Update: Long Term Follow up of Newborn Screening Conditions in New England

New England Newborn Screening Program

Secretary's Advisory Committee on Heritable Disorders in Newborns and Children

February 26, 2009

Anne Marie Comeau, Ph.D.
Deputy Director, NENSP

UMASS MEDICAL SCHOOL Commonwealth Medicine
Applied Knowledge in Public Service

Building Upon the Foundation of Six New England States' Comprehensive Newborn Screening Programs for Sustainable Follow-Up

Foundations

- New England longstanding NBS collaborative networks
- Massachusetts' experience
- Centralized NBS database, continuation of existing datasets

Goals

- Public Health Quality Assurance,
  - Public Health Quality Improvement and
    - Public Health Engagement in Research

Long-Term Follow Up Workgroup

Ellie Mulcahy, Gail Boaz -- Maine Genetics Program

Barbara McNeilly, Kristine Campagna -- Rhode Island NBS Program

Cindy Ingham – Vermont NBS Program

Marcia Lavochkin -- New Hampshire NBS Program

Vine Samuels-- Connecticut's Laboratory NBS Tracking Program

Janet Farrell – Massachusetts DPH

NENSP

Roger Eaton, Inderneel Sahai

Jaime Hale

Anne Comeau

Massachusetts Regulations

Stewardship and Authority

Massachusetts Regulations Governing Blood Screening of Newborns for Treatable Diseases and Disorders

(105 CMR 270.000 MGL c.111, ss3, 4E, 5, 6, 24A and 110A)

270.010: Follow-up of Newborn Blood Testing

For the purposes of quality assurance, quality improvement and ongoing evaluation of the effectiveness of the Newborn Blood Screening Program, including the determination of those disorders and diseases that should be screened for, the attending physician shall report to the Newborn Blood Screening Program, upon request, the following information within 30 days of the request:

(A) Diagnostic and long term outcomes for all newborns whose newborn screening results warranted diagnostic evaluation for a newborn screening disorder or disease; and

(B) Any additional, relevant information regarding these diagnostic and long term outcomes as specified by the Newborn Blood Screening Program.

Massachusetts Regulations Governing Blood Screening of Newborns for Treatable Diseases and Disorders

(105 CMR 270.000 MGL c.111, ss3, 4E, 5, 6, 24A and 110A)

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270.010: Follow-up of Newborn Blood Testing

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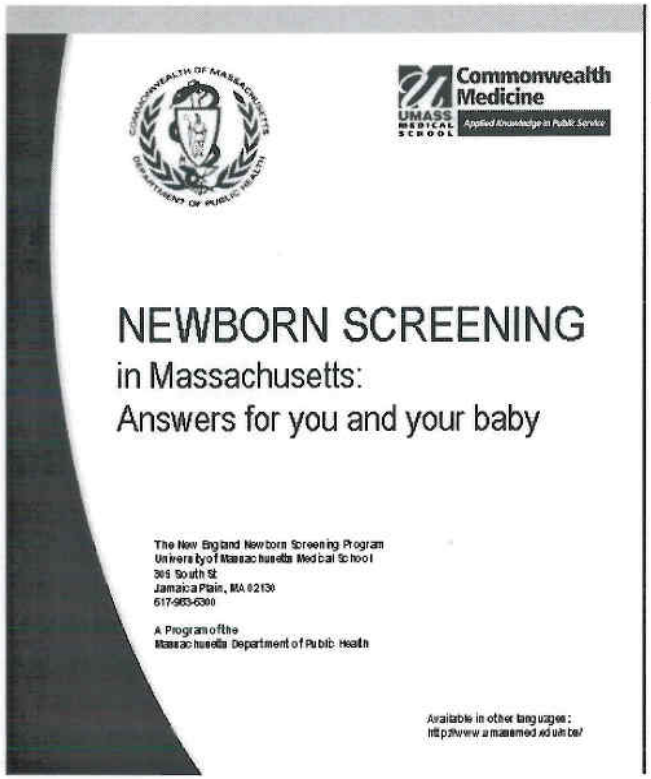
shall report to the Newborn Blood Screening Program

Diagnostic and long term outcomes

(B) Any additional, relevant information regarding these diagnostic and long term outcomes as specified by the Newborn Blood Screening Program.

Parent Notification of NBS Quality Assurance and Improvements in Massachusetts



NEWBORN SCREENING

QUALITY ASSURANCE AND IMPROVEMENTS

Newborn screening programs need to know that they are working well and need to know how to improve. This means that programs need to know whether the screening results match diagnostic results. This also means that programs need to know how babies who are diagnosed with newborn screening disorders are doing and whether they continue to get the care they need. Information on diagnoses and outcomes is collected for program-wide improvements.

Your baby's information and leftover blood may be stored for at least 10 years. Sometimes, the information or leftover blood will be used to make sure that newborn screening tests are working well. Sometimes the information or leftover blood will be used to make better tests for the newborn screening program. Other times, the information or leftover blood will be used for health studies. For any health studies, your written permission is needed before we release your baby's name to an external researcher.

In addition, if any information or leftover blood is going to be used for a study, the study has to be approved by two groups of people who make sure that your baby's rights are protected. These groups of people are called "Human Subjects Review Committees". One Human Subjects Review Committee is at the Department of Public Health, and the other is at the University of Massachusetts Medical School. The Federal Government sets the rules and regulates each Committee. For any proposed study, Human Subjects Review Committees decide whether your permission is needed. If either Committee decides that your permission is needed, the New England Newborn Screening Program will contact you before proceeding with the study.

Contacting you: We know that for many reasons, parents change health care providers and may change the name of their baby. If your baby has been diagnosed with a newborn screening disorder, or is being followed to find out if your baby has a newborn screening disorder, you may receive a letter from the New England Newborn Screening Program to ensure that your baby's information is up to date.

3 Foci for Data Collection and Best-Practice Development

Hemoglobinopathies

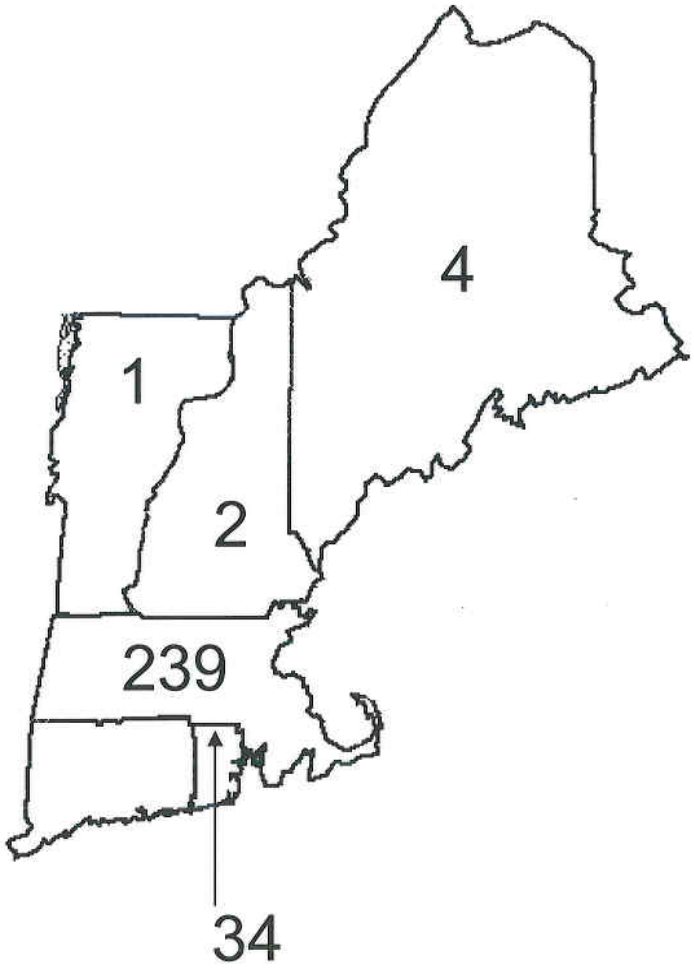
Cystic Fibrosis

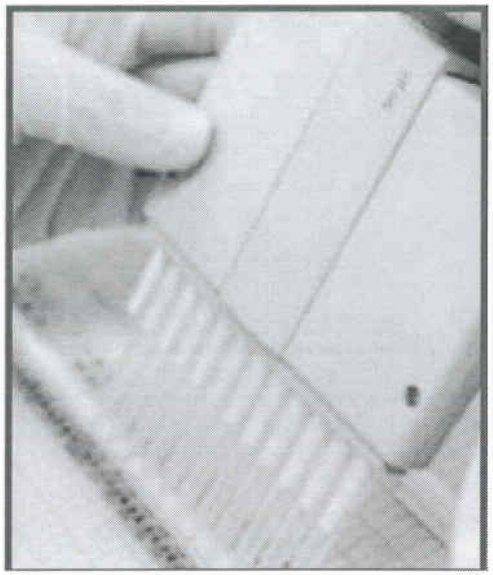
Metabolic Conditions

Sickling Hemoglobinopathies

Sickling Hemoglobinopathies Detected by the NENSP in New England

2003-present





A laboratory analyst transfers newborn sample extracts for sickle cell disease screening at the New England Newborn Screening Program.

The New England Hemoglobinopathies Newborn Screening Workgroup

Dr. Anne Marie Comeau Ms. Claire Hughes

Dr. Naheed Usmani

Dr. Philippa Sprinz Dr. Anjulika Chawla

Ms. Kathleen Ryan, RN Dr. Matthew Heeney

Dr. Karla Fuentes

Dr. Maria Pelidis

Dr. Mary Huang

Dr. David Ebb Dr. Anne Rossi

Dr. Farzana Pashankar

Dr. J. Nathan Hagstrom Dr. Joanna Luty

Boston Medical Center

Baystate Children's Hospital

Children's Hospital Boston

Connecticut Children's Medical Center

Floating Hospital for Children at Tufts Medical Center

MassGeneral Hospital for Children

Lifespan

Hasbro

The Barbara Bush Children's Hospital At Maine Medical Center

UMassMemorial Medical Center

A Member of UMass Memorial Health Care

Yale New Haven

LTFU Variables for Sickling Hemoglobinopathies

Defined by MA and Regional NBS Hgb Workgroups

Census

- Date of last clinic visit
- Date of most recent visit
- Alive; if no date & cause of death

General Demographics/Current Practices

- Height (cm) & Weight (kg) at last clinic visit
- TCD (Normal/Abnormal); date(s)

LTFU Variables for Sickling Hemoglobinopathies

continued

Clinical Status

- Clinical Stroke? if yes, date(s)
- Radiological Stroke? if yes, date(s)
- MRI/MRA Abnormal? date(s)
- Splenectomy? if yes, date

Notable Infections

- Febrile Episodes ? if yes, date(s)
- Culture + ? Sepsis? if yes, date(s)

Treatments and Clinical Episodes

- Hyper Transfusions? if yes, start & stop dates
- Prescribed Hydroxyurea in last 6 months? if yes start & stop dates
- Hospitalizations ?if yes, date(s)
- Acute Chest ? if yes, date(s)

Commonwealth Medicine
UMASS MEDICAL SCHOOL
Applied Knowledge in Public Service

New England Newborn Screening Program
University of Massachusetts Medical School
305 South Street
Jamaica Plain, MA 02130-3597
617-983-6300 (office) 617-522-2846 (fax)

Hemoglobinopathies LTFU Report

Last Name:

First Name:

DOB: NBS result:

Initial Clinic: Current Clinic:

Confirmatory HGB Result:

Date of most recent clinic visit: _____

Height (cm) _____ Date _____

Weight (kg) _____ Date _____

Date of 1st TCD: _____ Normal Abnormal

Date of Last TCD: _____ Normal Abnormal

MRI/MRA: Normal Abnormal Date _____

Hospitalizations: No Yes *If yes, date(s)* _____

Acute Chest Syndrome: No Yes *If yes, date(s)* _____

Clinically "Overt" Stroke: No Yes *If yes, date(s)* _____

Radiologic only "Silent" Stroke: No Yes *If yes, date(s)* _____

Febrile Episodes: No Yes *If yes, date(s)* _____

Culture + Bacteremia: No Yes *If yes, date(s)* _____

Prescribed hydroxyurea in last 6 months? Yes No

Start Date _____
End Date _____

Hyper Transfusions? Yes No

Start Date _____
End Date _____

Splenectomy: No Yes *If yes, date* _____

Is child living? No Yes *If no, date of death* _____

If no, cause of death _____

Data form for Hemoglobinopathies

Sent between NENSP and clinics

Sampling of LTFU Hgb data

30 patients (DOB 2003-present)

Variable	n	%
At least one clinic visit in the past 12 months	25	83
At least one TCD	8	27
At least one hospitalization in their life	7	23
Splenectomy	2	7
At least one event of acute chest in their life	2	7
Taken hydroxyurea	4	13
Clinical stroke *(Child has had 2 clinical strokes – at 2.5 and 3 years of age)*	1	3

Cystic Fibrosis

The Massachusetts CF NBS Workgroup

Representatives from NENSP and the 5 MA CF Centers

Dr. Anne Marie Comeau

Dr. Richard Parad

Baystate Children's Hospital

Dr. Robert (Bob) Gerstle

Children's Hospital Boston

Dr. Henry (Hank) Dorkin

Dr. Terry Spencer

MassGeneral Hospital for Children

Dr. Allen Lapey

Tufts-New England Medical Center

Dr. William (Bill) Yee

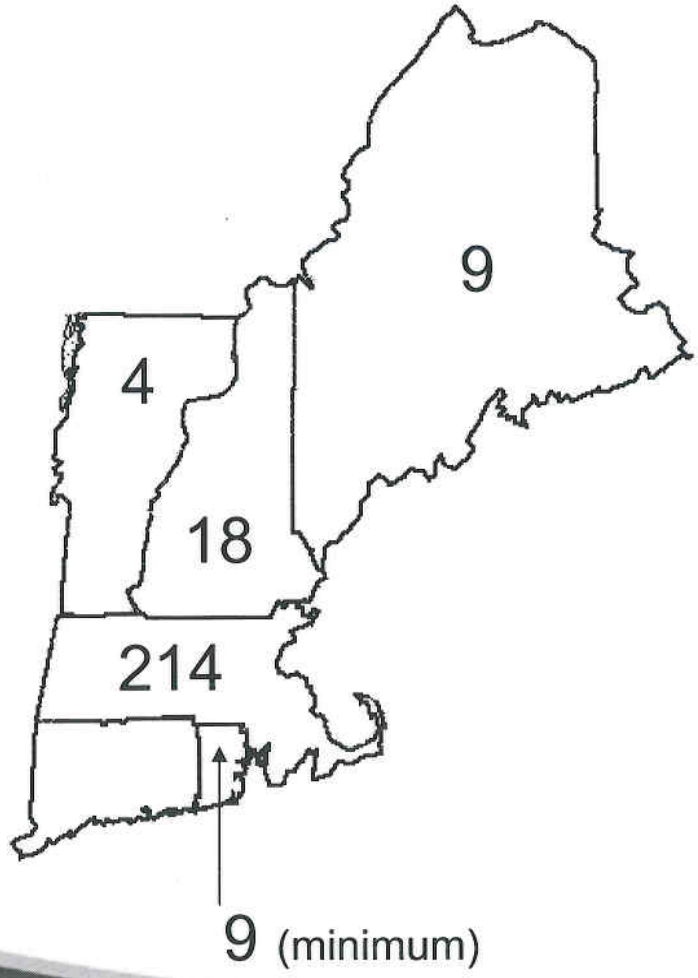
UMassMemorial Medical Center

A Member of UMass Memorial Health Care

Dr. Brian O'Sullivan

Cystic Fibrosis Cases Detected by the NENSP in New England

(From state's start date – January 31, 2009)



State	CF NBS start date
Massachusetts	2/1/1999
New Hampshire	5/1/2006
Rhode Island	7/1/2006
Vermont	3/1/2008
Maine	7/1/2008
Connecticut	—

Notable Trends in Cystic Fibrosis Cases Detected by the NENSP in New England

Massachusetts: Decrease of CF

Hale JE, Parad RB, and Comeau AM. Newborn screening showing decreasing incidence of cystic fibrosis. N Engl J Med. 2008 Feb 28;358(9):973-4.

The NEW ENGLAND JOURNAL of MEDICINE

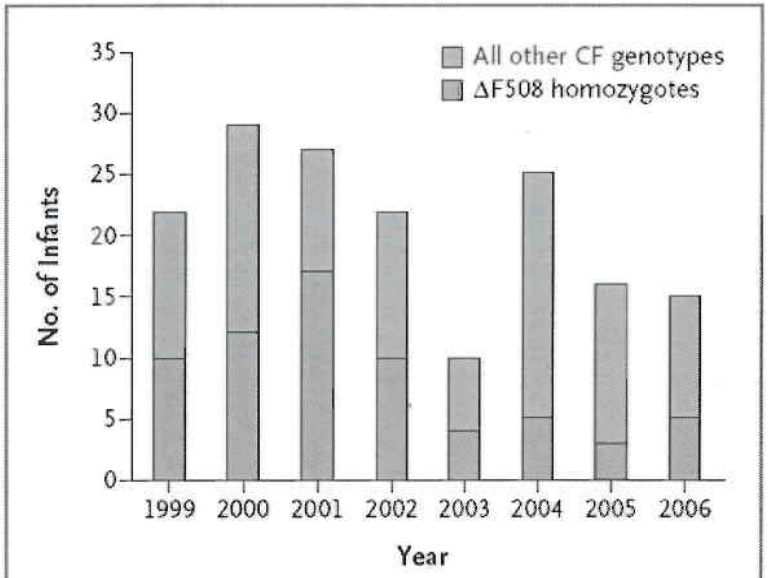


Figure 1. **Newborns with Cystic Fibrosis Identified by Newborn Screening for the Disease in Massachusetts.**

Bars indicate the number of first persons in a family with positive results of newborn screening and a diagnosis of cystic fibrosis (CF). Additional persons in a single family were excluded.

Notable Trends in Cystic Fibrosis Cases Detected by the NENSP in New England

Maine: CF NBS Case Projections vs. Actual Number

Projected Cases per Year

Northern Maine

2 CF Births per year

Central Maine

2 CF Births per year

Southern Maine

2 CF Births per year

6 TOTAL per year

Actual Cases Detected in 7 months of screening

Northern Maine

2 CF births

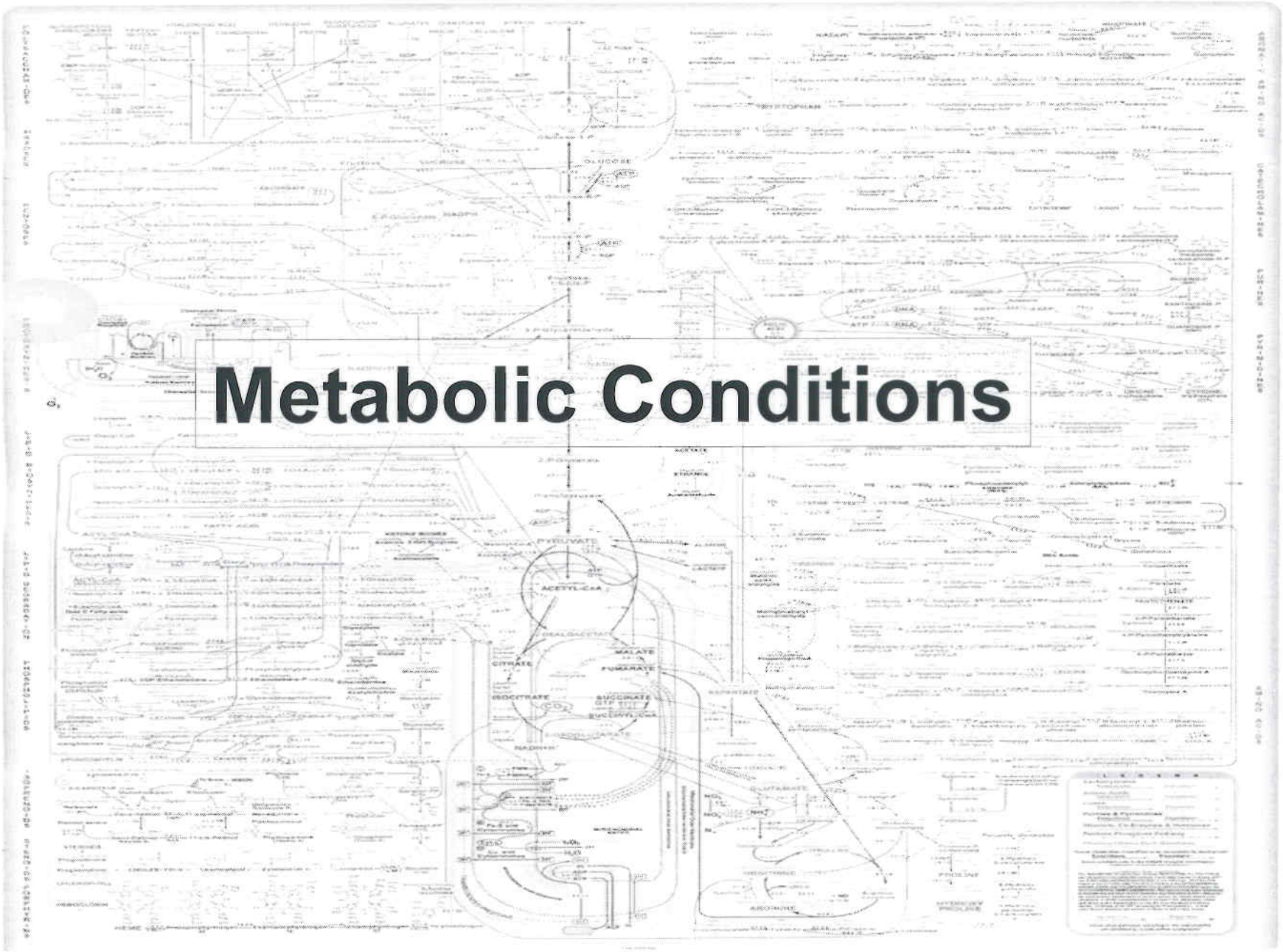
Central Maine

5 CF Births

Southern Maine

2 CF

9 TOTAL in 7 months



Metabolic Conditions

The New England Metabolic Newborn Screening Workgroup

Inderneel Sahai, MD (NENSP), Chair

Dr. Madelena Martin

Dr. Beverly Hay

Dr. Vivian Shih

Dr. Marsha F. Browning

Dr. Mark Korson

Dr. Cheryl Garganta

Dr. Gerald Berry

Dr. Harvey Levy

Dr. Chanika Phornphutkul

Dr. Thomas Brewster

Dr. Wendy Smith

Dr. Leah Burke

Dr. Greta Seashore

UMassMemorial Medical Center
A Member of UMass Memorial Health Care

Children's Hospital Boston

Lifespan
Hasbro

Eastern Maine Medical Center
Inspiring confidence in care

Yale New Haven

Floating Hospital for Children at Tufts Medical Center

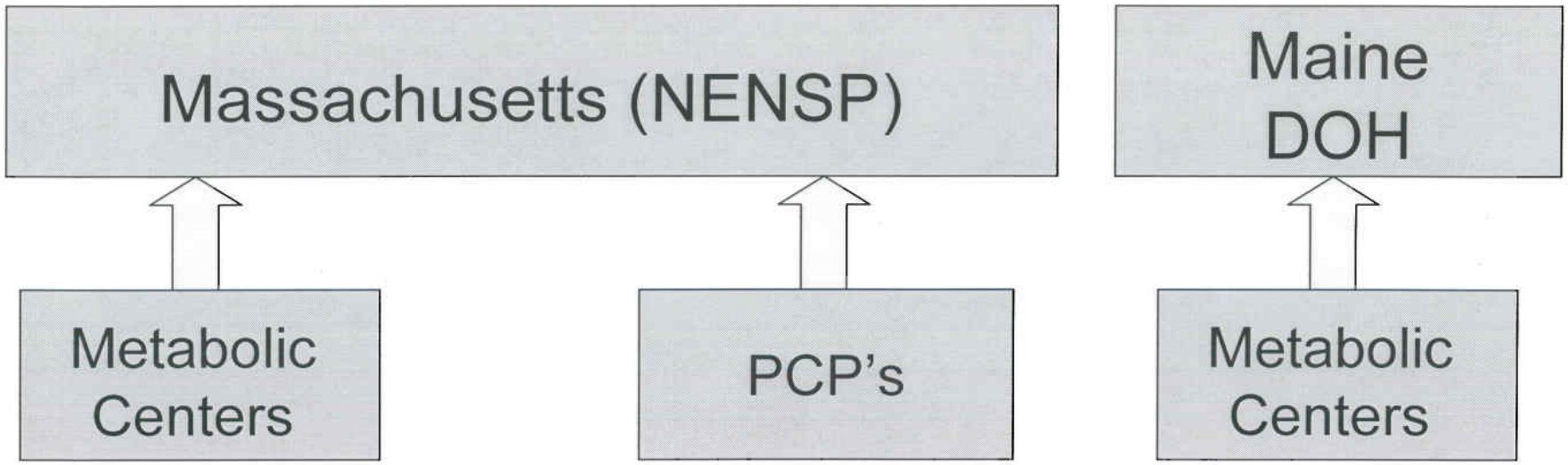
The Barbara Bush Children's Hospital
At Maine Medical Center

MassGeneral Hospital for Children

Fletcher Allen Health Care
In alliance with The University of Vermont

Connecticut Children's Medical Center

SOURCE OF NENSP LTFU DATA
(Metabolic Disorders)



~ 38 % Cases

~ 49 % Cases

~ 13 % Cases

Children's Hospital

Massachusetts General Hospital

University of Massachusetts Medical Center

Tufts Medical Center

Not evaluated by Specialist > 2 years.

Suggested follow- up by specialist

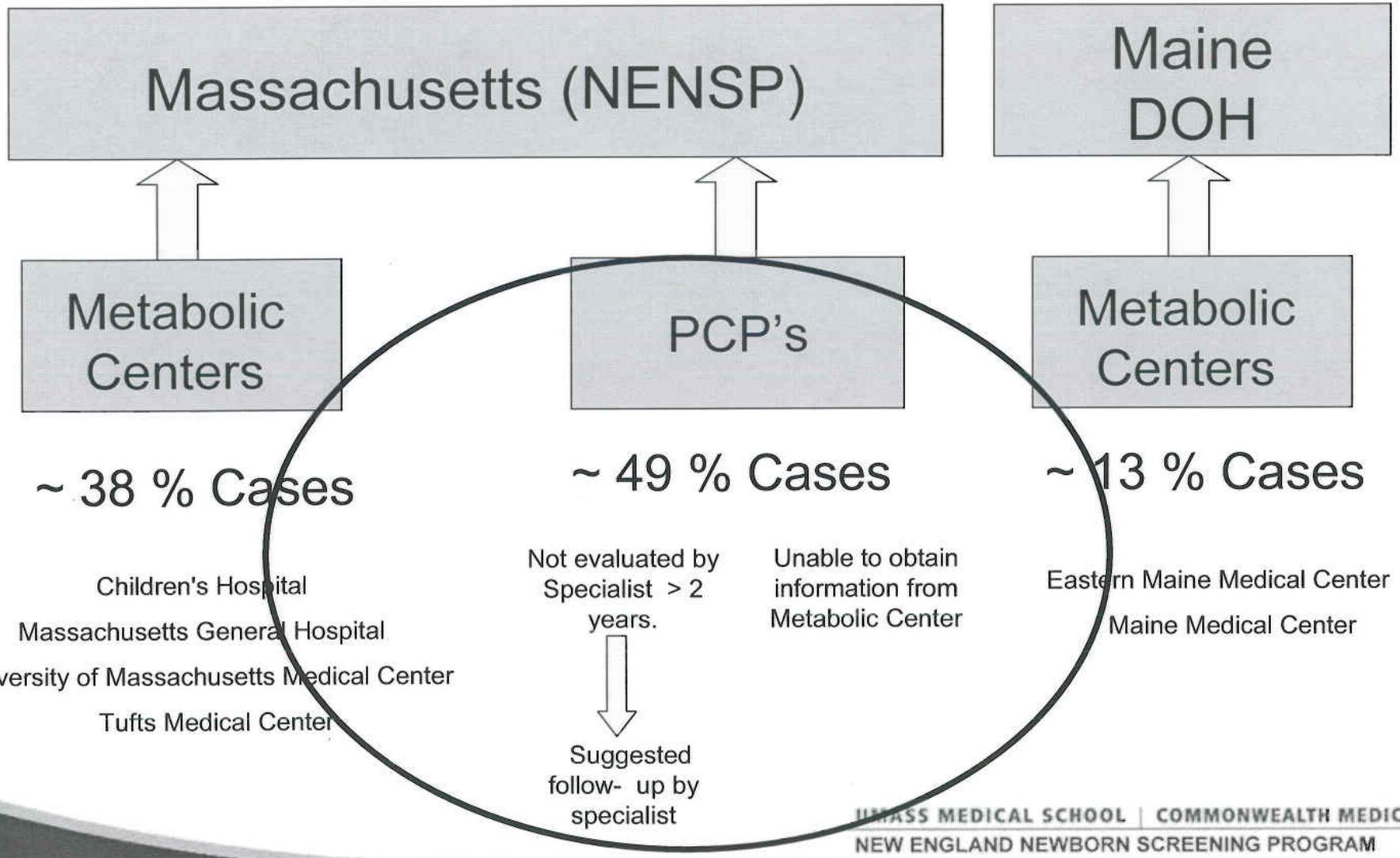
Unable to obtain information from Metabolic Center

Eastern Maine Medical Center

Maine Medical Center

SOURCE OF NENSP LTFU DATA

(Metabolic Disorders)

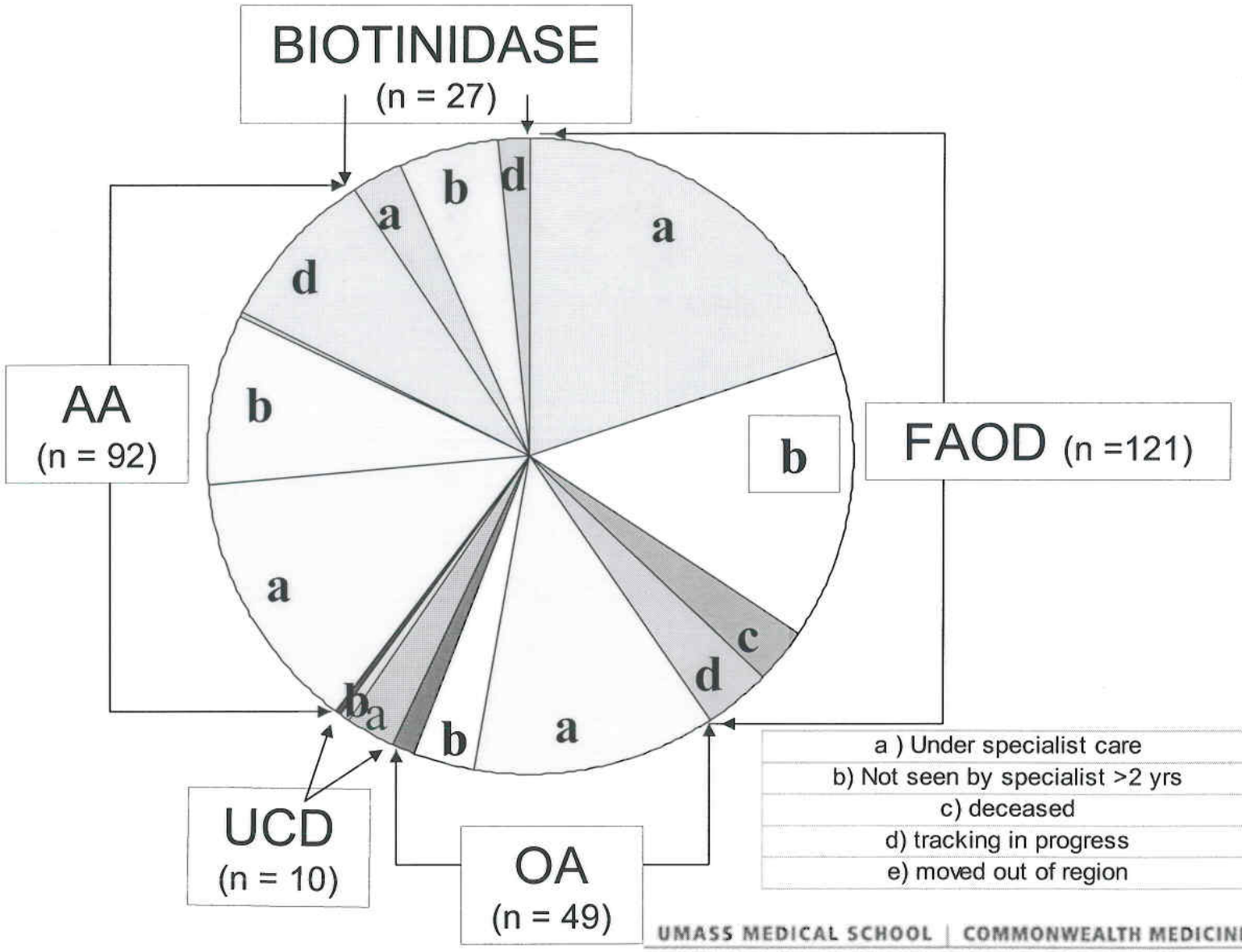


LTFU Status of Metabolic cases detected by NENSP in MA and ME

	Total n	Deceased	Moved	Tracking	LTFU Data	Not seen by specialist > 2 years
Fatty Acid Oxidation Defects	121	8	0	10	103	44
Organic Acidemias	49	0	3	0	46	9
Urea Cycle Defects	10	0	1	0	9	1
Amino Acid Disorders	92	1	0	25	66	26
Biotinidase Deficiency	27	0	0	5	22	15
TOTAL	299	9	4	40	246	95

95/246 children with LTFU data have not been seen by specialist in > 2 years

FOLLOW-UP SPECIALIST CARE



DISORDERS WITH LIMITED FOLLOW-UP WITH METABOLIC SPECIALIST

FAOD	•MCAD (19/39) •VLCAD (6/21) •CUD (4/10) •SCAD (15/28)
OA	•MCC (9/16) •MBCD (2/2)
UCD	•Citrullinemia I (1/4) •CPS (1/1)
AA	•Atypical PKU (6/40) •Hyper-PHE (17/18) •MAT (3/4)
Bio	•Profound (3/5) •Partial (12/17)

Reasons Stated for Follow-up Outside of Specialty Care

- Limited information provided by specialist (uncertain spectrum)
- No specific treatment provided
- Child has remained asymptomatic without treatment
- Unnecessary travel

Center-to-Center Transfers

Metabolic: ~ 48%

Cystic Fibrosis: ~20%

Hemoglobinopathies: <5%

LTFU of Metabolic Disorders Identified in Massachusetts & Maine (1999-2008)

Metabolic Case Outcomes.
Sahai et al

MCAD

Our records show that you are the primary care physician for a baby with MCAD deficiency

summarizes our experience to date, and alerts you of two late-occurring deaths among babies identified at birth in New England with MCAD.

Although most children with MCAD deficiency diagnosed by newborn screening have done well clinically, there have been two deaths, at age 11 months and 33 months. Both children had regular pediatric care and had no other medical conditions. One child had vomited several times but ate a snack before falling asleep. He was found unresponsive the next morning and could not be resuscitated. The other child had also vomited several times before becoming lethargic.

These deaths underscore the importance of close monitoring for early signs of illness and immediate medical attention to prevent severe hypoglycemia.

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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Spectrum of Medium-Chain Acyl-CoA Dehydrogenase Deficiency Detected by Newborn Screening

Ho-Wen Hsu, MD[a], Thomas H. Zytkovicz, PhD[a], Anne Marie Comeau, PhD[a], Arnold W. Strauss, MD[b], Deborah Marsden, MD[c], Vivian E. Shih, MD[d], George F. Grady, MD[a], Roger B. Eaton, PhD[a]

[a]Department of Pediatrics, New England Newborn Screening Program, University of Massachusetts Medical School, Jamaica Plain, Massachusetts; [b]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio; [c]Department of Pediatrics, Children's Hospital Boston, Boston, Massachusetts; [d]Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts

ABSTRACT

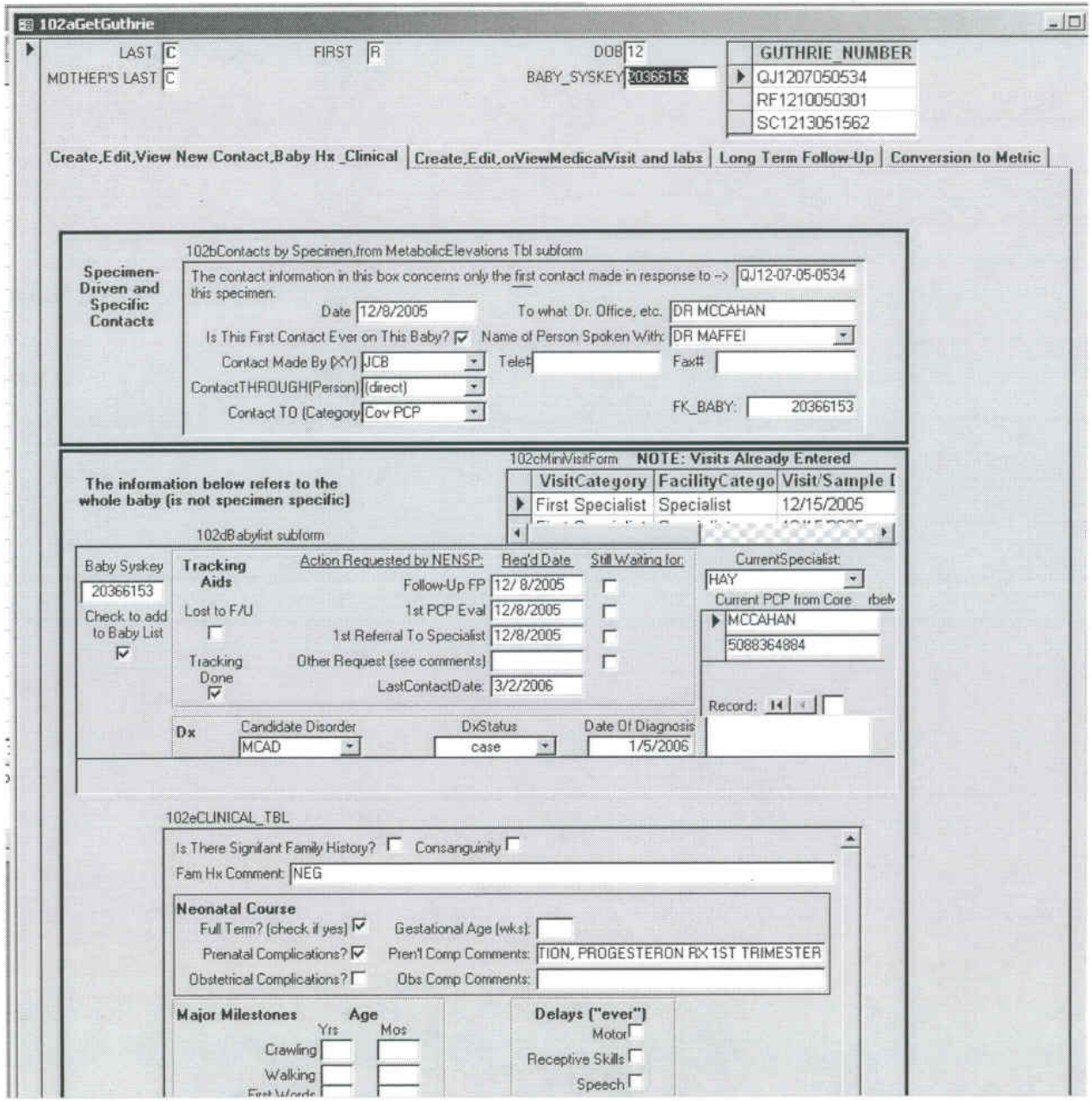
Objective: We describe the clinical spectrum of medium chain acyl-CoA dehydrogenase (MCAD) deficiency detected by routine newborn screening, assess factors associated with elevations of octanoyl carnitine (C8) in newborns, and characteristics associated with adverse clinical consequences of MCAD deficiency.

Pediatrics 2008;121;e1108-e1114

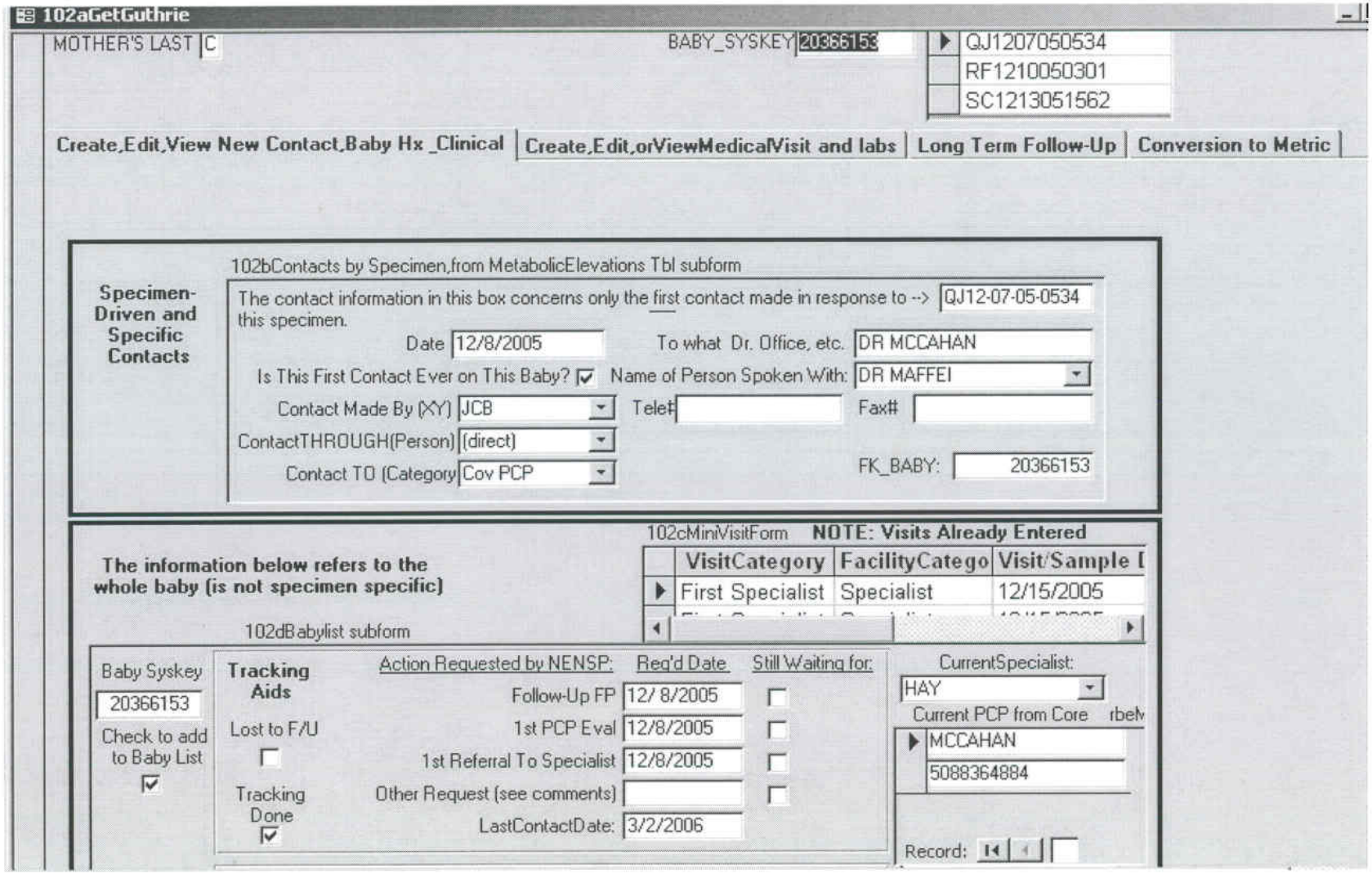
Back to the Foundations:

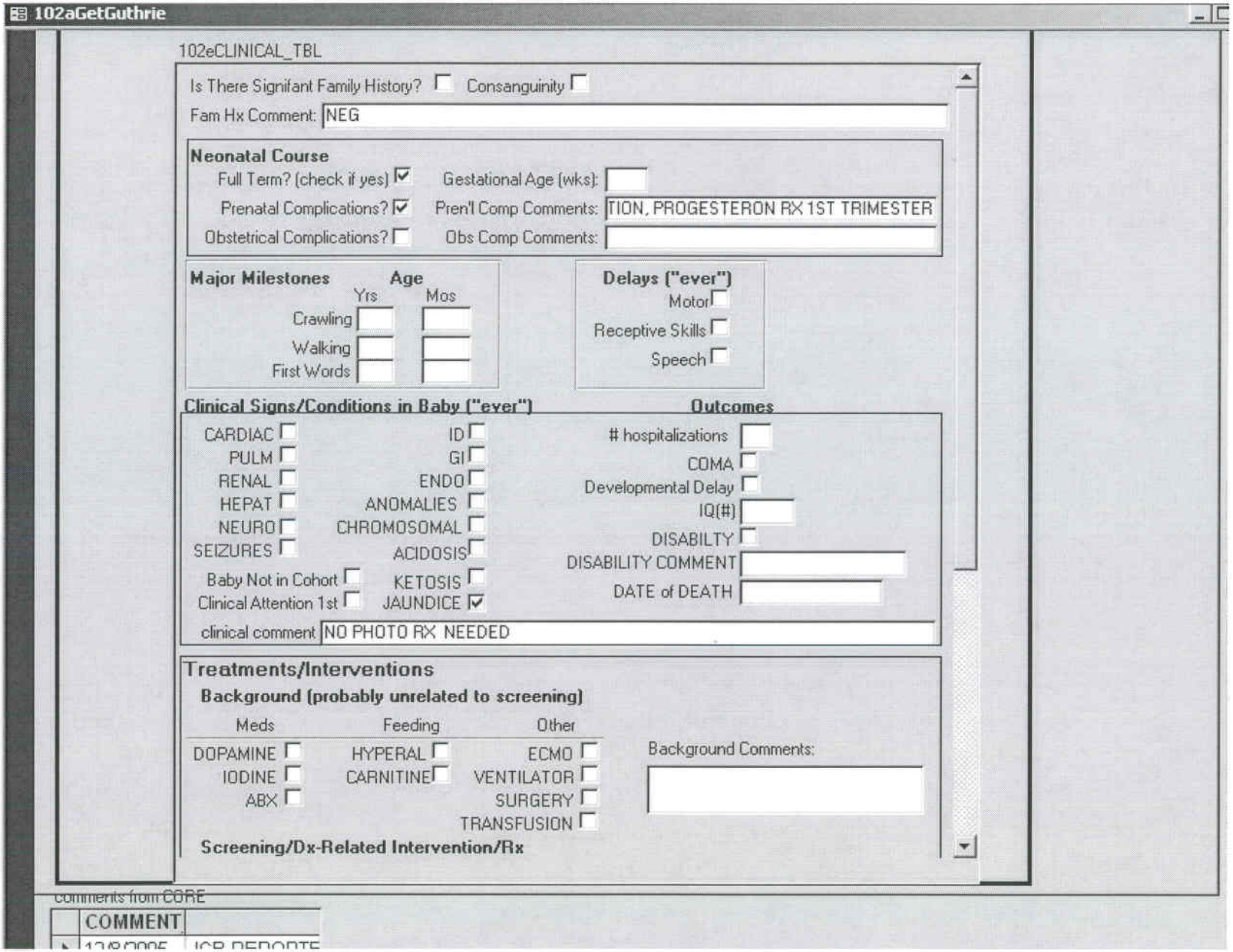
The Databases

Metabolic Database



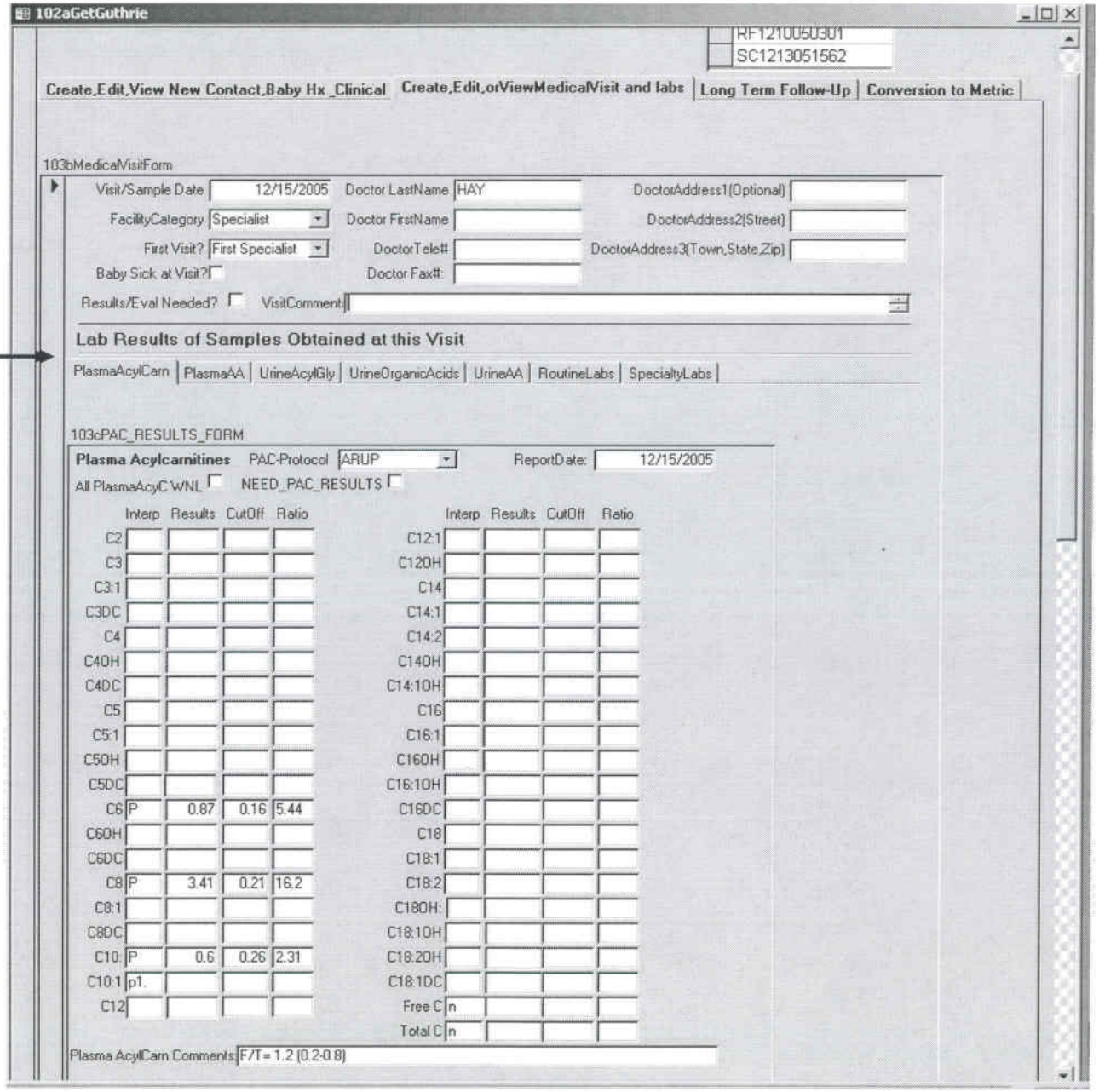
Metabolic Database




102aGetGuthrie
102eCLINICAL_TBL
Is There Signifant Family History?
Consanguinity
Fam Hx Comment: NEG
Neonatal Course
Full Term? (check if yes)
Gestational Age (wks):
Prenatal Complications?
Pren'l Comp Comments: TION, PROGESTERON RX 1ST TRIMESTER
Obstetrical Complications?
Obs Comp Comments:
Major Milestones
Age
Yrs
Mos
Crawling
Walking
First Words
Delays ("ever")
Motor
Receptive Skills
Speech
Clinical Signs/Conditions in Baby ("ever")
CARDIAC
PULM
RENAL
HEPAT
NEURO
SEIZURES
ID
GI
ENDO
ANOMALIES
CHROMOSOMAL
ACIDOSIS
KETOSIS
JAUNDICE
Baby Not in Cohort
Clinical Attention 1st
Outcomes
hospitalizations
COMA
Developmental Delay
IQ(#)
DISABILTY
DISABILITY COMMENT
DATE of DEATH
clinical comment: NO PHOTO RX NEEDED
Treatments/Interventions
Background (probably unrelated to screening)
Meds
Feeding
Other
DOPAMINE
IODINE
ABX
HYPERAL
CARNITINE
ECMO
VENTILATOR
SURGERY
TRANSFUSION
Background Comments:
Screening/Dx-Related Intervention/Rx
comments from CORE
COMMENT

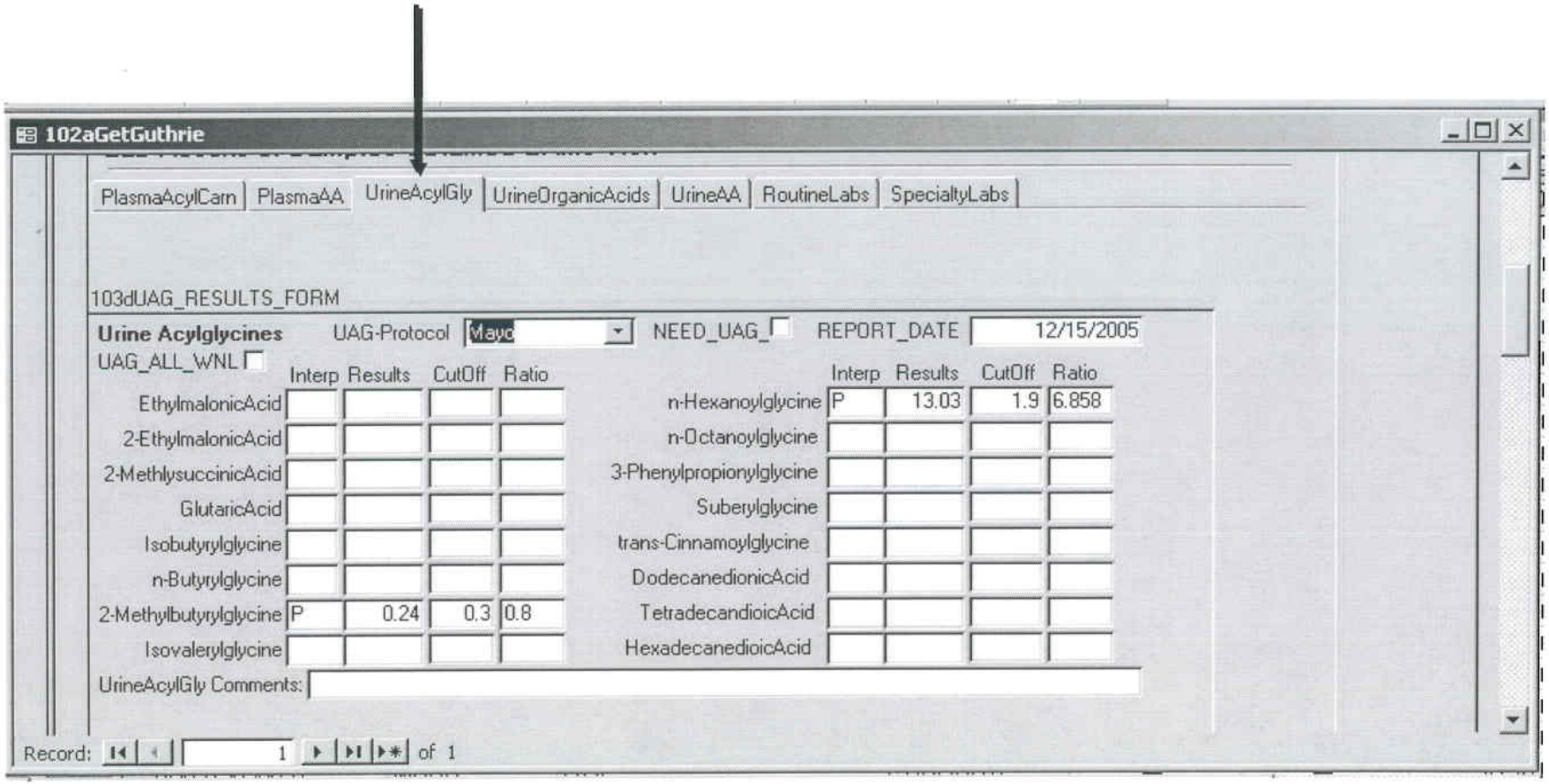
Diagnostic Labs

Plasma Acylcarnitines



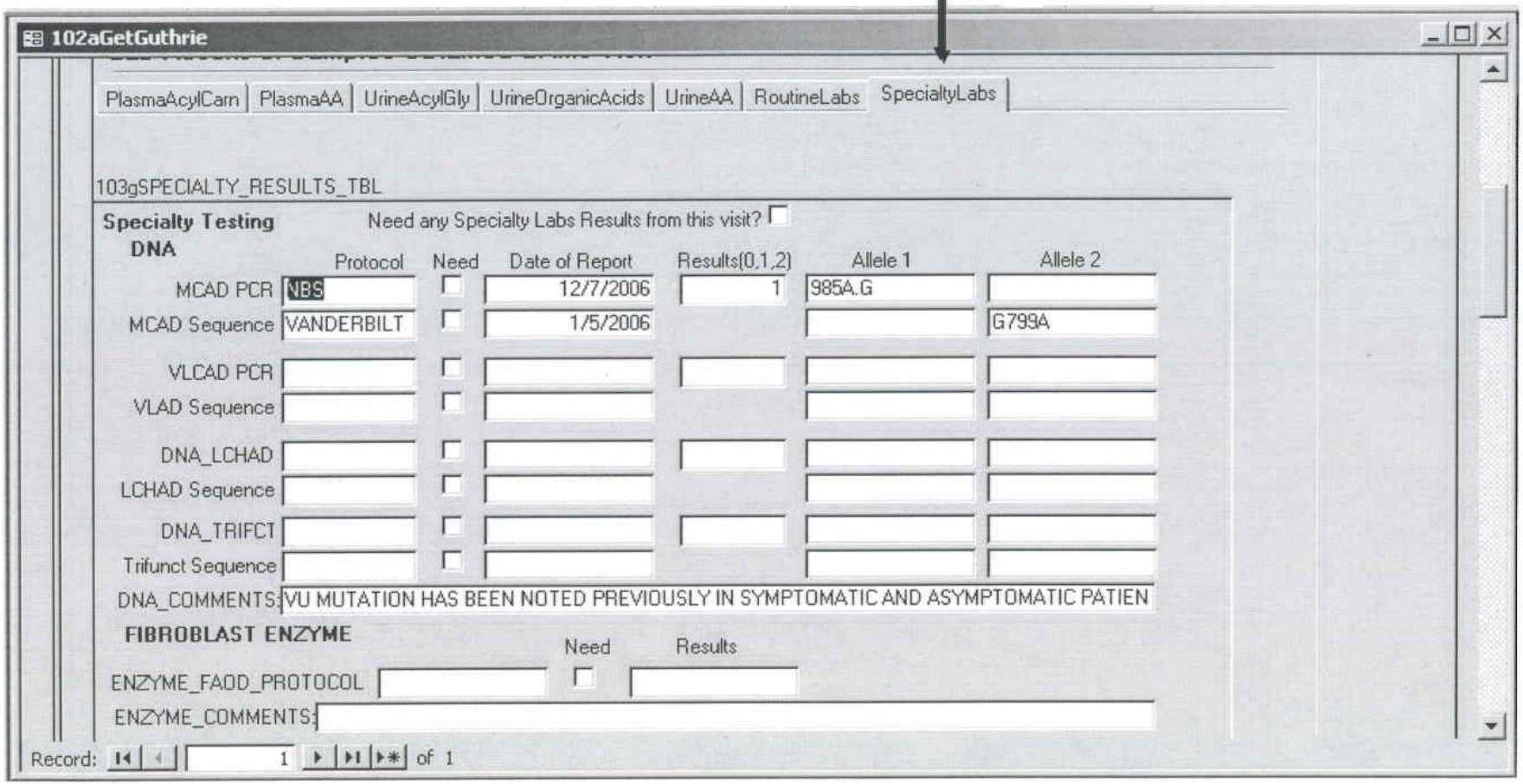
Diagnostic Labs

Urine Acylglycines

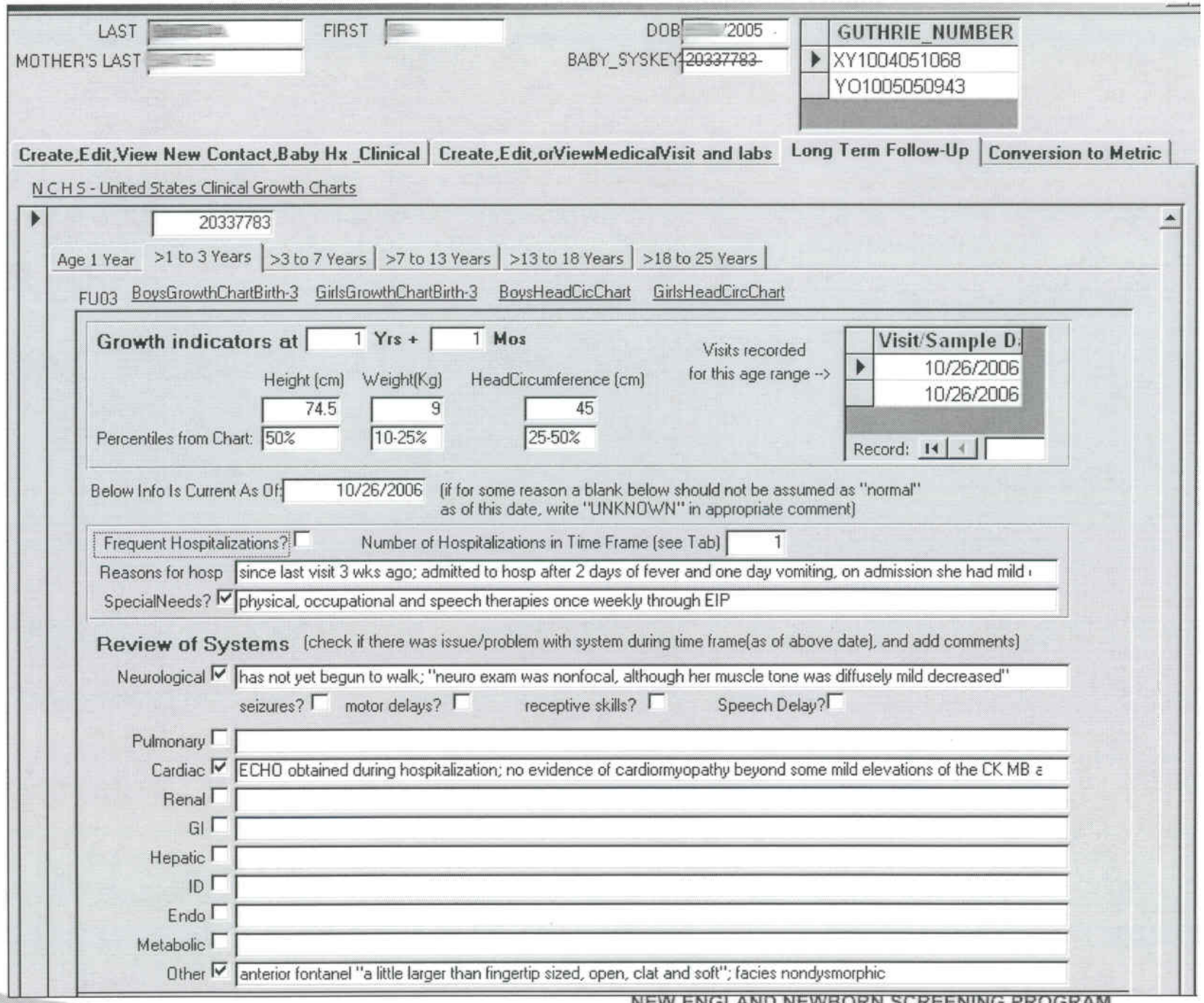


Diagnostic Labs

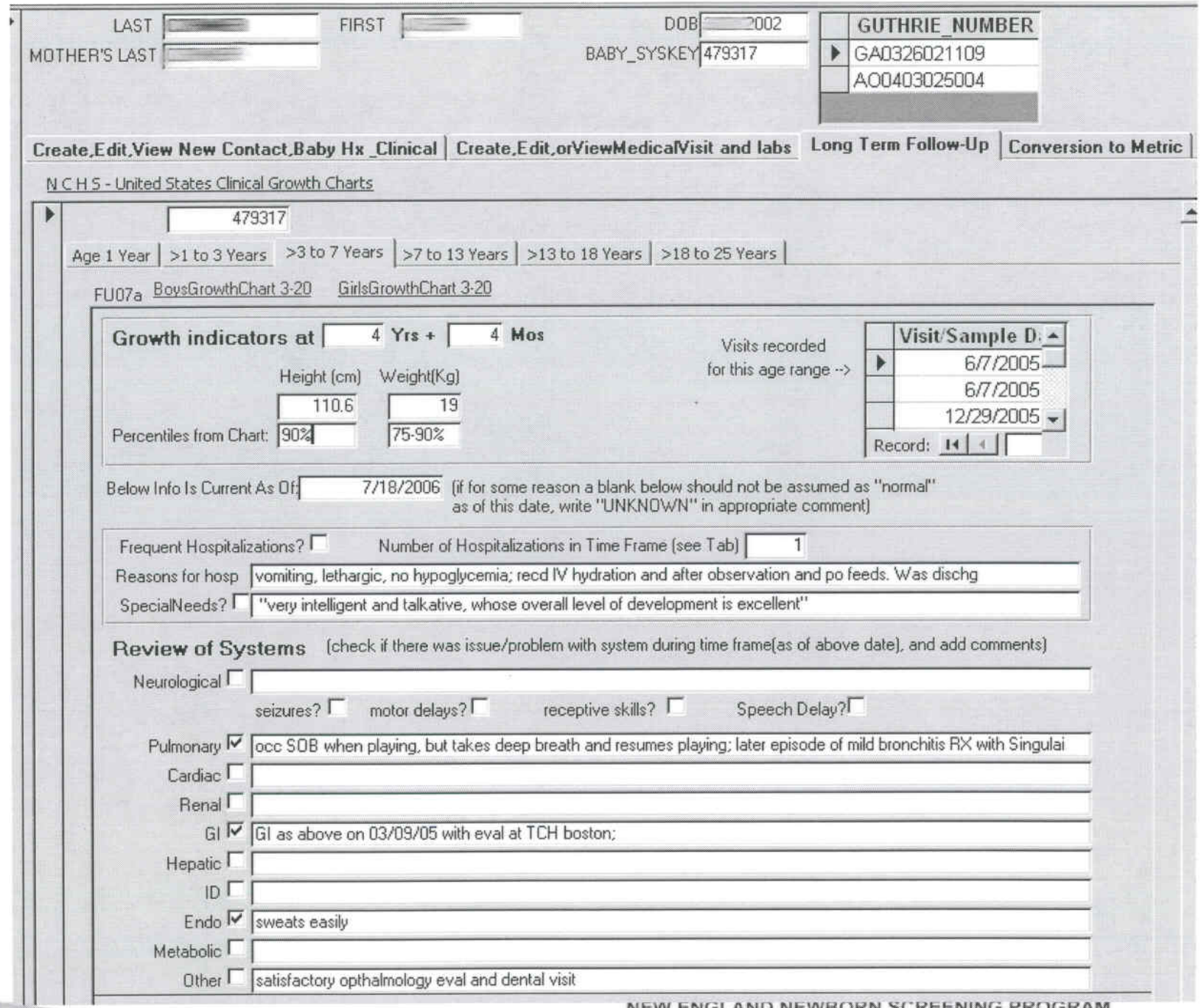
Specialty Labs



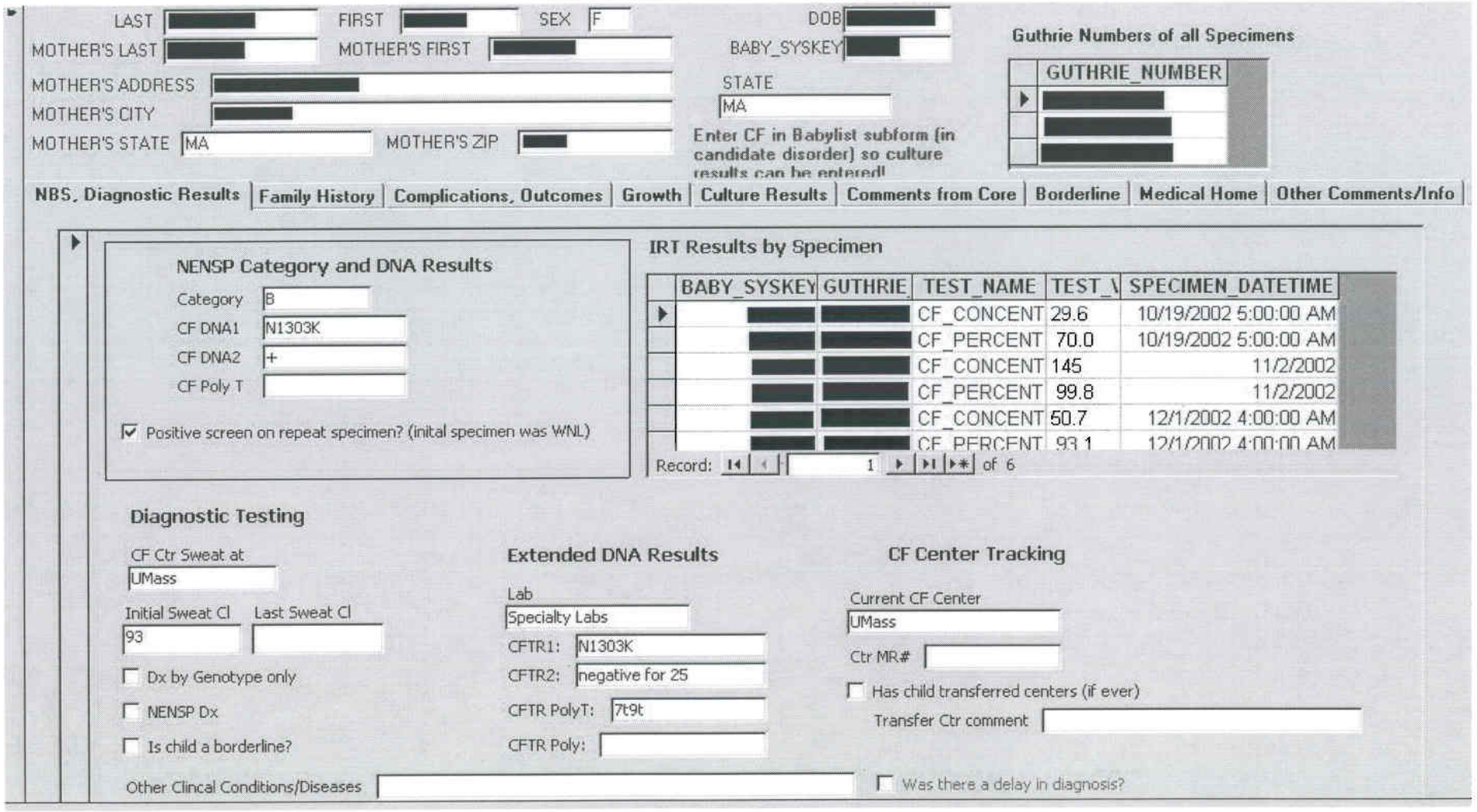
Long-term Follow-Up



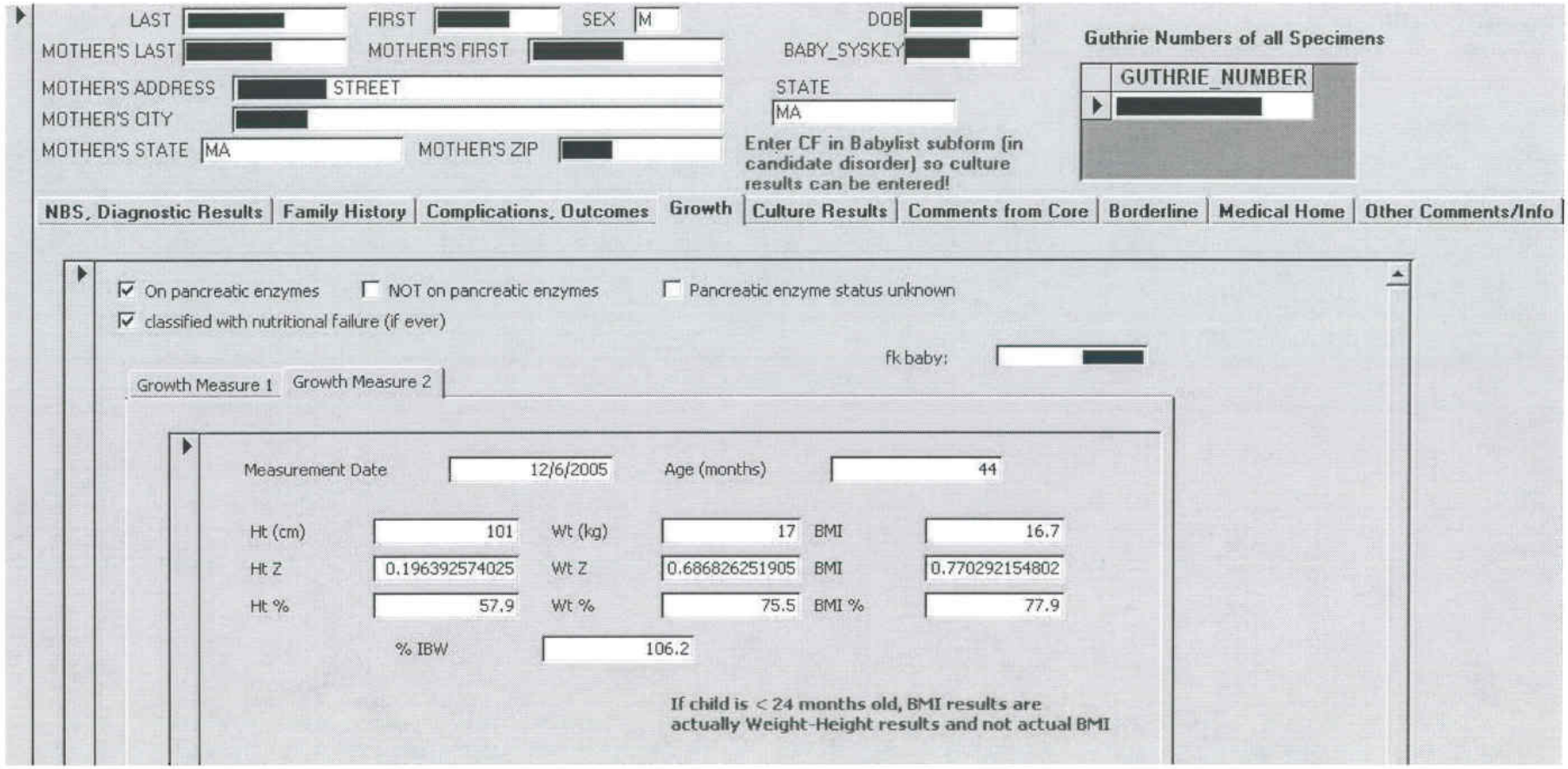
Long-term Follow-Up



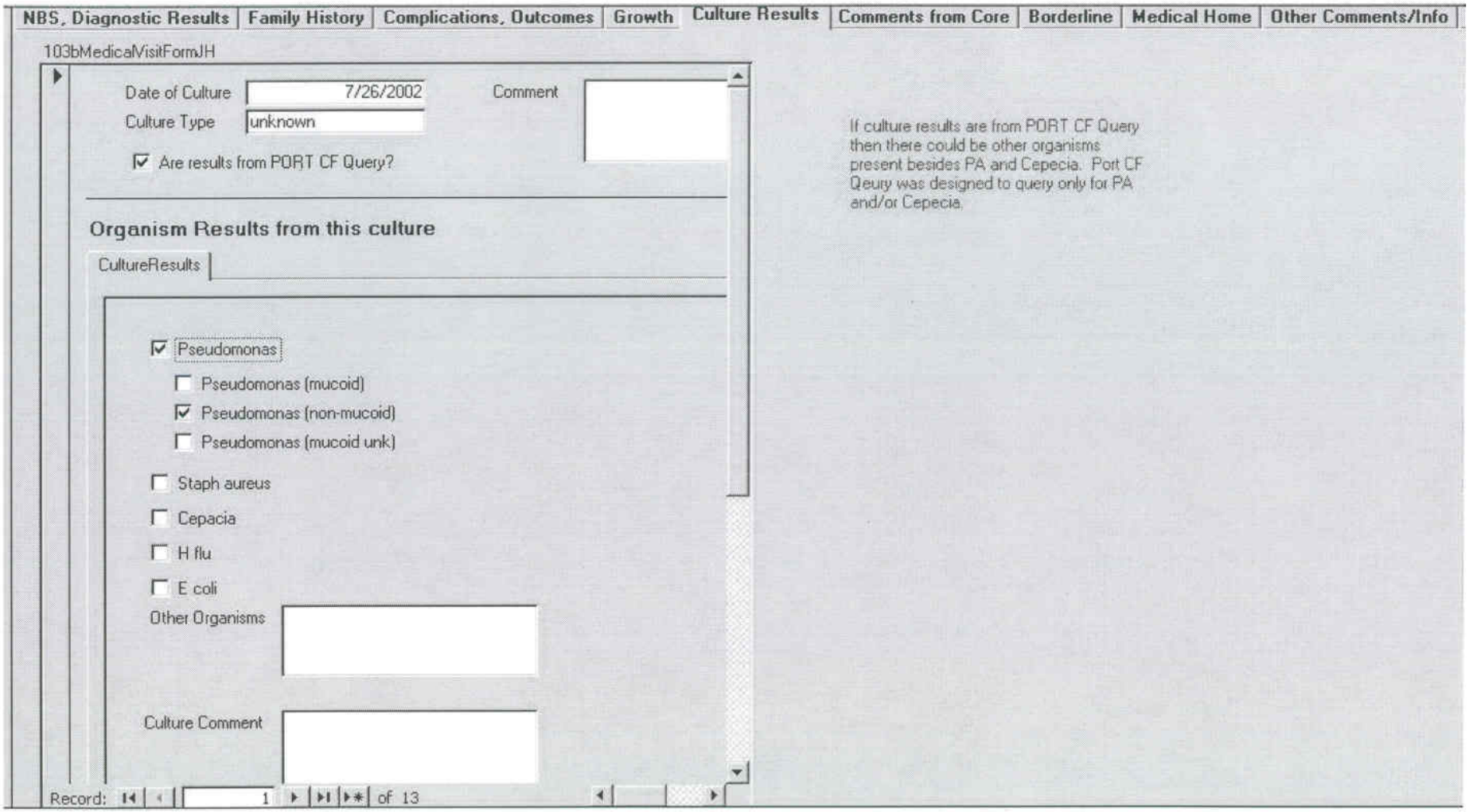
Cystic Fibrosis Database



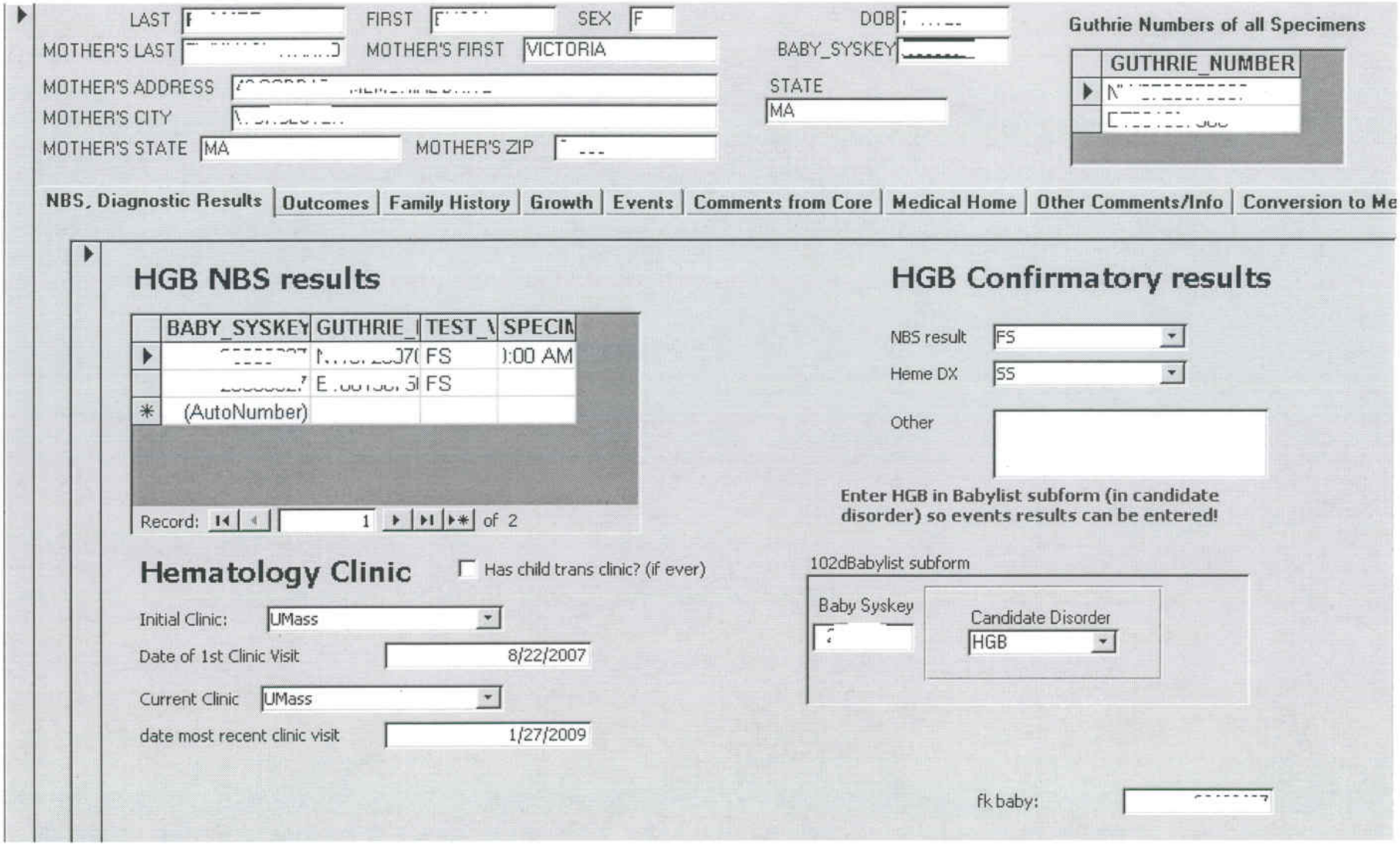
Cystic Fibrosis Database: Growth Measures



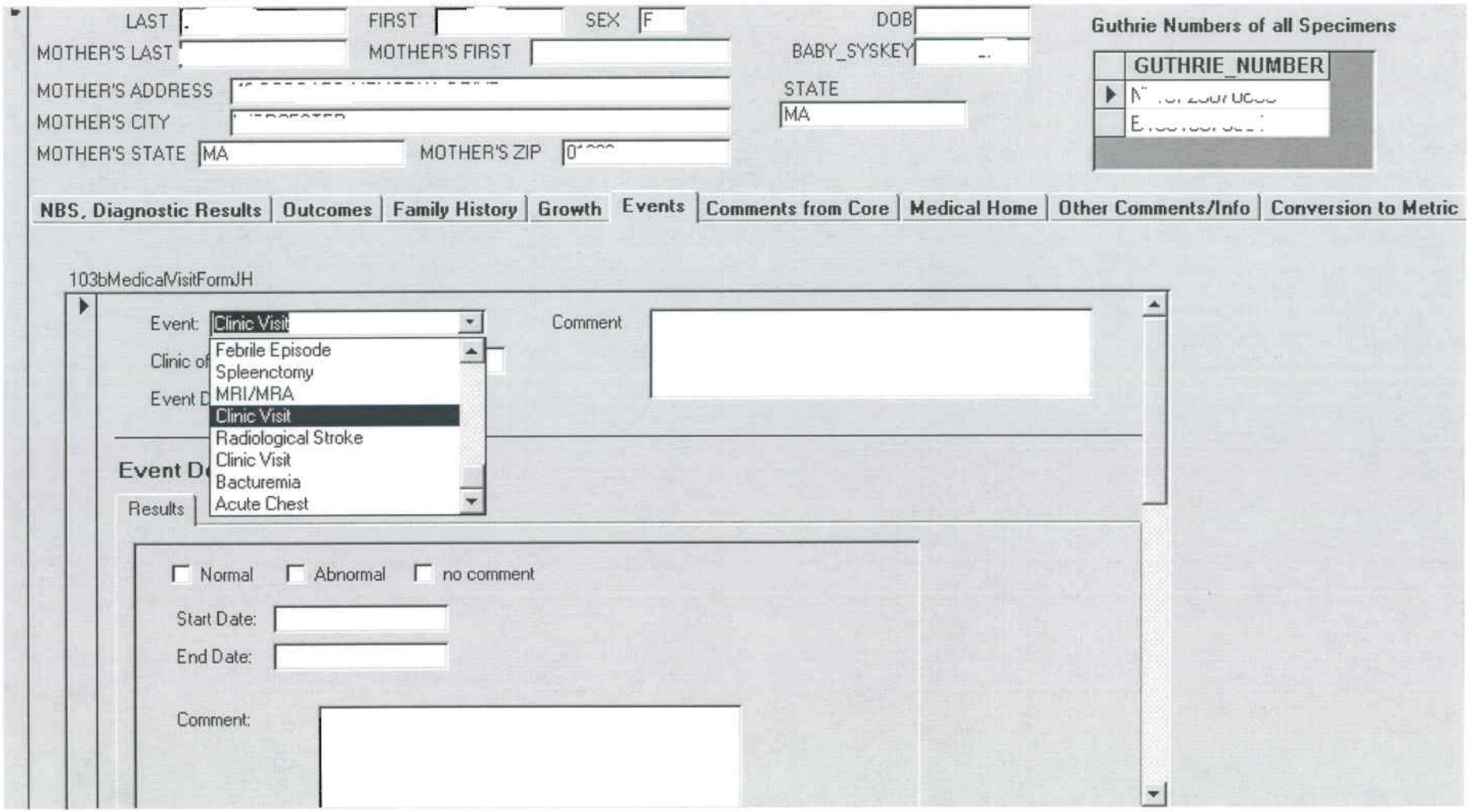
Cystic Fibrosis Database: Culture Results



Hemoglobin Database



Hemoglobin Database: Variables & Outcomes



Status of LTFU in New England States

Acknowledgements

This work is the funded by

the New England Newborn Screening Program,

State Newborn Screening Programs in New England

and Priority Focus 2 HRSA Award subcontracted through Region 1 Grant U22MC03959-04-00.

Lessons Learned from CF LTFU in Massachusetts

- In 2006 NENSP collected outcomes on 125 CF affected infants (born 1999-2004) identified by NBS
  - Height & Weights (at 1 year of age & most recent)
  - Culture Results (at 1 year of age & most recent) & later by organism cultured

* Not all CF infants are in PORT CF (the CFF registry)

* Center transfers offer a substantial challenge – local value

  ~ 20% of MA CF infants have transferred between the 5 MA CFF Centers

* Value of raw data: quality standards in collection, data entry and data translation. (various tools used to calculate height-weight, BMI and % Ideal Body Weight)

* Infection tracking confounded by successful treatments.

  - Focus on a particular organism such as *B. cepacia* or *Pseudomonas* and collect all dates that child had positive culture for that particular organism