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

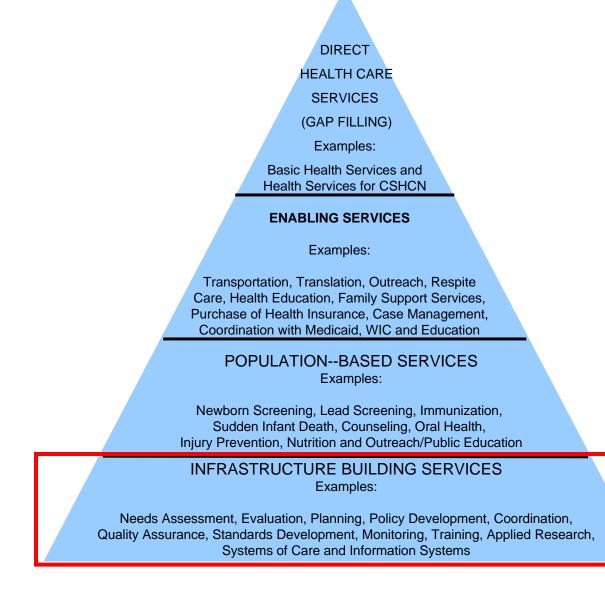
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Staff Support – Carrie Diener

Charge of Subcommittee

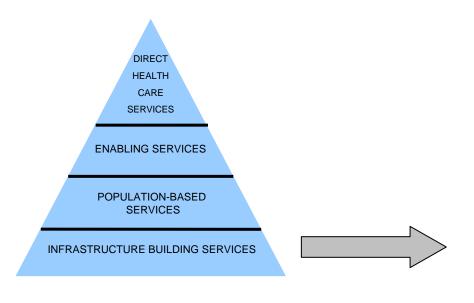
- Assessment of laboratory methodologies and standards for testing panels of inherited disorders in newborn and children
 - Process definition for addition/deletion
 of conditions to uniform panel
 - Evaluation of new technologies
 - Focus on infrastructure services

Focus on Infrastructure Building Services: Core Public Health Services Delivered by MCHB Agencies



[D]

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 preanalytical, 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

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Reporting

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

Performance Metrics

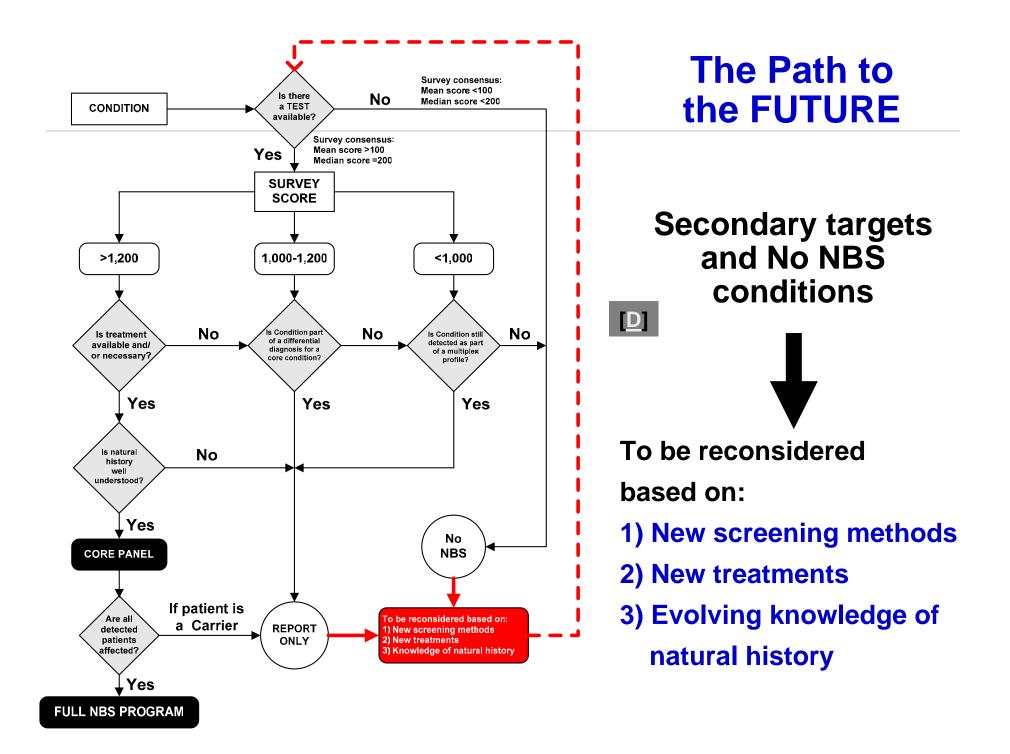
- Definition of targets
 - Detection rate
 - Cumulative
 - By condition
 - False positive rate
 - Cumulative
 - By analyte
 - Positive predictive value
 - Cumulative
 - By analyte
- Proficiency testing (beyond QC)

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



Prospective Evaluation Tool

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

NAME		Phone		
INSTITUTION		Fax		
DATE		E-mail		
ADDRESS				
	CHECK ALL CATEGORIE	ES THAT AP	PL	LY TO YOU
Provider of	Screening Services (TESTING)			Provider of Diagnostic Services
Provider of	Screening Services (FOLLOW UP)			Primary Care Provider
Provider of	Screening Services (ADMINISTRATION)			Specialty Care Provider
Provider of	Screening Services (POLICY)			Consumer
The evaluation	on tool includes:			

1 This page of INSTRUCTIONS

2 A page listing CRITERIA and 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/esclusion

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									
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INTRODUCTION This tool is to aid NBS **Advisory Committee of** individual States/ **Regions (or ad hoc** [<u>D</u>] expert panels) involved in the assessment of the NBS "fitness" of conditions currently not screened for in their program

Prospective Evaluation Tool

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PROJECT COO	RDINATOR		
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CONTENT

- Instructions
- Respondent profile
- CRITERIA
- **SCORES**
- A worksheet listing NBS
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Reference Conditions

Conditions to be evaluated

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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