Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children

Laboratory Standards & Procedures Subcommittee

April 22, 2005
Laboratory Standards & Procedures Subcommittee

- Duane Alexander
- Amy Brower (chair)
- Peter B. Coggins
- R. Rodney Howell
- Marie Mann (staff)
- Piero Rinaldo

Staff Support – Carrie Diener
Charge of Subcommittee

- Assessment of laboratory methodologies and standards for testing panels of inherited disorders in newborn and children
  - Process definition for addition/deletion of conditions to uniform panel
  - Evaluation of new technologies
  - Focus on infrastructure services
Focus on Infrastructure Building Services: Core Public Health Services Delivered by MCHB Agencies

DIRECT HEALTH CARE SERVICES (GAP FILLING)
Examples:
Basic Health Services and Health Services for CSHCN

ENABLING SERVICES
Examples:
Transportation, Translation, Outreach, Respite Care, Health Education, Family Support Services, Purchase of Health Insurance, Case Management, Coordination with Medicaid, WIC and Education

POPULATION--BASED SERVICES
Examples:
Newborn Screening, Lead Screening, Immunization, Sudden Infant Death, Counseling, Oral Health, Injury Prevention, Nutrition and Outreach/Public Education

INFRASTRUCTURE BUILDING SERVICES
Examples:
Infrastructure Building Services

- Nomenclature
- Testing strategies
- Cut-off values
- Reporting
- Performance metrics
Nomenclature

- Provide guidelines for standardized "counting" of conditions
  - Clinical phenotype
  - Group of conditions
  - Primary marker
  - Test platform
  - Response to treatment
  - Number of loci
  - Ad hoc criteria (to be established)

- Facilitate communication to professionals and consumers by providing structural feedback to education subcommittee
Testing Strategies

- Evaluation and standardization of pre-analytical, analytical, and post-analytical practices
  - Time of collection
  - 2nd collection
    - All cases
    - First abnormal (repeat test)
  - 2nd tier tests
    - Biochemical
    - Molecular
    - New technologies
  - Interpretation (profile evaluation)
  - Timing of confirmatory testing
Cut-off Values

- Disease range vs. normal range
- Use of analyte ratios
- Monitoring of abnormal results
  - True positives
  - Reported abnormal, false positive
  - Interpreted as not significant
- Normalization (abnormals/10,000 cases)
- Impact of 2nd tier tests
Reporting

- Standardization of required elements
- Quantitative results
- Cut-off
- Prior experience (range)
- Interpretation
  - Differential diagnosis, if applicable
  - Recommendations for confirmatory testing
Performance Metrics

- Definition of targets
  - Detection rate
    - Cumulative
    - By condition
  - False positive rate
    - Cumulative
    - By analyte
  - Positive predictive value
    - Cumulative
    - By analyte
- Proficiency testing (beyond QC)
Cross Cutting Focus Areas

- Evaluation
  - Cost-effectiveness
  - Assessment methodology
    - Clinical validity and utility
  - Health outcomes
- Information technology
  - Data integration
  - Data access
  - Privacy
- Financing
Addition/Deletion of Conditions: Process Evaluation

- Dynamic, open-ended process
- Driven by stakeholders
  - Consumer advocates
  - Clinical investigators
  - Researchers (basic, transitional)
  - Providers of laboratory services
  - Industry
- Use of prospective evaluation tool
The Path to the FUTURE

Secondary targets and No NBS conditions

To be reconsidered based on:
1) New screening methods
2) New treatments
3) Evolving knowledge of natural history
**INTRODUCTION**

This tool is to aid NBS Advisory Committee of individual States/Regions (or ad hoc expert panels) involved in the assessment of the NBS "fitness" of conditions currently not screened for in their program but included in the HRSA/ACMG uniform condition panel.

**INSTRUCTIONS**

Name: 
Institution: 
Date: 
Address: 

**CHECK ALL CATEGORIES THAT APPLY TO YOU**

- Provider of Screening Services (Testing)
- Provider of Screening Services (Follow Up)
- Provider of Screening Services (Administration)
- Provider of Screening Services (Policy)
- Provider of Diagnostic Services
- Primary Care Provider
- Specialty Care Provider
- Consumer

**The evaluation tool includes:**

1. This page of INSTRUCTIONS
2. A page listing CRITERIA and SCORES
3. A worksheet listing NBS REFERENCE CONDITIONS. Scoring these well known conditions is encouraged to self-assess how the respondent's scores compare with the results of the HRSA/ACMG survey (listed at the top)
4. A blank worksheet where to list the condition(s) under evaluation for inclusion/exclusion

To better define a condition under evaluation, consider including the name of the deficient enzyme and the OMIM number together with the common name of the disorder

For each criterion, enter one of the scores provided. If unsure, enter "U". A BLANK means ZERO

After completing the tool, please mail or fax it to your project coordinator (see below)

Thank you for your participation

**PROJECT COORDINATOR**

Name: 
Address: 
Phone: 
Fax: 
E-mail:
**Prospective Evaluation Tool**

**CONTENT**
- Instructions
- Respondent profile
- CRITERIA
- SCORES
- A worksheet listing NBS REFERENCE CONDITIONS

Scoring these well known conditions is encouraged to self-assess how the respondent's scores compare with the results of the HRSA/ACMG survey (listed at the top)
- A blank worksheets where to list the condition(s) under evaluation for inclusion/exclusion

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**HRSA/ACMG UNIFORM CONDITION PANEL EVALUATION TOOL**

**INSTRUCTIONS**
This tool is to aid NBS Advisory Committee of individual States/Regions (or ad hoc expert panels) involved in the assessment of the NBS "fitness" of conditions currently not screened for in their program but included in the HRSA/ACMG uniform condition panel.

<table>
<thead>
<tr>
<th>NAME</th>
<th>Phone</th>
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<td>INSTITUTION</td>
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<td>DATE</td>
<td>E-mail</td>
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**CHECK ALL CATEGORIES THAT APPLY TO YOU**
- Provider of Screening Services (TESTING)
- Provider of Screening Services (FOLLOW UP)
- Provider of Screening Services (ADMINISTRATION)
- Provider of Screening Services (POLICY)

**The evaluation tool includes:**
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2. A page listing CRITERIA and SCORES
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<thead>
<tr>
<th>NAME</th>
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<tbody>
<tr>
<td>ADDRESS</td>
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<tr>
<td>PHONE</td>
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# Reference Conditions

Reference Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>MCAD</th>
<th>CH</th>
<th>PKU</th>
<th>SCA</th>
<th>CAH</th>
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<tbody>
<tr>
<td>Incidence of condition</td>
<td>1799</td>
<td>1718</td>
<td>1663</td>
<td>1642</td>
<td>1533</td>
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<tr>
<td>Age at onset</td>
<td>240</td>
<td>240</td>
<td>240</td>
<td>240</td>
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<tr>
<td>Nutritional diagnosis</td>
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<tr>
<td>Genetic diagnosis</td>
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<td>240</td>
<td>240</td>
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<tr>
<td>Screening test sensitivity</td>
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<td>240</td>
<td>240</td>
<td>240</td>
<td>240</td>
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<tr>
<td>Treatment availability</td>
<td>240</td>
<td>240</td>
<td>240</td>
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<tr>
<td>Cost of treatment</td>
<td>240</td>
<td>240</td>
<td>240</td>
<td>240</td>
<td>240</td>
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<tr>
<td>Potential effectiveness of existing treatment</td>
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<td>240</td>
<td>240</td>
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<td>Benefits of early intervention</td>
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<td>240</td>
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<td>Early diagnosis and treatment perinatal mortality</td>
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<td>Diagnostic confirmation</td>
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<td>Clinical management</td>
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<td>Mortality of therapy</td>
<td>240</td>
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</tbody>
</table>

# Conditions to be evaluated

Conditions to be evaluated

| SCID | Pompe | Krabbe | Wilson | HyperBIL |
|------|-------|--------|--------|---------|----------|
| Incidence of condition | 240 | 240 | 240 | 240 | 240 |
| Age at onset | 240 | 240 | 240 | 240 | 240 |
| Nutritional diagnosis | 240 | 240 | 240 | 240 | 240 |
| Genetic diagnosis | 240 | 240 | 240 | 240 | 240 |
| Screening test sensitivity | 240 | 240 | 240 | 240 | 240 |
| Treatment availability | 240 | 240 | 240 | 240 | 240 |
| Cost of treatment | 240 | 240 | 240 | 240 | 240 |
| Potential effectiveness of existing treatment | 240 | 240 | 240 | 240 | 240 |
| Benefits of early intervention | 240 | 240 | 240 | 240 | 240 |
| Early diagnosis and treatment perinatal mortality | 240 | 240 | 240 | 240 | 240 |
| Diagnostic confirmation | 240 | 240 | 240 | 240 | 240 |
| Clinical management | 240 | 240 | 240 | 240 | 240 |
| Mortality of therapy | 240 | 240 | 240 | 240 | 240 |
Outline of Process

- Collect survey data from local group
  - Providers of services
  - Consumers
- Calculation of score(s)
- Application of evaluation flow chart
- Review updated literature evidence
- Make recommendations
New Technologies

- **Type**
  - Molecular
  - Expression
  - Proteomics

- **Uses**
  - New approach to existing panel
  - Testing of additional conditions
  - Identification of new conditions

- **Other**
  - Multiplex testing
  - Point of Care (POC)
  - Direct to Consumers (DOC)
Subcommittee Invitees (Preliminary)

- Participation confirmed
  - Don Chace, Pediatrix
  - Harry Hannon – Biochemical Branch, CDC
  - Gary Hoffman – WI State Laboratory of Hygiene
  - Jana Monaco, Parent
  - Larry Sweetman – Baylor University Medical Center

- Participation under consideration
  - John Sherwin, Genetic Disease Branch, California Department of Health Services