

CDC Recommendations for Good Laboratory Practices in Biochemical Genetic Testing and Newborn Screening

Bin Chen, PhD, FACMG

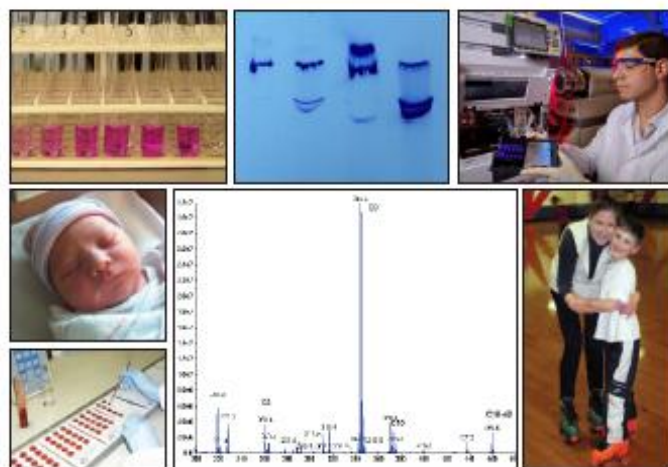
Centers for Disease Control and Prevention (CDC)

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Good Laboratory Practices for Biochemical Genetic Testing and Newborn Screening for Inherited Metabolic Disorders



U.S. Department of Health and Human Services
 Centers for Disease Control and Prevention

Recommendations and Reports

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Disclosure of Relationship

CDC, our planners, and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use. CDC does not accept commercial support.

Front cover photos: Top row, left to right: colorimetric biotinidase assay; thin layer chromatography analysis for macropolymerization, a group of lysosomal disorders; laboratorian using tandem mass spectrometry. Second row, left to right: sleeping newborn; acylcarnitine profile indicating elevated CR, a biochemical marker for medium-chain acyl-CoA dehydrogenase deficiency; mother and her son, who are able to skate together because of effective laboratory monitoring and clinical management of an inherited metabolic disorder. Bottom left: dried blood spot samples for proficiency testing.

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Developing Recommendations for Good Laboratory Practices in BGT and NBS

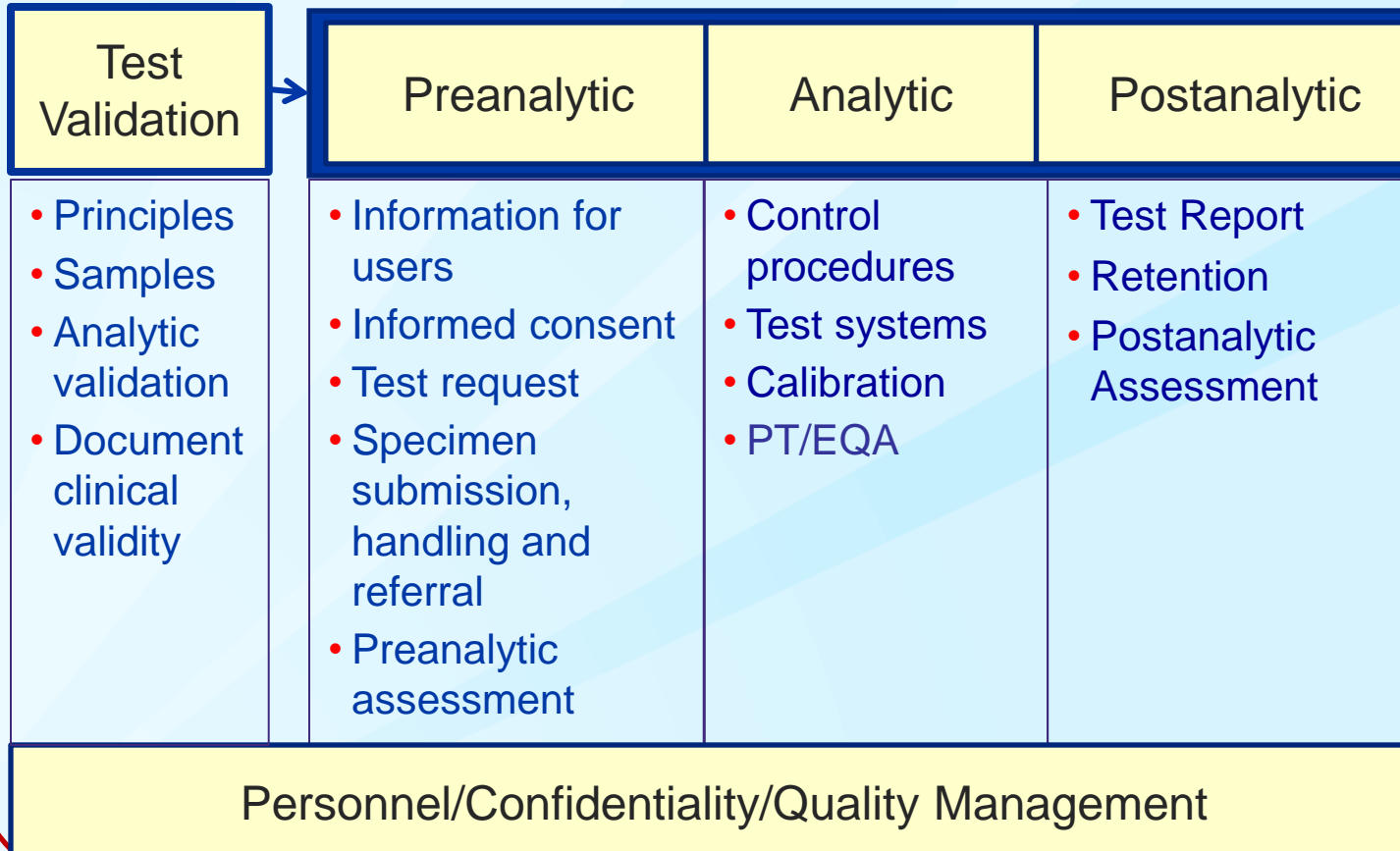
- ❖ 2009: CLIAC BGT workgroup
 - 13 experts representing key BGT & NBS perspectives
 - Comprehensive evaluation of laboratory standards and guidelines
- ❖ Feb. 2010 CLIAC meeting
 - CLIAC reviewed BGT workgroup report
 - Recommendations formulated (<http://wwwn.cdc.gov/cliac/default.aspx>)
- ❖ 2010: Additional input to complement CLIAC recommendations
 - SACGHS
 - SACHDNC
 - Association of Public Health Laboratories

CDC Preparation of Recommended Practices

- ❖ Intent of recommendations
 - Provide quality management guidance for genetic testing performed for screening, diagnosis, monitoring, and treatment of heritable metabolic disorders
 - Consider BGT and NBS separately when practices differ
 - Clarify CLIA requirements and provide additional good laboratory practice recommendations
 - Complement 2009 CDC guideline for molecular genetic testing

Highlights of Recommended Practices

Total Laboratory Testing Process



Test Performance Establishment and Verification

- ❖ Ensure adequate establishment/verification of analytic performance AND document available information on clinical validity
 - Sample considerations (adequate number of positive and normal samples, representative sample types, variance of sample conditions)
 - Performance characteristics and specifications
 - Use of reference ranges in certain situations with disclosure and ongoing monitoring/adjustment
 - “Truth in advertising”
 - Additional considerations for NBS

Specimen Submission and Referral

- ❖ Provide guidance for patient preparation when appropriate
- ❖ Written criteria for specimen acceptance/rejection:
 - Consistent with sample types and conditions in test validation when practical and feasible
 - Variable specimen conditions in clinical testing
 - Note exceptions on test report
- ❖ Refer tests only to CLIA-certified laboratories

Specimen Submission and Referral (cont'd.)

- ❖ Specific recommendations for NBS specimen acceptance and handling
 - Inform submitters specimens should be sent to the laboratory < 24 hrs after birth
 - Address time-sensitive issues of testing and handling for varying conditions of infant
 - Address whether “unsatisfactory” specimens meet the established acceptance criteria
 - Request a second specimen for all unsatisfactory specimens

Control Procedures

- ❖ Use control materials to monitor entire analytic process
- ❖ Perform control procedures each day or with each batch
- ❖ Controls should be
 - comprehensive
 - selected based on patient population
 - prevalence of the disease
 - purpose of testing
- ❖ Acceptable control practices for
 - Time-consuming testing using single-channel/single-column instruments
 - Rare disease assays = rare positive controls
 - Appropriate alternative control

Test Reports

- ❖ Provide information necessary for accurate understanding and interpretation of test results
- ❖ Comply with CLIA general test report requirements
- ❖ Inform or update users when test methods change to meet CLIA requirements*
- ❖ Written in plain language, understood by non-geneticist health professionals when possible
- ❖ Separate recommendations for BGT and NBS test reports

* Based on CLIA requirements but more specific

Retention of Test Reports, Records, and Tested Specimens

- ❖ Test reports indicating genotypes: At least 21 years
- ❖ Test records: CLIA and other applicable requirements
- ❖ Tested specimens:
 - Longest possible timeframe as permitted by sample stability/integrity, technology, space, cost
 - BGT: At least until after final result reporting; if possible until next PT or alternative performance assessment
 - NBS: Subject to federal, state, local requirements

Laboratory Personnel: Qualifications & Responsibilities

- ❖ Laboratory directors: Meet CLIA requirements for high complexity testing
- ❖ Technical supervisors for BGT
 - Equivalent to CLIA qualification requirements for clinical cytogenetics technical supervisors (42CFR §493.1449[p])
 - Current certification in BGT by an HHS-approved board
- ❖ Technical supervisors for public health NBS:
 - CLIA requirements for high complexity testing
 - Four years of laboratory training or experience in NBS
 - Meet additional state requirements
- ❖ Clinical consultants, general supervisors, testing personnel:
 - Meet CLIA qualifications
 - Relevant training and/or experience

Intended Audiences and Outcomes

- ❖ Intended audiences
 - Laboratory professionals
 - Laboratory surveyors and inspectors
 - Users of laboratory services
 - Standard-setting organizations
 - Professional societies
 - IVD manufacturers
- ❖ Expected outcomes
 - Improve quality of laboratory genetic services
 - Enhance oversight for genetic testing using the current regulatory framework
 - Improve healthcare outcomes from genetic testing

Continuing Education Activity

❖ Participation (till 08/14/2012):

- Registered: 107
- Completed: 69 (43% CEU, 33% CNE, 16% CME, 6% CHES)

❖ General comments and suggestions:

- “The contents were very helpful”; “informative”; “excellent”; “great learning experience”
- “Would have liked to see more information on how to explain the lab practices for genetic testing/newborn screening in easier terms to patients/parents”
- “a lot to absorb”; “hard to read”
- “make it worth more CE hours”
- “make the CE activity system more user-friendly”
- “keep up the great work”

Feedback from Continuing Education Activity

- ❖ The content and learning materials addressed a need or a gap in my knowledge or skills
Strongly agree: 31% Agree: 63%
- ❖ This activity effectively met my educational needs
Strongly agree: 34% Agree: 58%
- ❖ If given an opportunity, I can apply the knowledge gained as a result of this activity
Strongly agree: 25% Agree: 66%
- ❖ Availability of CE credit influenced my decision to participate in this activity
Strongly agree: 38% Agree: 58%

Feedback from Continuing Education Activity

- ❖ Changes to competence, skills, practice:
 - “The document helped me improve my understanding of quality management of newborn screening testing”
 - “After reading the materials I will start to collect newborn screenings on time”
 - “better understanding of lab practice”
 - “Enhanced my knowledge of newborn screening and how it relates to CLIA”
 - “It reaffirmed my understanding of the quality practices required by NB Screening and assisted me with designing a performance validation protocol”

Feedback from Continuing Education Activity

- ❖ I plan to use these recommendations as the basis for:
 - Education materials: 45%
 - Laboratory policies and procedures: 20%
 - Laboratory standards or guidelines: 11%
 - Public policy: 5%
 - Other: 19%

- ❖ Best educational way(s) to increase awareness and uptake of these recommendations:
 - Wider electronic dissemination: 40%
 - Interactive, web-based training: 20%
 - Dissemination of printed recommendations: 13%
 - Onsite educational sessions: 11%
 - Educational sessions at professional conferences: 10%

Resources

❖ Links to the CDC recommendations:

- CDC MMWR site: <http://www.cdc.gov/mmwr/pdf/rr/rr6102.pdf>
- CDC Online Newsroom “Have You Heard?”:
http://www.cdc.gov/media/haveyouheard/stories/Genetic_Testing.html
- CDC CLIA website: <http://wwwn.cdc.gov/clia/default.aspx>
- CDC Laboratory Science, Policy and Practice Program Office Genetic Testing Quality Practices site:
http://www.cdc.gov/osels/lspppo/Genetic_Testing_Quality_Practices/index.html

❖ Link to continuing education activity:

- http://www.cdc.gov/mmwr/cme/serial_conted.html

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Thank You!

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SACHDNC Affirmation of Value to the Heritable Disorders and Newborn Screening Community