

CDC Guidelines for Good Laboratory Practices in Genetic Testing

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Centers for Disease Control and Prevention (CDC)
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Outline

- ❖ Development of Clinical Laboratory Improvement Advisory Committee (CLIA) recommendations for good laboratory practices in genetic testing
- ❖ CDC guideline for molecular genetic testing (MGT) and upcoming guideline for biochemical genetic testing (BGT) and newborn screening (NBS) for inherited metabolic diseases
- ❖ Issues for SACGHS input

Current Oversight for Genetic Testing

❖ CLIA regulations

- General requirements for non-waived testing as applicable
- Specialty of clinical cytogenetics
 - Specific QC requirements
 - Qualification requirements for technical supervisor
- Requirements for molecular amplification procedures
- No specialty for molecular or biochemical genetic testing

❖ FDA requirements for IVD products

❖ State programs

❖ Accreditation standards

❖ Professional practice guidelines

❖ Good laboratory practices

Clinical Laboratory Improvement Advisory Committee (CLIAC)

- ❖ Federal advisory committee established under Public Health Service Act [42 USC §217a] in 1992
- ❖ Provides scientific and technical advice regarding
 - CLIA regulations
 - Impact on medical and laboratory practice
 - Modifications to accommodate technological advances
- ❖ Reports to HHS Secretary/Assistant Secretary for Health, CDC Director, CMS Administrator, FDA Commissioner
- ❖ Managed by CDC Division of Laboratory Science and Standards (DLSS)



Developing Good Laboratory Practice Guidance for Genetic Testing

- ❖ 1997: Federal agencies (CDC, CMS, FDA, NIH) working with advisory committees, other stakeholders to consider quality assurance and oversight for genetic testing
- ❖ 2007: CMS action plan to enhance oversight of genetic testing
 - Providing guidance rather than prescriptive regulations
 - Training, education, data collection, collaboration
- ❖ 2008: SACGHS report - U.S. System of Oversight of Genetic Testing
- ❖ 2008: CLIAC recommendations for good laboratory practices (GLPs) in MGT, need for separate guideline to address BGT
- ❖ 2009: CDC *Morbidity and Mortality Weekly Report* (MMWR) guideline



MMWR™

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Recommendations and Reports

June 12, 2009 / Vol. 58 / No. RR-6

Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions

INSIDE: Continuing Education Examination

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

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Continuing Education Activity.....6CE-1

Process of Developing Recommended Practices for BGT and NBS

- ❖ 2009: CLIAC BGT workgroup
- ❖ Feb. 2010: CLIAC recommendations for BGT and NBS for diagnosis and monitoring of inborn errors of metabolism (<http://wwwn.cdc.gov/cliac/default.aspx>):
 - Total testing process (preanalytic, analytic, and postanalytic phases of BGT and NBS)
 - Personnel qualifications, responsibilities and competency
 - Factors to consider when introducing new tests
 - Confidentiality procedures
 - Potential benefits of quality management system approach
- ❖ 2011: Prospective MMWR guideline



Highlights of Good Laboratory Practices for Genetic Testing

Scope and Applicability

- ❖ MGT MMWR:
 - MGT for heritable diseases and conditions
 - MGT aspects of tests encompassing MGT and other methods
- ❖ Upcoming MMWR for BGT and NBS: Genetic testing for screening, diagnosis and management of inborn errors of metabolism (IEMs)
 - BGT (including diagnostic testing for presumptive positive NBS cases)
 - NBS for IEMs
 - BGT aspects of tests encompassing BGT and other methods

Highlights of Good Laboratory Practices for Genetic Testing

Recommended practices in preanalytic phase –

- ❖ *Information to be provided to users of laboratory services*
- ❖ *Informed consent*
- ❖ Test request
- ❖ Specimen submission, handling and referral
- ❖ Preanalytic system assessment

Highlights of Good Laboratory Practices for Genetic Testing

- ❖ Laboratories should provide test information to users to facilitate -
 - Selecting and requesting appropriate molecular or biochemical genetic tests
 - Collection, handling, transport, and submission of specimens
 - Obtaining patient information needed by the laboratory to perform testing and report test results
 - Informed decision making

Highlights of Good Laboratory Practices for Genetic Testing

- ❖ Information to be provided for each molecular or biochemical genetic test:
 - Intended use (analyte or nucleic acid target, specimen type, purpose of testing, recommended patient population)
 - Indications for testing
 - Test method to be used
 - Analytic performance specifications, clinical validity, limitations
 - FDA approval or clearance
 - Specimen collection, handling, transport, and submission
 - Types of patient information needed by the laboratory for effective testing, accurate laboratory interpretation and result reporting
 - Likelihood of test results to have implications for family members
 - Availability of laboratory consultation and discussion
 - Cost information when possible and practical

Highlights of Good Laboratory Practices for Genetic Testing

❖ Informed consent for MGT and BGT –

- Provide users with information necessary to make informed decisions whether informed consent (IC) is required or not
- Unless mandated, obtaining IC for patient testing generally not a laboratory responsibility
- When IC is required, assist in determining appropriate level of IC and include method for documentation on test request forms

❖ Informed consent for NBS -

- Explicit parental consent not necessary for mandated public health NBS if meeting accepted criteria
- New tests not meeting criteria should require explicit consent
- Parental and provider education should be integral to NBS programs regardless of consent requirement
- Research use of tested specimens should have appropriate human subjects protection procedures

Highlights of Good Laboratory Practices for Genetic Testing

Recommended practices in analytic phase -

- ❖ Performance establishment and verification
 - Ensure adequate establishment/verification of analytic performance
 - Include adequate number, type, and variety of samples
 - Document available information on clinical validity
 - “Truth in advertising”
- ❖ Control procedures
 - Specific QC measures for MGT: MGT MMWR
 - QC measures in BGT and NBS: Upcoming MMWR
- ❖ Specific analytic issues for BGT and NBS
 - Reagents, standards/reference materials, supplies, equipment
 - Calibration and calibration verification
- ❖ Proficiency testing (PT) and alternative performance assessment

Highlights of Good Laboratory Practices for Genetic Testing

Recommended practices in postanalytic phase -

❖ Test report

- Provide information necessary for accurate understanding and interpretation of test results
- Comply with CLIA general test report requirements
- Include recommended additional information for MGT, BGT and NBS (details in MGT MMWR and summary of CLIA recommendations)

❖ Report retention

- MGT reports: At least 25 years
- BGT reports indicating genotypes: At least 21 years
- NBS reports: Comply with CLIA and state requirements

Highlights of Good Laboratory Practices for Genetic Testing

Recommended practices in postanalytic phase –

- ❖ Record retention: CLIA and other applicable requirements
- ❖ Retention of tested specimens:
 - MGT: As long as possible, at least until next PT or alternative performance assessment
 - BGT: As long as possible, at least until after final result reporting. If possible until next PT or alternative performance assessment
 - NBS: Subject to federal, state, local requirements
- ❖ Postanalytic Systems Assessment

Highlights of Good Laboratory Practices for Genetic Testing

Recommended personnel qualifications -

- ❖ Laboratory directors: Meet CLIA requirements for high complexity testing
- ❖ Technical supervisors:
 - MGT: Equivalent qualifications to CLIA requirements for clinical cytogenetics technical supervisors or current certification in MGT by an HHS-approved board
 - BGT: Equivalent qualifications to CLIA requirements for clinical cytogenetics technical supervisors or current certification in BGT by an HHS-approved board
 - Public health NBS: CLIA requirements for high complexity testing, 4 years of training/experience in NBS, additional state requirements
- ❖ Clinical consultants, general supervisors, testing personnel: Meet CLIA qualifications and have relevant training or experience

Intended Users

- ❖ Laboratories performing MGT, BGT or NBS for inherited metabolic diseases
- ❖ Users of laboratory services
- ❖ Health professionals evaluating laboratory practices and policies
- ❖ Standard-setting organizations and professional societies
- ❖ Federal and state agencies
- ❖ IVD manufacturers
- ❖ General public



Current Efforts

- ❖ MGT MMWR-
 - Information sheets for laboratories, health professionals, patients, consumers
 - Questions and answers on DLSS website
 - Continuing education activity
- ❖ MMWR guideline for BGT and NBS –
 - Collaborative effort with input from CMS, FDA
 - Publication expected in early 2011



Outlook

- ❖ Good laboratory practice guidelines intended to –
 - Improve quality of laboratory genetic services
 - Enhance oversight for genetic testing under the current regulatory framework
 - Improve healthcare outcomes from genetic testing



Resources

❖ CLIAC Recommendations for BGT and NBS:

- <http://wwwn.cdc.gov/cliac/default.aspx>

❖ MGT MMWR:

- <http://wwwn.cdc.gov/dls/default.aspx> or <http://www.cdc.gov/mmwr/pdf/rr/rr5806.pdf>

❖ MMWR Continuing Education:

- <http://www.cdc.gov/mmwr/cme/conted.html>

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MMWR - Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions [\[HTML\]](#) [\[PDF\]](#)
 MMWR - Good Laboratory Practices for Waived Testing Sites
 Coagulation Laboratory Testing Practices

CDC Home | Search | Health Topics A-Z

CDC **MMWR**

Continuing Education
Contact CE Coordinator

These Activities Are Available For Credit.

1	<p>NEW Recommendations for Diagnosis of Shiga Toxin-Producing <i>Escherichia coli</i> Infections by Clinical Laboratories</p> <p>Course Detail  View MMWR Vol.58 No. RR-12 in Adobe Acrobat Format</p> <p style="text-align: right;">Expires 10/16/2011</p>	<p>Click Here to Register and Take Exam</p> <p>CEU CECH CME: Phys CNE</p>
2	<p>MMWR Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children : Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics</p> <p>Course Detail  View MMWR Vol.58 No. RR-11 in Adobe Acrobat Format</p> <p style="text-align: right;">Expires 09/04/2012</p>	<p>Click Here to Register and Take Exam</p> <p>CEU CECH CME: Phys CNE</p>
3	<p>MMWR Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions</p> <p>Course Detail  View MMWR Vol.58 No. RR-06 in Adobe Acrobat Format</p> <p style="text-align: right;">Expires 06/12/2011</p>	<p>Click Here to Register and Take Exam</p> <p>CEU CECH CME-NP CME CNE</p>

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For SACGHS Feedback

- ❖ Among the CLIAC recommendations, are there issues that should be specifically explained or clarified for the laboratory community and other stakeholders?
- ❖ Are there issues or topic areas that are of particular interest to SACGHS? If so what are they?
- ❖ How should we encourage the implementation of the recommended practices once the prospective MMWR guideline is published? What efforts should be taken and who should be reached as partners or collaborators to help with these efforts?



Thank You!

Questions or comments:

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