Update

Hemoglobinopathy Issues and Answers Conference

CHORI – May 25, 2010

SACHDNC – September 16, 2010

Brad Therrell, PhD
NNSGRC - Austin, Texas

Jelili Ojodu, MPH
APHL – Silver Spring, Maryland

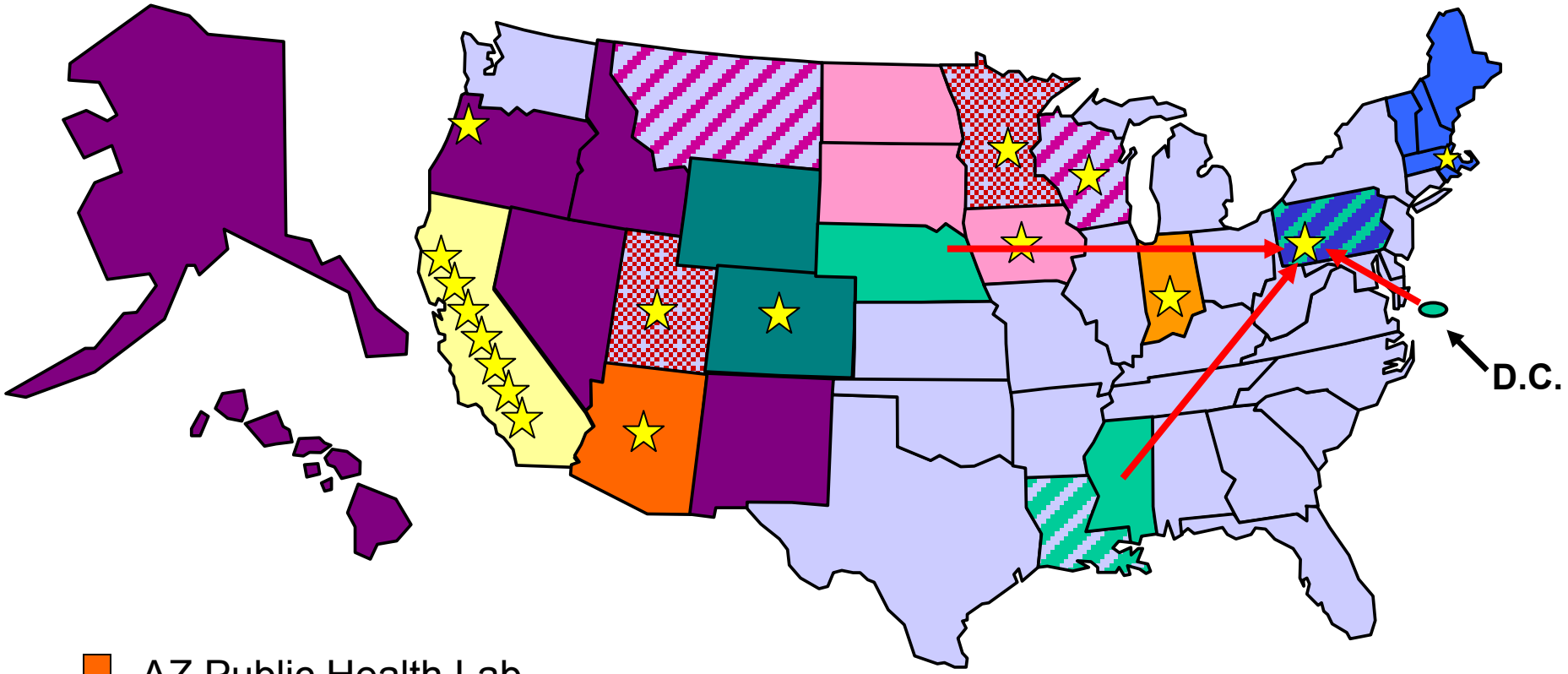
Current Status of Newborn Hemoglobinopathy Screening in the United States

May 25, 2010

Brad Therrell, Ph.D., Director

National Newborn Screening and Genetics Resource Center

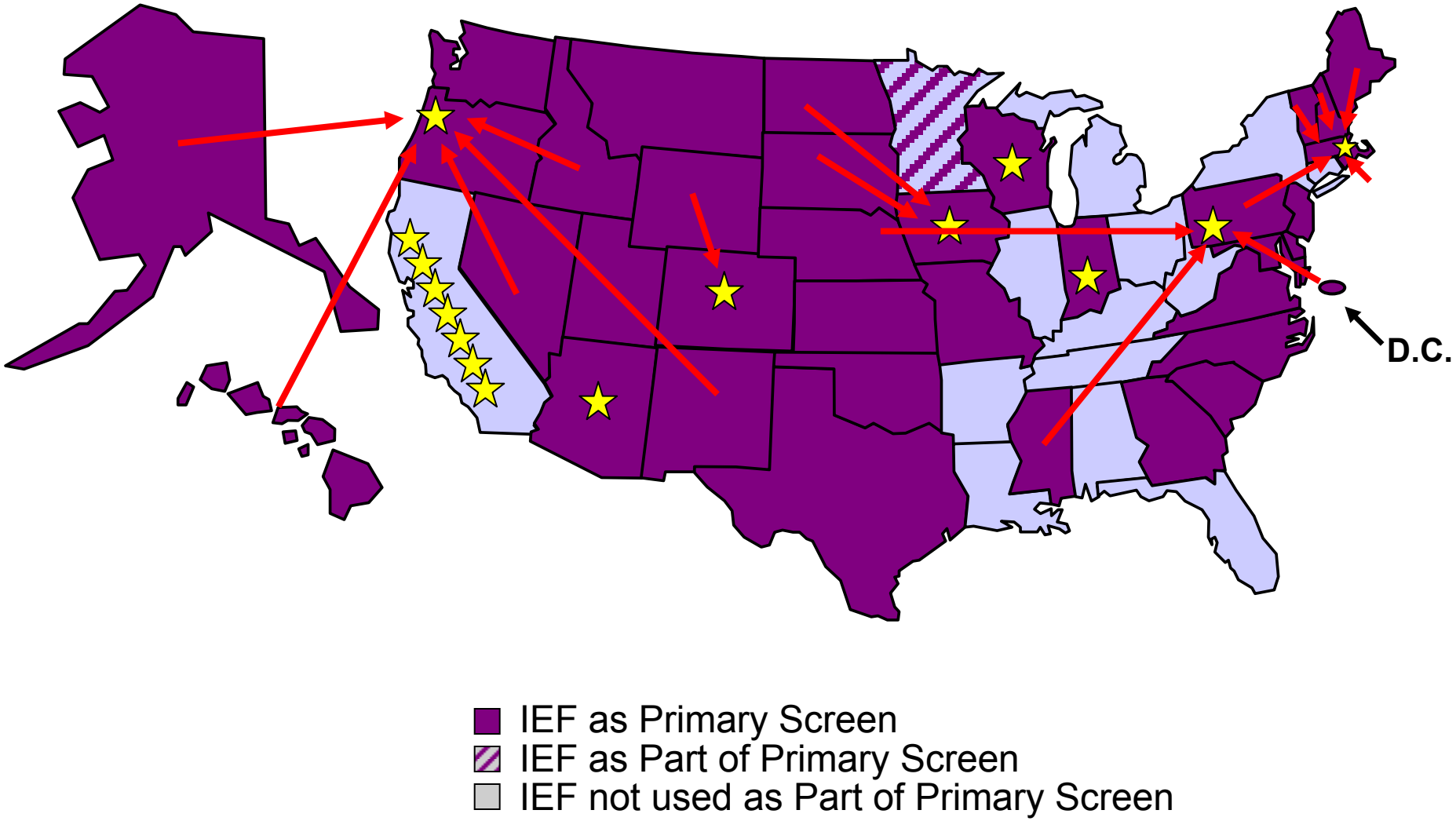
Austin, Texas



- AZ Public Health Lab
- OR Public Health Lab
- WI Public Health Lab
- IA Public Health Lab
- CO Public Health Lab
- U Mass Lab
- Allows Commercial Lab Competition
- 7 Contracted Labs
- 1 Pathology Lab
- 1 Med Ctr Lab
- 1 Commercial Screening Lab
- 2 Contracted Labs
- Share – Public Health/Med Ctr

Laboratory Service Delivery Models 2010
States Using Contract Screening Laboratories and Public and/or Commercial/Non-profit

National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC



Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

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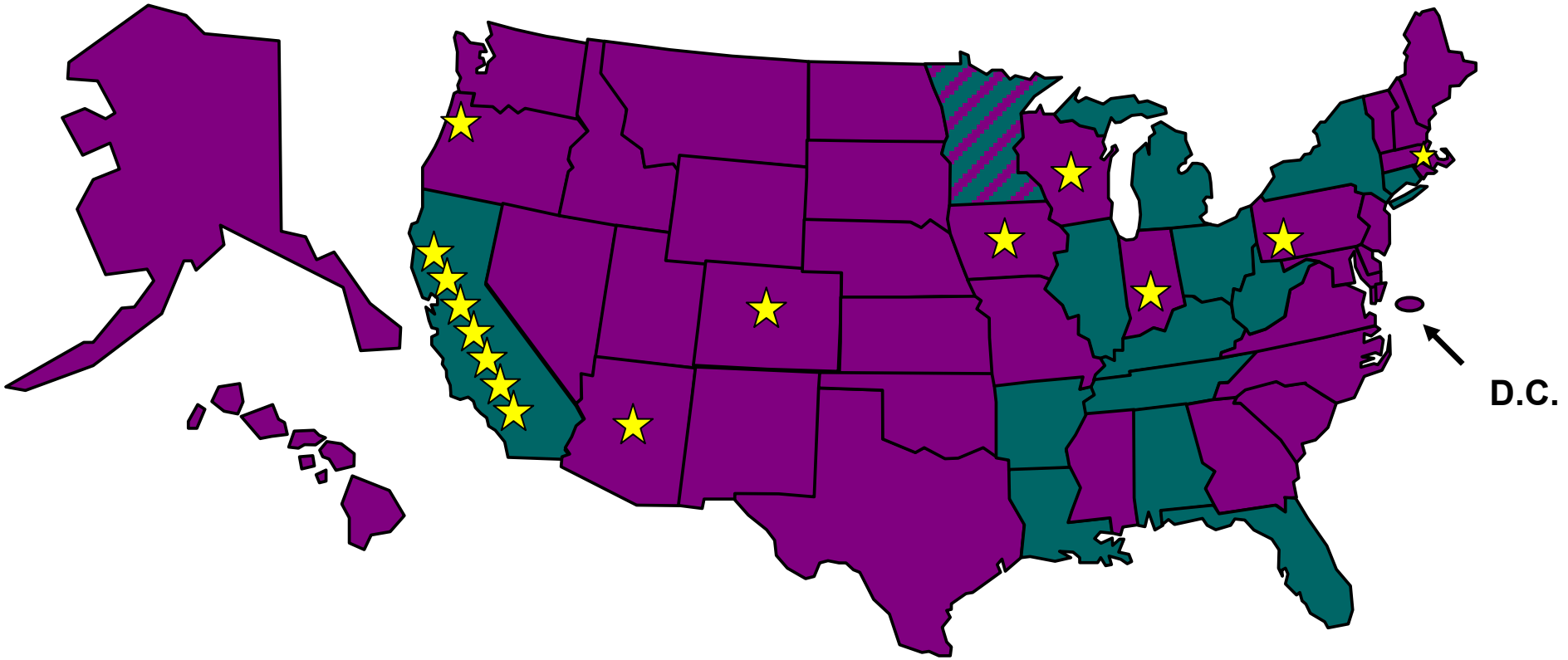

Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

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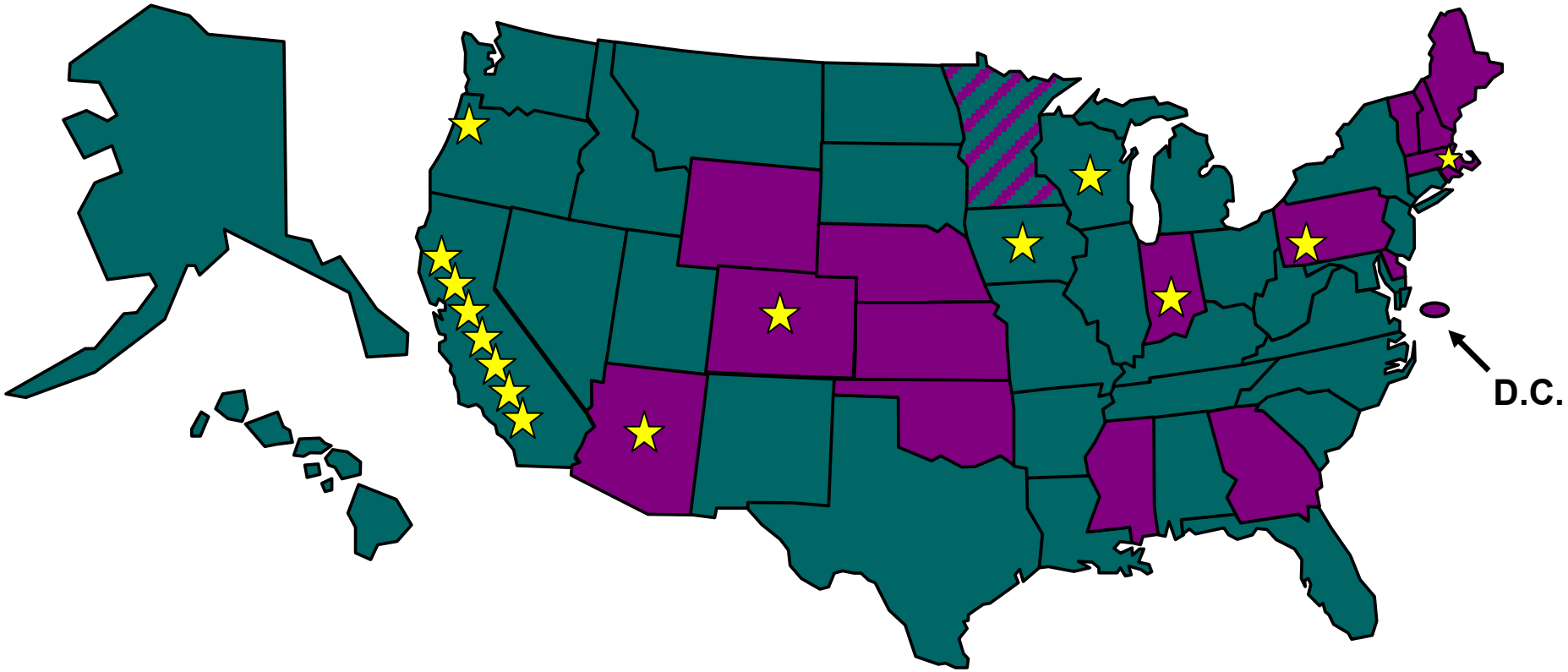

HPLC Not Available
IEF and HPLC on All Newborns
HPLC Available – First or Second Tier Screen

Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

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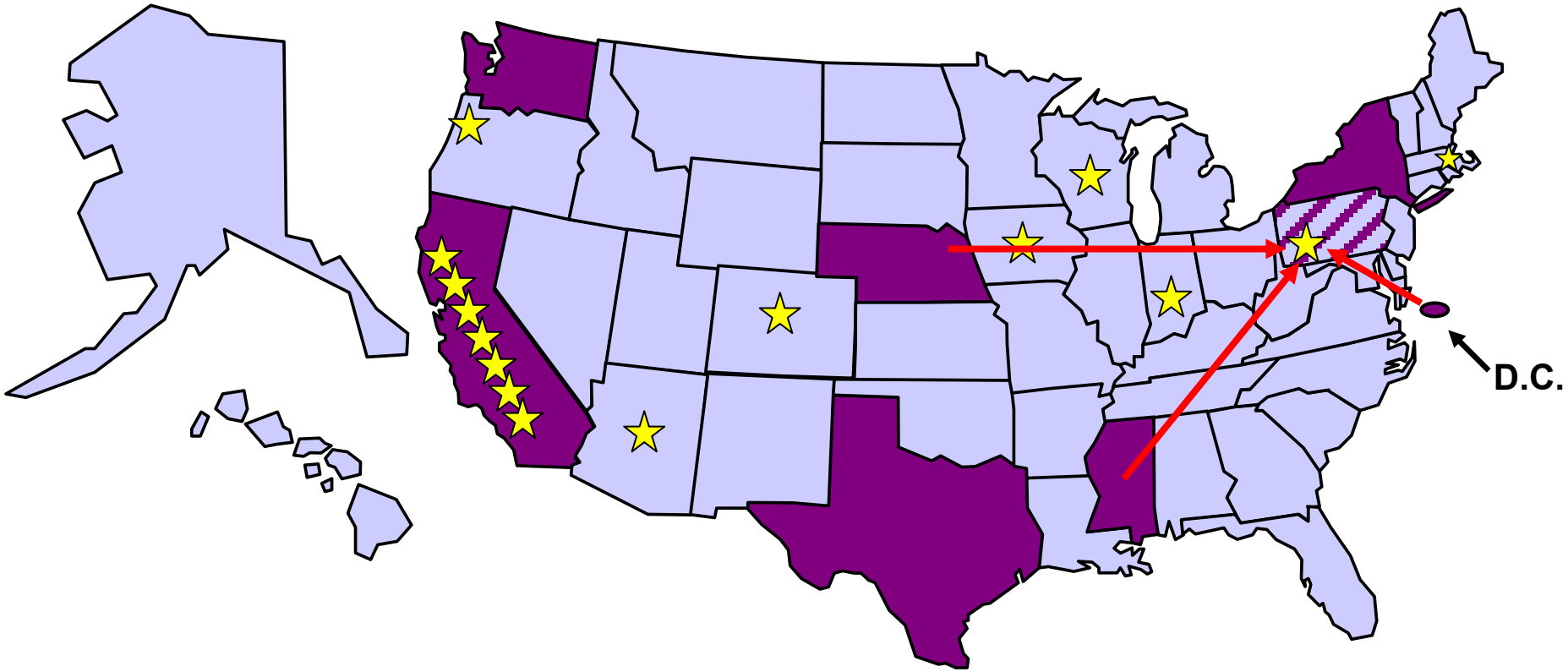

DNA Available as Second Tier
DNA Available to Some Infants as Second Tier
DNA Not Commonly Used as Second Tier Screen

Laboratory Service Delivery Models 2010
Hemoglobinopathy Screening

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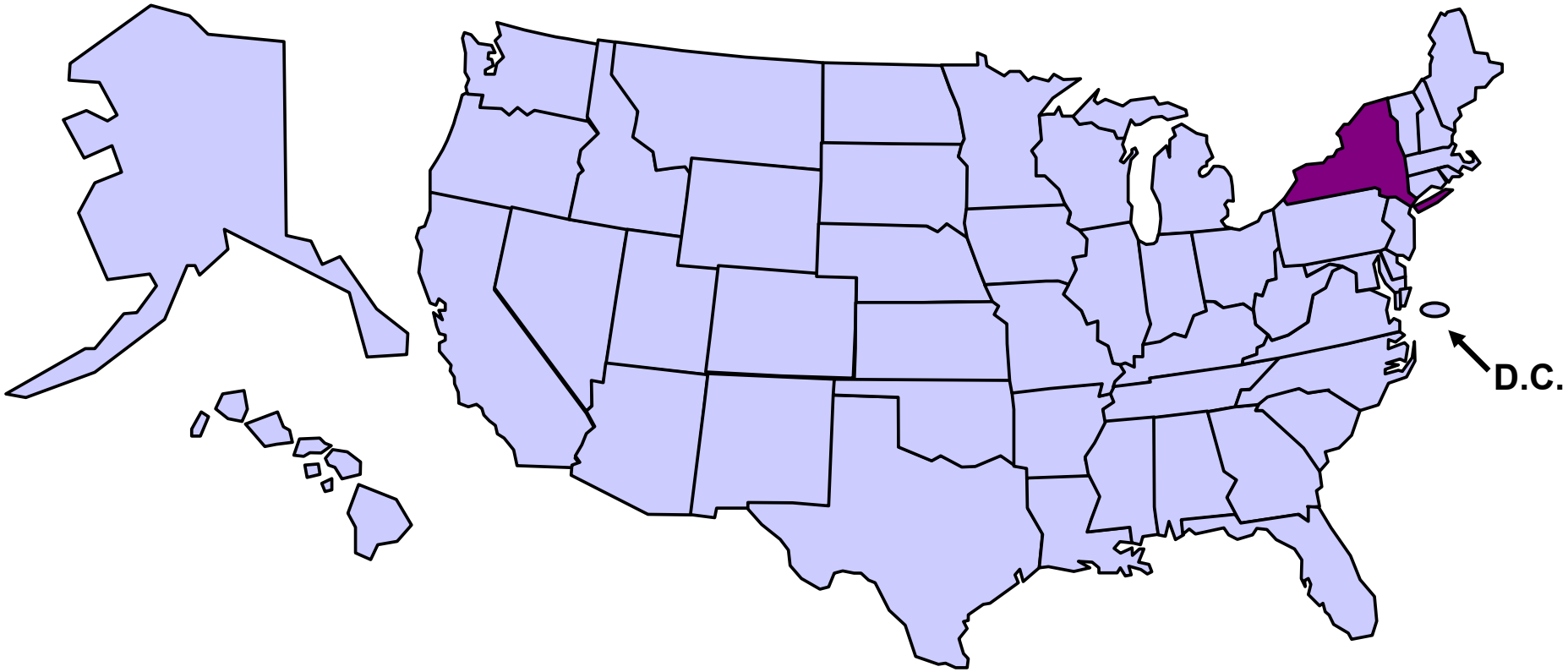


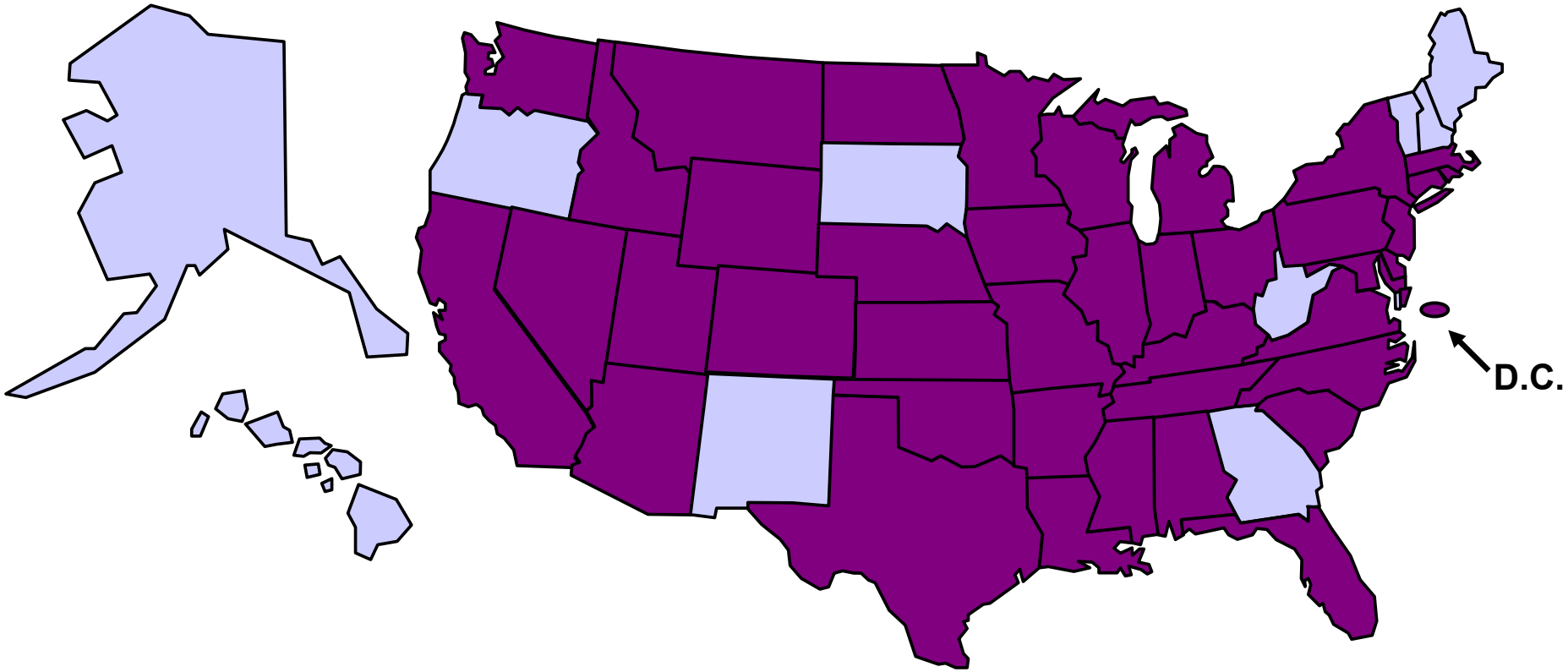
Universal Newborn Hemoglobinopathy Screening Mandated

Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening April 1, 1975

National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC

Benson and Therrell. Semin Perinatol 34:134-144 (2010).



Universal Newborn Hemoglobinopathy Screening Mandated

Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening By January 1, 1995

National Newborn Screening and Genetics Resource Center
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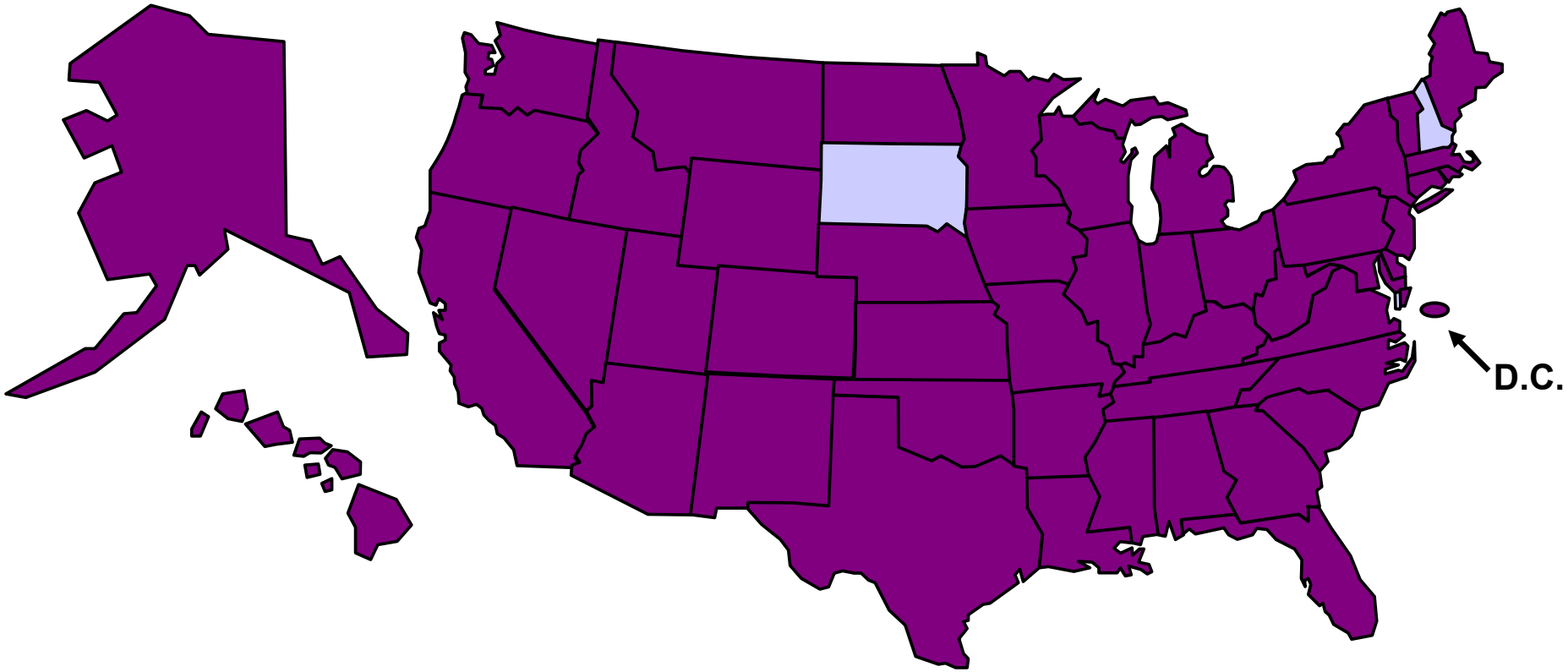
Benson and Therrell. Semin Perinatol 34:134-144 (2010).



Universal Newborn Hemoglobinopathy Screening Mandated

Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening By January 1, 2005

National Newborn Screening and Genetics Resource Center
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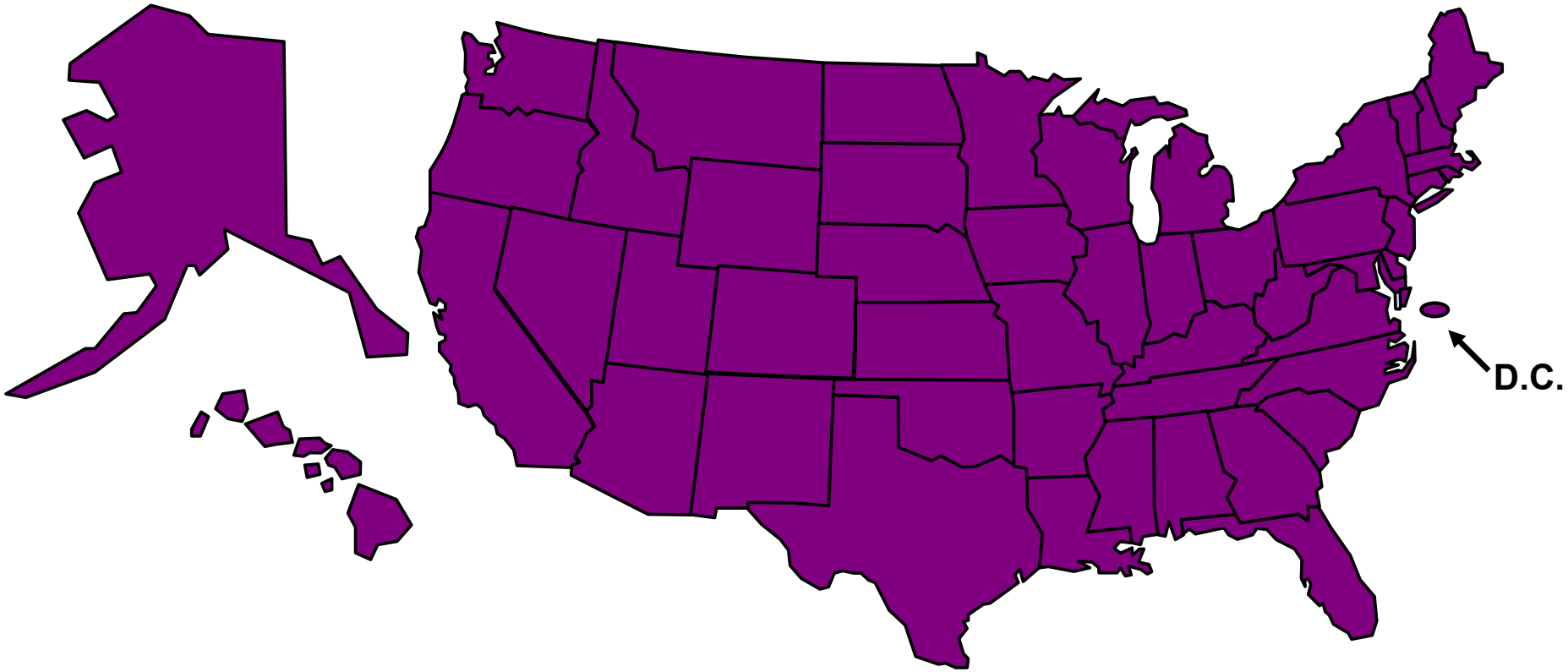
Benson and Therrell. Semin Perinatol 34:134-144 (2010).



Universal Newborn Hemoglobinopathy Screening Mandated

Newborn Hemoglobinopathy Not Universally Mandated

U.S. History of Hemoglobinopathy Screening By May 1, 2006 All 51 Programs

National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC

Benson and Therrell. Semin Perinatol 34:134-144 (2010).

Issues and Answers Series

Hemoglobinopathy Newborn Screening

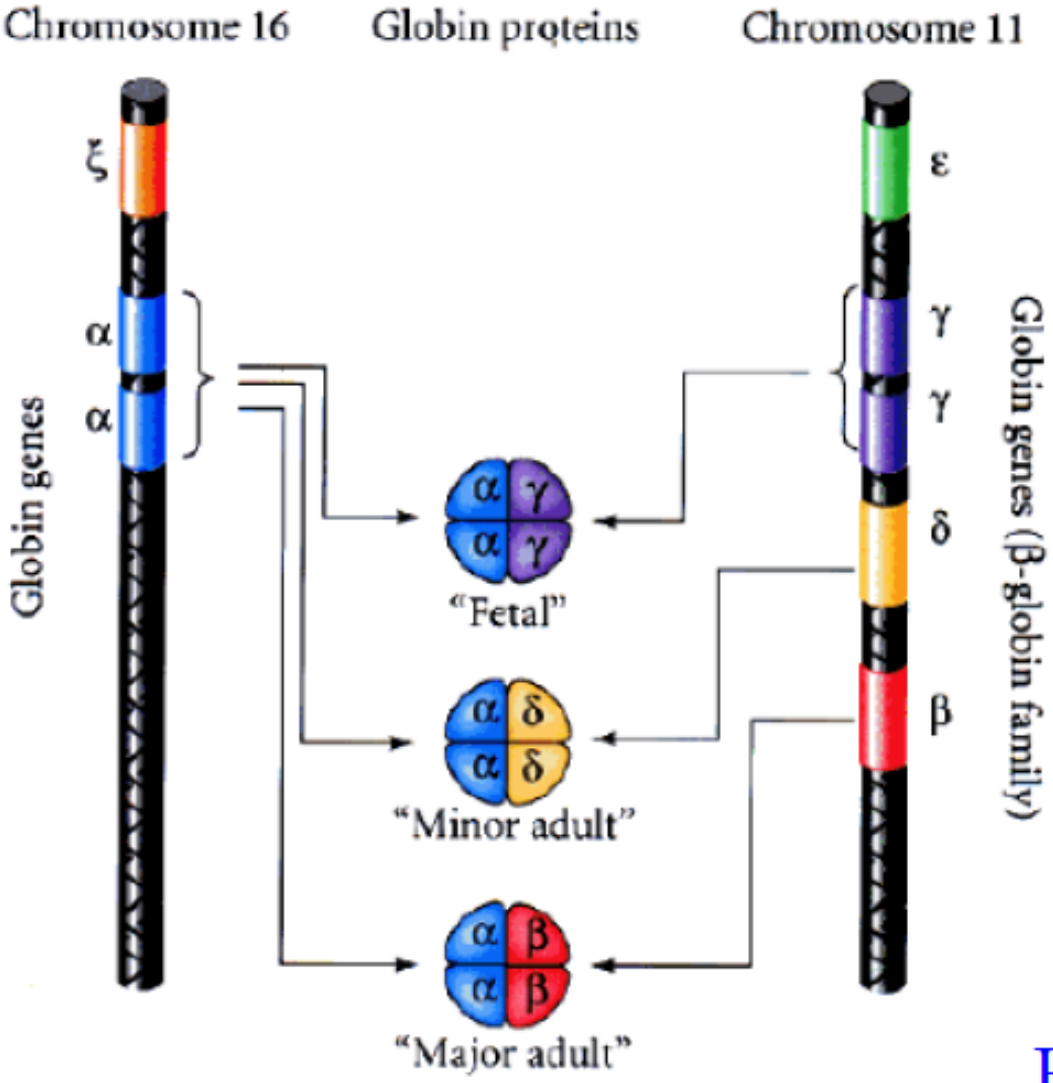
Nomenclature and Hemoglobinopathy 101

Kwaku Ohene-Frempong, M.D.

The Children's Hospital of Philadelphia
University of Pennyslvania

Genetics of Hemoglobinopathies

Human Hemoglobin Genes and Products



F:	$\alpha_2\gamma_2$	60-90%
A2:	$\alpha_2\delta_2$	<1%
A:	$\alpha_2\beta_2$	10-40%

Hemoglobins at Birth

Nomenclature in SCD

Common Types of Sickle Cell Disease

Genotype	Common Term	Preferred Term	Preferred Acronym
β^S / β^S	Sickle cell anemia	Sickle cell disease SS	SCD-SS
	Hemoglobin SS disease		
β^S / β^C	Sickle cell hemoglobin C disease	Sickle cell disease SC	SCD-SC
	Hemoglobin SC disease		
β^S / β^o	Hemoglobin S beta-zero thalassemia	Sickle cell disease $S\beta^o$ thalassemia	SCD-$S\beta^o$ th
β^S / β^+	Hemoglobin S beta-plus thalassemia	Sickle cell disease $S\beta^o$ thalassemia	SCD-$S\beta^+$ th

Hemoglobinopathies Newborn Screening

Newborn with Hemoglobin Bart's

Hemoglobin St. Bartholomew's (Hb Bart's):

- Abnormal tetramer of gamma globin ($\gamma 4$) suggests excess gamma globin and by inference, deficiency of alpha globin (α thalassemia) to make Hb F ($\alpha 2 \gamma 2$)

- Relative quantity of Hb Bart's reflects degree of alpha thalassemia

Reporting Hemoglobin Bart's

FA + Bart's

FX + Bart's

FYZ + Bart's

Sickle Cell Disease and Other Hemoglobinopathies

Proficiency Testing Program

Carla Cuthbert, PhD FACMG

Newborn Screening and Molecular Biology Branch
Centers for Disease Control and Prevention

Hemoglobinopathy PT program

- Hemoglobinopathy PT program has been in operation since 1991
- Current participants include 51 domestic and 26 international laboratories
- Extent of participant enrollment by NSQAP is limited by availability of materials

Results by Year (2000-2009)

Year	Total # Specimens	Percentage of Errors	
		Phenotype	Clinical Assessment
2000	1000	0.5	0.3
2001	920	0.4	0.4
2002	1020	0.1	0.1
2003	884	0.2	0.3
2004	1080	1.0	0.9
2005	1100	0.5	0.6
2006	1094	0.8	0.6
2007	1020	0.3	0.1
2008	786	0.0	0.0
2009*	1056	1.2	1.2

* 1st year single donor specimens used

Future Directions for Hb Program

- NSQAP is expanding our current program to increase the number and variety of specimens
- New partnerships are being developed to achieve expansion
- Expansion will allow us to serve those laboratories currently on the waiting list

Testing for Hemoglobinopathies in the Texas Newborn Screening Program

Rachel C. Lee and Chris Moore

Texas Department of State Health Services
Austin, Texas

Hemoglobinopathy Screening Procedures in Texas

- Isoelectric Focusing (IEF) to screen all specimens
  - ~800,000 specimen per year
  - ~2,700 specimens per day (6 days a week)
- Retest IEF for all abnormal specimens
  - ~100 specimens per day
- HPLC for certain abnormal specimens
  - ~10 specimens per day
- 2nd tier molecular testing
  - ~500 per year
- Identify an average of 35 clinically significant results per month

California Newborn Screening for Hemoglobinopathies

Shellye Lessing, MS, CGC

Genetic Disease Screening Program

California Department of Public Health

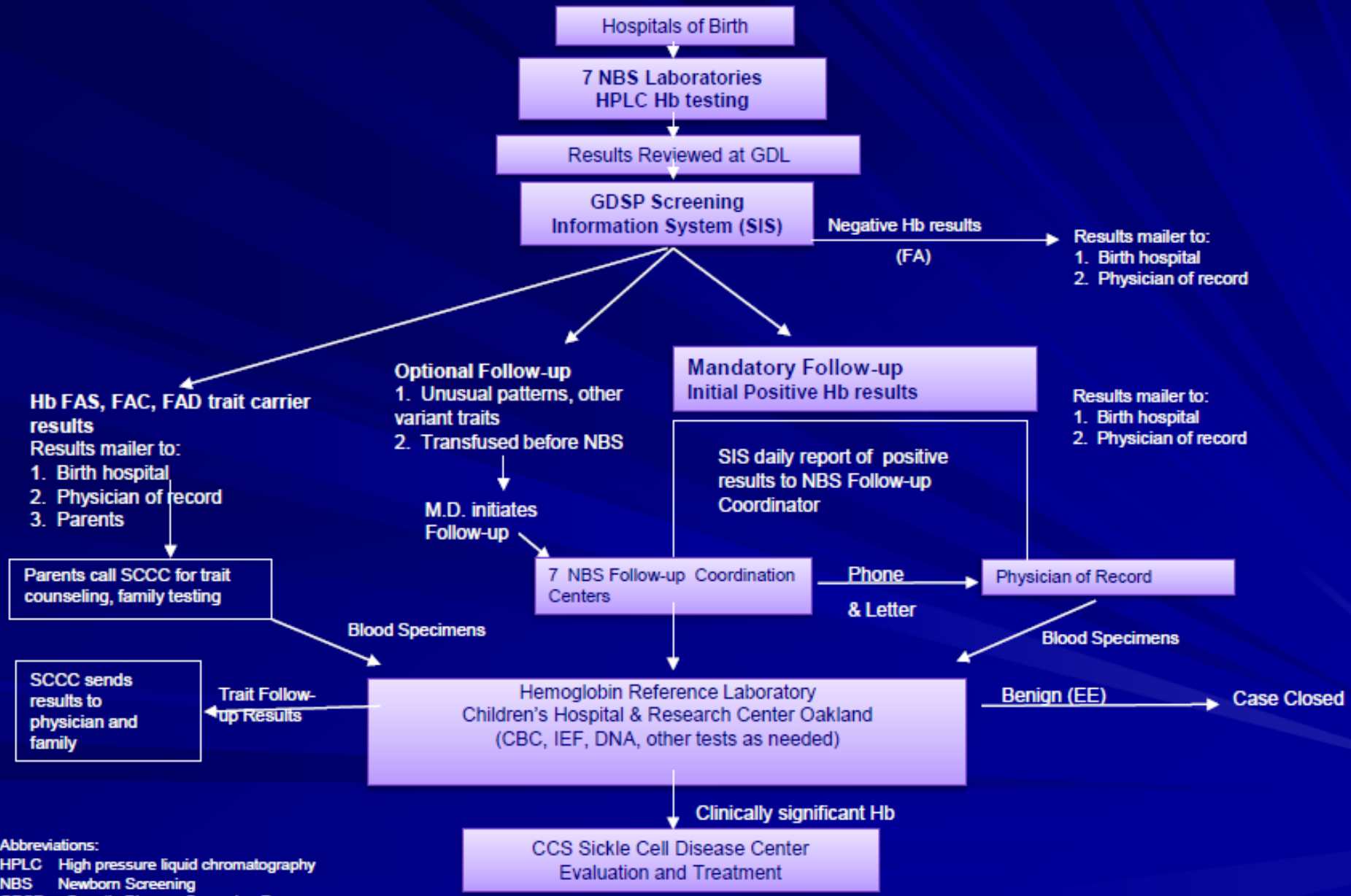
May 25, 2010

Newborn Screening Laboratory Methodology

- High pressure liquid chromatography (HPLC)
- Identifies hemoglobins F, A, S, D, C, E, Bart's, and 5 unknown Variants

CALIFORNIA NEWBORN SCREENING PROGRAM

Hemoglobinopathy Screening



Abbreviations:

HPLC High pressure liquid chromatography
NBS Newborn Screening
GDSP Genetic Disease Screening Program
SCCC Sickle Cell Counseling Center
CCS California Childrens Services

Non-Targeted Hemoglobinopathies: Challenges and Considerations

Kathryn Hassell, M.D.

Professor of Medicine, Division of Hematology

Director, Colorado Sickle Cell Treatment and Research Center

NBS Hemoglobinopathy Follow-Up Program, Colorado and Wyoming

Harmonizing laboratory reporting Is It Possible?

Issues and Answers Series – Hemoblobinopathy NBS
Children's Hospital Oakland Research Institute
May 25, 2010

Roger B. Eaton, PhD, Director
New England Newborn Screening Program

The BIG ISSUE
Standardization vs. Idiosyncracy

- 54089-8 Newborn Screening Panel, American Health Information Community (AHIC)
  - HPLC : 79 codes
  - IEF : 79 codes

- 15 State NBS labs (*after grouping*): about 272 patterns

Remaining Issues

- **LA12057-8** =
  "Hb F, A, and other than C,D,E,S,O-Arab"
  Similar for
  FSV, FV, FACV, FADV, FAEV, FASV
  FSV, FVB, FAVB, SV, V, AV
- **LA11982-8** = "Hb F, D"
  Many labs acknowledge they can not reliably distinguish D/G
- Have not discussed "Disorder List" today
- Have not addressed "method specificty" issue
- >20 labs not represented
- Hundreds of patterns still not covered …

Introduction to Hb H-Disease Epidemiology and Natural History

Elliott Vichinsky, MD
Hematology/Oncology

May 25, 2010

Hemoglobin H Disease
Longitudinal Observations During Childhood

Ash Lal, M.D.
Hematology/Oncology
Nutrition & Metabolism Center

California Newborn Screening Program for Thalassemias

APHL Hemoglobinopathy Lab Workshop
Children's Hospital Oakland
May 26, 2015

Fred Lorey, Ph.D
Genetic Disease Screening Program
CA Department of Public Health

California Newborn Screening Program for Thalassemias: Confirmatory Testing and Follow-up

Issues and Answers Series
Hemoglobinopathy Newborn Screening
May 25, 2010

Carolyn Hoppe, MD
Hemoglobinopathy Reference Laboratory
Children's Hospital & Research Center Oakland

CHILDREN'S HOSPITAL & RESEARCH CENTER OAKLAND

Report from Evidence Review

Advisory Committee on Heritable Disorders in Newborns and Children

May 14, 2010

Alex R. Kemper, MD, MPH, MS
Department of Pediatrics, Duke University

DUKE CHILDREN'S Hospital & Health Center

MassGeneral Hospital for Children

http://genes-r-us.uthscsa.edu

National Newborn Screening and Genetics Resource Center
Austin, Texas USA
NNSGRC