resources and support. Proposed venues included a satellite workshop at the 2004 annual meeting of the American Society of Human Genetics, a companion meeting at the 2004 annual meeting of AMP, and a symposium at the 2005 annual meeting of ACMG 2005.
- A publication should be developed based on the subcommittee accomplishments and recommendations.

At the end of the meeting, participants expressed appreciation for CDC for supporting and coordinating activities in QC material development and asked that CDC continue this role. Dr. Boone suggested that the subcommittee reports be posted at the CDC website to make the progress and recommendations available to the public and to help obtain additional input for moving the process forward. The next meeting is proposed for November 9th, 2004, in Los Angeles, CA.