NewSTEPs

A Program of the Association of Public Health Laboratories™

Case Worksheets for Newborn Screening

Last Updated: December 5, 2024

Case Information Worksheet:
Information Collected for ALL Cases

Infant Demographic Information	
State Unique ID? (alphanumeric)* *A state unique ID is a number and or letters that your program provides to tag or track each confirmed case and update information as needed.*	Unique IDs should only include numbers, letters, hyphens, and underscores
Gestational Age? (in weeks)	
Birth Information	
Date of Birth? (mm/dd/yyyy)*	
Time (hh:mm AM/PM) *If time of birth is not available, only enter the date*	
Year* *Year of birth is stored to calculate Quality Indicators*	*Automatically populated based on date of birth*
Birth Weight? (in grams)	
Biological Sex?	☐ Male ☐ Female ☐ Unspecified ☐ Unknown
Race? (Select all that apply)	☐ White ☐ Black or African American ☐ American Indian or Alaskan Native ☐ Asian ☐ Native Hawaiian or other Pacific Islander ☐ Not Reported ☐ Unknown
Ethnicity?	☐ Hispanic, Latino(a) or Spanish origin ☐ Not of Hispanic, Latino(a), or Spanish origin ☐ Not Reported ☐ Unknown
Screening Information	
Which newborn screen result indicated this infant was at risk for the disorder?	☐ Initial Screen ☐ Subsequent Screen ☐ Second Required Screen
Was prenatal testing done that indicated that this infant was at risk for this disorder?	☐ Yes ☐ No ☐ Unknown
Was there family history that indicated that this infant was at risk for this disorder?	☐ Yes ☐ No

	☐ Unknown
Was this individual identified outside of the newborn screening?	☐ Yes ☐ No ☐ Unknown
What was the reason the infant was missed? (IF diagnosed later in life=Yes)	☐ Parental Refusal ☐ Lost to follow-up after unsatisfactory specimen ☐ Biologic false negative/result within normal range ☐ Did not have valid screen due to error ☐ Other (please describe below)
Initial & Subsequent Specimen Collection Information	
Specimen Collection	
Date of specimen collection (mm/dd/yyyy)?	
Time (hh:mm AM/PM)	
Time Elapsed Since Birth (in hours)	*Automatically calculated from birth and specimen collection dates; some states can enter directly*
Receipt by Lab	
Date of receipt by lab (mm/dd/yyyy)?	
Time (hh:mm AM/PM)	
Time Elapsed Since Birth (in days)	*Automatically calculated from birth and receipt date; some states can enter directly*
Release of Out-of-Range Results	
Date of release of out-of-range results (mm/dd/yyyy)?	
Time (hh:mm AM/PM)	
Time Elapsed Since Birth (in days)	*Automatically calculated from birth and report date; some states can enter directly*
Intervention, Follow-up, and Diagnosis	
Intervention by Appropriate Medical Provider	
Date of intervention by appropriate medical provider (mm/dd/yyyy)?	
Time (hh:mm AM/PM)	
Time Elapsed Since Birth (in days)	*Automatically calculated from birth and intervention date; some states can enter directly*
Confirmation of Diagnosis	
Date of confirmation of diagnosis (mm/dd/yyyy)?	

Time (hh:mm AM/PM)	
Time Elapsed Since Birth (in days)	*Automatically calculated from birth and diagnosis date; some states can enter directly*
Is infant receiving treatment/care out-of-state?	☐ Yes; enter where state receives care ☐ No ☐ Unknown
Is this diagnosis reversed (does not refer to the therapeutic interventions to address a condition (i.e., surgery, treatment, therapy, etc.)	☐ Yes; enter Year diagnosis reversed ☐ No ☐ Unknown

Newborn Screening Surveillance Case Definitions:

Case Confirmatory Diagnosis Follow-Up

Developed by the Health Resources and Services Administration (HRSA) and NewSTEPs in cooperation with the newborn screening medical sub-specialty community, standard surveillance case definitions for newborn screening conditions allow for determination of true prevalence and incidence of disorders, and for comparison of outcomes across states. The case definition forms can be found in the pages to follow, stratified by disorder type. Additionally, you can find case definition classification tables linked here that can be used as a reference resource.

Table of Contents

Note: standard surveillance case definitions have not been developed for 3-Hydroxy-3-methyglutaric aciduria (HMG), ß-Ketothiolase deficiency (ßKT), Mucopolysaccharidosis Type II, Guanidinoacetate methyltransferase deficiency (GAMT) and Infantile Krabbe Disease (Krabbe). These are forthcoming.

Metabolic Disorders

Organic Acid Disorders

Glutaric Acidemia/ Aciduria Type I (GA1)

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 3-OH Glutaric acid level ☐ Elevated ☐ Normal ☐ Unknown Was Glutaric acid level ☐ Elevated ☐ Normal ☐ Unknown
Were serum organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 3-OH Glutaric acid level ☐ Elevated ☐ Normal ☐ Unknown Was Glutaric acid level ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C5 -DC level ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for Glutaric Acidemia enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	

Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *GCDH* ☐ Other gene:_____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Holocarboxylase Synthetase (Multiple Carboxylase) Deficiency (MCD) or Other Biotin Disorders

**Not Biotindase Deficiency*

Final Diagnosis as determined by clinician performing follow-up:

- ☐ Holocarboxyase Synthetase Deficiency (MCD)
- ☐ Maternal 3-methylcrotonyl-CoA carboxylase deficiency
- ☐ MT-ATP6 related mitochondrial disorders
- ☐ Other Biotin Disorder (not biotindase deficiency)
- ☐ Unknown

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 3OH Isovaleric acid level: ☐ Elevated ☐ Normal ☐ Unknown Was 3OH Propionic acid level: ☐ Elevated ☐ Normal ☐ Unknown Was 3-methylcrotonyl glycine level: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C3 level ☐ Elevated ☐ Normal ☐ Unknown Was C5-OH level ☐ Elevated ☐ Normal ☐ Unknown

Were infant chemistries (biotinidase) studies completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were infant chemistries (biotinidase) studies: ☐ Normal ☐ Abnormal ☐ Unknown

Was enzyme analysis for holocarboxylase synthetase deficiency enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *HLCS* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Isovaleric Acidemia/ Aciduria (IVA)

Final Diagnosis as determined by clinician performing follow-up:

- ☐ Isovaleric Acidemia/ Aciduria (IVA)
- ☐ Short/branched chain acyl-CoA dehydrogenase Deficiency (SBCAD) or 2-methylbutyrl CoA dehydrogenase deficiency
- ☐ Unknown

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 3OH Isovaleric acid level ☐ Elevated ☐ Normal ☐ Unknown Was Isovaleryl glycine level ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C5 -DC level ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for Glutaric Acidemia enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *IVD* ☐ Other gene:_____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

3-Methylcrotonyl-CoA Carboxylase Deficiency (3-MCC)

Final Diagnosis as determined by clinician performing follow-up:

- ☐ 3-Methylcrotonyl-CoA Carboxylase Deficiency (3-MCC)
- ☐ Maternal MCC deficiency
- ☐ MT-ATP6 related mitochondrial disorders
- ☐ Unknown

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 3OH Isovaleric acid level ☐ Elevated ☐ Normal ☐ Unknown Was 3-methylcrotonyl glycine level ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C5 -OH level ☐ Elevated ☐ Normal ☐ Unknown
Was maternal 3-MCC level tested and ruled out? ☐ Yes ☐ No ☐ Unknown	
Was enzyme analysis for 3-MCC enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *MCCC1* ☐ *MCCC2* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Propionic Acidemia/ Aciduria (PROP)

Final Diagnosis as determined by clinician performing follow-up:

- ☐ Propionic Acidemia (PROP)
- ☐ Maternal vitamin B12 deficiency
- ☐ Succinate-CoA ligase deficiency
- ☐ Unknown

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Please indicate which of the following metabolites were detected: Propionyl glycine? ☐ Yes ☐ No ☐ Unknown Tiglyglycine? ☐ Yes ☐ No ☐ Unknown Methylcitrate? ☐ Yes ☐ No ☐ Unknown 3OH Propionic acid level? ☐ Yes ☐ No ☐ Unknown MMA? ☐ Yes ☐ No ☐ Unknown Methylcrotonyl glycine? ☐ Yes ☐ No ☐ Unknown

Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C3 level: ☐ Elevated ☐ Normal ☐ Unknown

Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *PCCA* ☐ *PCCB* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Methylmalonic Acidemia (methylmalonyl-CoA mutase; MUT)

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Mutase(-) (mut-)
- ☐ Mutase (0) (mut0)
- ☐ Maternal vitamin B12 deficiency
- ☐ Succinate-CoA ligase deficiency
- ☐ Unknown

Enzymatic	
Was serum MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in serum: ☐ Elevated ☐ Normal ☐ Unknown
Was urine MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in urine: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C3 level ☐ Elevated ☐ Normal ☐ Unknown
Was maternal vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was maternal vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown
Was infant vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was infant vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown
Was total plasma homocysteine tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was total plasma homocysteine: ☐ Elevated ☐ Normal ☐ Unknown

Were enzyme complementation studies completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were complementation studies: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *METHYLMALONYL-CoA MUTASE* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Methylmalonic Acidemia (cobalamin disorders; Cbl A, Cbl B, Cbl Dv2)

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Cobalamin A deficiency (Cbl A)
- ☐ Cobalamin B deficiency (Cbl B)
- ☐ Cobalamin Dv2 deficiency (Cbl Dv2)
- ☐ Maternal vitamin B12 deficiency
- ☐ Succinate-CoA ligase deficiency
- ☐ Unknown

Enzymatic	
Was serum MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in serum: ☐ Elevated ☐ Normal ☐ Unknown
Was urine MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in urine: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C3 level ☐ Elevated ☐ Normal ☐ Unknown
Was maternal vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was maternal vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown
Was infant vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was infant vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown
Was total plasma homocysteine tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was total plasma homocysteine: ☐ Elevated ☐ Normal ☐ Unknown

Were enzyme complementation studies completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were complementation studies: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *MMAA gene* ☐ *MMAB gene* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Methylmalonic Acidemia with Homocystinuria (Cbl C, Cbl D, Cbl F, Cbl Dv1, Cbl J)

**Secondary RUSP Condition*

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Cobalamin C deficiency (Cbl C)
- ☐ Cobalamin D deficiency (Cbl D)
- ☐ Cobalamin F deficiency (Cbl F)
- ☐ Cobalamin Dv1 deficiency (Cbl Dv1)
- ☐ Cobalamin J deficiency (Cbl J)
- ☐ Maternal vitamin B12 deficiency
- ☐ Succinate-CoA ligase deficiency
- ☐ Other cobalamin deficiency
- ☐ Unknown

Enzymatic	
Was serum MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in serum: ☐ Elevated ☐ Normal ☐ Unknown
Was urine MMA level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was MMA level in urine: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C3 level ☐ Elevated ☐ Normal ☐ Unknown
Was maternal vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was maternal vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown
Was infant vitamin B12 levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was infant vitamin B12 deficient? ☐ Yes ☐ No ☐ Unknown

Was total plasma homocysteine tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was total plasma homocysteine: ☐ Elevated ☐ Normal ☐ Unknown

Were enzyme complementation studies completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were complementation studies: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *MMACHC* ☐ *MMADHC* ☐ *LMBRD1* ☐ *ABCD4* ☐ *HCFC1* ☐ *C2ORF25* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Fatty Acid Disorders

Primary Carnitine Deficiency/ Carnitine Uptake Deficiency (CUD)

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Carnitine Uptake Deficiency (CUD)
- ☐ Maternal Carnitine Deficiency (primary and secondary)
- ☐ Unknown

Enzymatic	
Was urine carnitine tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was fractional excretion of free carnitine level: ☐ Elevated ☐ Normal ☐ Unknown Was 3-methylcrotonyl glycine level ☐ Elevated ☐ Normal ☐ Unknown
Were plasma carnitine levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was free carnitine (C0) ☐ Low ☐ Normal ☐ Unknown
Were other causes for carnitine loss ruled out? ☐ Yes ☐ No ☐ Unknown	
Was enzyme analysis for carnitine deficiency enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *SCL22A5* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Medium-chain acyl-CoA Dehydrogenase Deficiency (MCAD)

Enzymatic	
Were urine organic acids or aclyglycines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Hexanoylglycine level: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C8 level: ☐ Elevated ☐ Normal ☐ Unknown Was repeat C8 level: ☐ Elevated ☐ Normal ☐ Unknown Was C8>C10 level: ☐ Yes ☐ No ☐ Unknown Was C8>C6 level: ☐ Yes ☐ No ☐ Unknown Was C6 level: ☐ Elevated ☐ Normal ☐ Unknown Was C10 level: ☐ Elevated ☐ Normal ☐ Unknown

Was functional analysis of fatty acid oxidation in cultured fibroblasts performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was functional fibroblast analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Was enzyme analysis for MCAD enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *ACADM* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Trifunctional Protein Deficiency (TFP)

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C12-OH dicarboxylic acid level: ☐ Elevated ☐ Normal ☐ Unknown Was C10-OH dicarboxylic acid level: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C16-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C16:1-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C18-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C18:1-OH level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for TFP enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown

Was functional analysis of fatty acid oxidation in cultured fibroblasts performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was functional fibroblast analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *HADHA* ☐ *HADHB* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Long-chain L-3 Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)

Enzymatic	
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C12-OH dicarboxylic acid level: ☐ Elevated ☐ Normal ☐ Unknown Was C10-OH dicarboxylic acid level: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C16-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C16:1-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C18-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C18:1-OH level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for TFP enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown

Was functional analysis of fatty acid oxidation in cultured fibroblasts performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was functional fibroblast analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *HADHA* ☐ *HADHB* ☐ Other gene: _____
	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Very Long-chain acyl-CoA Dehydrogenase Deficiency (VLCAD)

Enzymatic	
Were plasma acylcarnitines tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was C14:1 level: ☐ Elevated (on more than one sample) ☐ Normal ☐ Unknown Was C14:2-OH level: ☐ Elevated ☐ Normal ☐ Unknown Was C14 level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for VLCAD enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Was functional analysis of fatty acid oxidation in cultured fibroblasts performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was functional fibroblast analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *ACADVL* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Amino Acid Disorders

Argininosuccinic Acidemia/ Aciduria (ASA)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Argininosuccinic Acidemia/ Aciduria (ASA)
- ☐ Pyruvate carboxylase deficiency
- ☐ Unknown

Enzymatic	
Were plasma amino acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was plasma ASA level: ☐ Elevated ☐ Normal ☐ Unknown Was Citrulline level: ☐ Elevated ☐ Normal ☐ Unknown
Were plasma urine acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was urine ASA level? ☐ Elevated ☐ Normal ☐ Unknown Was urine Citrulline level? ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for ASA enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	

Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *ASL* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Citrullinemia, Type I (CIT)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up

- ☐ Citrullinemia, Type I
- ☐ Pyruvate Carboxylase Deficiency
- ☐ Unknown

Enzymatic	
Were plasma amino acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was plasma ASA level: ☐ Present ☐ Absent ☐ Unknown Was Citrulline level: ☐ Elevated ☐ Normal ☐ Unknown
Was blood ammonia levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was blood ammonia level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for Citrullinemia type 1 enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *ASS1* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Classic Phenylketonuria (PKU) and Hyperphenylalaninemia (Hyperphe)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Classic phenylketonuria (PKU)
- ☐ Benign hyperphenylalaninemia (H-PHE)
- ☐ HyperPhe diet controlled
- ☐ Dihydropterine reductase deficiency (DHPR)
- ☐ DNAJC12
- ☐ Parenteral nutrition
- ☐ Maternal PKU
- ☐ Unknown

Enzymatic	
Were plasma amino acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Phe level: ☐ Elevated (>120umol/L on unrestricted diet) ☐ Normal ☐ Unknown Was Phe/Tyr level: ☐ Elevated ☐ Normal ☐ Unknown
Were biopterin studies done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were biopterin studies: ☐ Normal ☐ Abnormal ☐ Unknown
Was enzyme analysis for Hyperphe (inclusive of classic PKU) enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *PAH* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Homocystinuria (Cystathionine Beta-Synthase (CBS) Deficiency; HCY)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Classic Homocystinuria
- ☐ Methionine Adenosyltransferase (MAT I/III Deficiency)
- ☐ Glycine n-methyltransferase (GNMT)
- ☐ Adenosylhomocysteine Hydrolase Deficiency
- ☐ Unknown

Enzymatic	
Were plasma amino acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Methionine level: ☐ Elevated ☐ Normal ☐ Unknown
Was plasma Homocysteine tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was plasma Homocysteine level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for CBS enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *CBS* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Maple Syrup Urine Disease (MSUD)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Maple Syrup Urine Disease, Type IA
- ☐ Maple Syrup Urine Disease, Type IB
- ☐ Maple Syrup Urine Disease, Type II
- ☐ Maple Syrup Urine Disease, Type III
- ☐ Hydroxyprolinemia
- ☐ Unknown

Enzymatic	
Were plasma amino acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Alloisoleucine level: ☐ Elevated ☐ Normal ☐ Unknown Was Leucine level: ☐ Elevated ☐ Normal ☐ Unknown Was Isoleucine level: ☐ Elevated ☐ Normal ☐ Unknown Was Valine level: ☐ Elevated ☐ Normal ☐ Unknown Was Leu>Val level: ☐ Yes ☐ No ☐ Unknown

Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was 2-ketoisocaproic acid level: ☐ Elevated ☐ Normal ☐ Unknown Was 2-OH Isovaleric acid level: ☐ Elevated ☐ Normal ☐ Unknown Was 2-ketomethyl valeric acid level ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for MSUD enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	
Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *DBT* ☐ *BCKDHB* ☐ *DLD* ☐ *BCKDHA* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Tyrosinemia Type I (TYR-1)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Tyrosinemia, Type I (hepatorenal)
- ☐ Transient Tyrosinemia of the neonate (TTN)
- ☐ Unknown

Enzymatic	
Were plasma organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was plasma succinylacetone level: ☐ Elevated ☐ Normal ☐ Unknown Was plasma tyrosine level: ☐ Elevated ☐ Normal ☐ Unknown
Were urine organic acids tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was urine succinylacetone level: ☐ Elevated ☐ Normal ☐ Unknown Was urine tyrosine level: ☐ Elevated ☐ Normal ☐ Unknown
Was enzyme analysis for fumarylacetoacetate hydrolase completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme analysis: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	

Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *FAH* ☐ Other gene: _____

	[For each gene selected] Check the types of variants found on: *Allele 1:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Endocrine Disorders

Congenital Hypothyroidism (CH)

Final Diagnosis as determined by clinician performing follow-up:

- ☐ Primary Congenital Hypothyroidism
- ☐ Secondary Congenital Hypothyroidism
- ☐ TBG Deficiency (Thyroxine Binding Globulin) or other protein binding defect
- ☐ Transient Congenital Hypothyroidism
- ☐ Unknown

Enzymatic	
Was Serum TSH tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the level: ☐ TSH > 10 mU/L ☐ TSH 6-10 mU/L ☐ TSH <10 mU/L ☐ TSH <6 mU/L ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No ☐ Unknown
Was Serum Total T4 tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Serum Total T4 below the age-established reference range? ☐ Yes ☐ No ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No ☐ Unknown

Was Serum Free T4 tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Serum Free T4 below the age-established reference range? ☐ Yes ☐ No ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No ☐ Unknown
Does this baby have other pituitary hormone deficiencies? ☐ Yes ☐ No ☐ Unknown	
Does this baby have midline defects? ☐ Yes ☐ No ☐ Unknown	
Was TBG tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was TBG below the age established reference range? ☐ Yes ☐ No ☐ Unknown
Was T3 or T4 resin uptake tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was T3 or T4 resin uptake above the age-established reference range? ☐ Yes ☐ No ☐ Unknown

Congenital Adrenal Hyperplasia (CAH)

Final Diagnosis as determined by clinician performing follow-up:

- ☐ Classic 21-Hydroxylase Deficiency-Salt Wasting
- ☐ Classic 21-Hydroxylase Deficiency-Simple Virilizing
- ☐ Other Adrenal disorder: other final diagnosis name _____
- ☐ Unknown

Enzymatic	
Societal Sex ☐ Male ☐ Female ☐ Unknown ☐ Unspecified	
Was confirmatory serum 17-OHP level obtained? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was there a value at baseline: ☐ >10,000 ng/dl ☐ 1000-10,000 ng/dl; ☐ < 1000 ng/dl; ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No Was there a result after ACTH stimulation: ☐ >10,000 ng/dl ☐ 1000-10,000 ng/dl; ☐ < 1000 ng/dl; ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No
Was tandem mass spectrometry urinary steroid profile obtained? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Were the urinary spectrometry steroid profile results: ☐ Indicative of 21-Hydroxylase Deficiency CAH ☐ Unknown

Was serum sodium level measured before initiation of treatment? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was the sodium level: ☐ < 135 mEq/L ☐ > 135 mEq/L ☐ Unknown
Was plasma renin activity level measured at time of initiation of treatment? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was plasma renin activity normal for age? ☐ Yes ☐ No ☐ Unknown Was it tested before initiation of treatment? ☐ Yes ☐ No
Clinical Results	
Is there evidence of salt wasting (e.g., shock or severe failure to thrive)? ☐ Yes ☐ No ☐ Unknown	
Is there supportive clinical or laboratory evidence of CAH? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Is the evidence (check all that apply): ☐ Ambiguous genitalia, with 46 XX karyotype ☐ Normal genitalia, with 46 XY karyotype ☐ Other hormonal evidence of CAH
Molecular Genetics	
Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *CYP21A2* ☐ Other gene:_____

	[For each gene selected] Check the types of variants found on: *Allele 1* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Hemoglobinopathies

Presence of Hb S

Final diagnosis as determined by a clinician performing the follow-up:

- ☐ S, Beta 0-thalassemia – HB S/B0Th
- ☐ S,S Disease (Sickle Cell Anemia) – HbSS
- ☐ S, Beta + Thalassemia – HbS/B + Th
- ☐ S,C Disease – Hb S/C
- ☐ S, Other; other result name _____
- ☐ Unknown

Diagnostic Workup	
Was qualitative (IEF or HPLC) testing completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FS ☐ FSC ☐ FSA ☐ FSA_2 ☐ $FSAA_2$ ☐ Other; other result name_____ ☐ Unknown
Was quantitative (HPLC or electrophoresis) testing completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FS ☐ FSC ☐ FS with high A_2 ☐ FSA with high A_2 ☐ FSA ☐ Other; other result name_____ ☐ Unknown

Was mutation analysis performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Check the type of variant found on: *Allele 1* ☐ *S* ☐ *C* ☐ *Beta + Thal* ☐ *Beta^0 + Thal* ☐ Other; _____ ☐ Unknown *Allele 2* ☐ *S* ☐ *C* ☐ *Beta + Thal* ☐ *Beta^0 + Thal* ☐ Other; other name_____ ☐ Unknown
NBS result ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FS ☐ FSC ☐ FSA ☐ FSA_2 ☐ Other ☐ Unknown
Was a CBC performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ Normal – high MCV ☐ Low MCV ☐ Unknown

Were family studies (in parents) done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Maternal Status: what were the results? ☐ Carrier *S* ☐ Carrier *C* ☐ Carrier *Beta + Thal* ☐ Carrier *Beta^0 Thal* ☐ Other: _____ ☐ Unknown Paternal Status: what were the results? ☐ Carrier *S* ☐ Carrier *C* ☐ Carrier *Beta + Thal* ☐ Carrier *Beta^0 Thal* ☐ Other: _____ ☐ Unknown
Was there a positive family history? ☐ Yes ☐ No ☐ Unknown	
Were HPLC & IEF tested on the same sample from the infant? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FS ☐ FSC ☐ FSA_2 ☐ $FSAA_2$ ☐ Other ☐ Unknown
Were Hgb tests (electrophoresis or HPLC) performed on family members? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ Positive ☐ Negative ☐ Unknown

Presence of Other Hb Variant

**This is a Secondary RUSP Condition*

Final diagnosis as determined by a clinician performing the follow-up:

- ☐ Hemoglobin C Disease
- ☐ Hemoglobin D Disease
- ☐ Hemoglobin E Disease
- ☐ Hemoglobin O-Arab Disease
- ☐ Other Hemoglobin Disease; please describe
- ☐ Unknown

Diagnostic Workup	
Alpha thalassemia present? ☐ Yes ☐ No ☐ Unknown	
Was qualitative (IEF or HPLC) testing completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FC ☐ FD ☐ FE ☐ FO_{ARAB} ☐ Other; other result name_____ ☐ Unknown
Was quantitative (HPLC or electrophoresis) testing completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FC ☐ FD ☐ FE ☐ FO_{ARAB} ☐ Other; other result name_____ ☐ Unknown

Was mutation analysis performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Check the type of variant found on allele 1: ☐ *C* ☐ *D* ☐ *E* ☐ O_{ARAB} ☐ Other; other name_____ ☐ Unknown Check the type of variant found on allele 2: ☐ *C* ☐ *D* ☐ *E* ☐ O_{ARAB} ☐ *Beta + Thal* ☐ $Beta^{0}$ *+ Thal* ☐ Other; other name_____ ☐ Unknown
NBS result ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ FC ☐ FD ☐ FE ☐ FO_{ARAB} ☐ Other; other result name_____ ☐ Unknown
Was a CBC performed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ Normal – high MCV ☐ Low MCV

Were family studies (in parents) done? ☐ Yes ☐ No ☐ Unknown	Maternal Status: what were the results? ☐ Carrier *C* ☐ Carrier *D* ☐ Carrier *E* ☐ Carrier O_{Arab} ☐ Carrier *Beta + Thal* ☐ Carrier $Beta^0$ *Thal* ☐ Other: _____ ☐ Unknown Paternal Status: what were the results? ☐ Carrier *C* ☐ Carrier *D* ☐ Carrier *E* ☐ Carrier O_{Arab} ☐ Carrier *Beta + Thal* ☐ Carrier $Beta^0$ *Thal* ☐ Other: _____ ☐ Unknown
Was there a positive family history? ☐ Yes ☐ No ☐ Unknown	
Were Hgb tests (electrophoresis or HPLC) performed on family members? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the results? ☐ Positive ☐ Negative ☐ Unknown

Lysosomal Storage Disorders

Note: Case Confirmatory Diagnosis Follow-up for Mucopolysaccharidosis Type II (MPS II) is in development

Mucopolysaccharidosis Type I (MPS I)

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ MPS I—Severe
- ☐ MPS I—Severity not determined
- ☐ MPS I—attenuated
- ☐ Uncertain Type/Onset
- ☐ Unknown

Enzymatic	
Was enzyme activity tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the enzyme level? ☐ Within lab known affected range ☐ Normal ☐ Unknown
Were urine GAGS tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the urine GAG level? ☐ Elevated ☐ Normal ☐ Unknown

Clinical symptoms/lab findings? ☐ Symptoms present and documented by specialists. Public health (PH) program continued to collect data through the development of symptoms ☐ No symptoms by the time the PH Program closes follow-up (either due to child being lost to follow-up OR program policy on follow-up time ☐ Unknown	*Clinical symptoms consistent with MPS-I include: Hepatosplenomegaly, Coarse facial features, Hydrocephalus, Skeletal deformities (dysostosis multiplex), Corneal clouding, Large tongue, Prominent forehead, Joint stiffness, Short stature, frequent ear infections and hearing loss, hernia*

Molecular Genetics	
Were variants detected in genes known to be associated with MPS I? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Check the types of variants found on: *Allele 1:* ☐ Pathogenic variant and associated with SEVERE disease ☐ Pathogenic or likely pathogenic variant ☐ Variant of unknown significance ☐ Variant known to be associated with ATTENUATED disease. ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Pathogenic variant and associated with SEVERE disease ☐ Pathogenic or likely pathogenic variant ☐ Variant of unknown significance ☐ Variant known to be associated with ATTENUATED disease. ☐ Wild Type (Normal) ☐ Unknown

Pompe Disease

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Infantile Onset (IO) Pompe Disease
- ☐ Late Onset (LO) Pompe Disease
- ☐ Uncertain Type/Onset
- ☐ Unknown

Enzymatic	
Was enzyme activity tested in blood (not DBS sample)? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the enzyme level? ☐ Within lab known affected range for infantile onset (IO) ☐ Low (above affected range, for IO, may or may not be in late-onset (LO range), but should not be above LO range)) ☐ Within lab known affected range for late onset (LO) ☐ Low (above affected range, for LO not normal) ☐ Unknown
Was enzyme activity tested in skin/muscle? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the enzyme activity? ☐ Positive skin or muscle biopsy ☐ Unknown
Was there cardiac involvement consistent with Pompe? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Findings: ☐ Positive findings on chest X-ray/EKG/ECHO in newborn period ☐ Positive findings on chest X-ray/EKG/ECHO
Lab findings for CK/AST/ALT/LDH/Urine Hex4? ☐ Elevated ☐ Not Present ☐ Unknown ☐ Untested	

Were there any clinical findings? ☐ Symptoms present after one year of age and documented by specialists. PH program continue to collect data through the development of symptoms ☐ Symptoms present before one year of age, but no cardiac involvement ☐ Unknown or not reported to PH by the end of the follow-up period	*Clinical symptoms consistent with Pompe Disease: progressive muscle weakness, need for respiratory assistance, swaying gait or waddle, Lordosis, kyphosis, or scoliosis*
Molecular Genetics	

Were variants detected in genes known to be associated with Pompe Disease? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Check the types of variants found on: *Allele 1:* ☐ Pathogenic ☐ Pathogenic variant and associated with infantile onset ☐ Novel variant that is likely pathogenic ☐ Pathogenic variant or likely pathogenic variant, with deletion or duplication consistent with infantile onset ☐ Pathogenic and associated with non-classical disease, or variant of uncertain significance ☐ Pathogenic or likely pathogenic variant, no other variants found; duplication/deletion testing not done or not known ☐ Pathogenic or likely pathogenic variant; no other variants found ☐ Wild Type (Normal) ☐ Unknown *Allele 2:* ☐ Pathogenic ☐ Pathogenic variant and associated with infantile onset ☐ Novel variant that is likely pathogenic ☐ Pathogenic variant or likely pathogenic variant, with deletion or duplication consistent with infantile onset ☐ Pathogenic and associated with non-classical disease, or variant of uncertain significance ☐ Pathogenic or likely pathogenic variant, no other variants found; duplication/deletion testing not done or not known ☐ Pathogenic or likely pathogenic variant; no other variants found ☐ Wild Type (Normal) ☐ Unknown

Other Disorders

Biotinidase Deficiency (BIOT)

Final Diagnosis as determined by metabolic geneticist or clinician performing follow-up:

- ☐ Profound Biotinidase deficiency
- ☐ Partial Biotinidase deficiency
- ☐ Unknown

Enzymatic	
Was enzyme analysis for biotinidase enzyme activity completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was enzyme activity: ☐ <10% ☐ 10-30% ☐ Normal ☐ Unknown
Molecular Genetics	
Was a mutation analysis performed for biotinidase deficiency? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ BTD ☐ Other gene:_____
	[For all genes selected] **Check the types of variants found on:** *Allele 1:* ☐ Variant known to be disease causing (Unknown) ☐ Variant known to be disease causing (known to be associated with profound enzyme deficiency) ☐ Variant known to be disease causing (known to be associated with partial enzyme deficiency [“mild” mutation (D44H)] ☐ Variant of unknown significance ☐ Wild Type (Normal) ☐ Unknown *Allele 2* ☐ Variant known to be disease causing (Unknown) ☐ Variant known to be disease causing (known to be associated with profound enzyme deficiency) ☐ Variant known to be disease causing (known to be associated with partial enzyme deficiency [“mild” mutation (D44H)] ☐ Variant of unknown significance ☐ Wild Type (Normal) ☐ Unknown

Galactosemia (GALT)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ Classic Galactosemia
- ☐ Duarte variant galactosemia
- ☐ Unknown

Enzymatic	
Were GALT levels tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was GALT level: ☐ <10% ☐ 10-30% ☐ Normal ☐ Unknown
Was Gal-1-P tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Gal-1-P level: ☐ Elevated ☐ Normal ☐ Unknown
Was Urine Galactitol tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Was Urine Galactitol level: ☐ Elevated ☐ Normal ☐ Unknown
If Variant Galactosemia, was protein phenotyping completed? ☐ Yes ☐ No ☐ Unknown ☐ Not applicable	*[IF YES]* Did result indicate: ☐ Phenotype consistent with variant ☐ Phenotype NOT consistent with variant ☐ Unknown
If Arginase Deficiency, were enzyme studies completed? ☐ Yes ☐ No ☐ Unknown ☐ Not applicable	*[IF YES]* Was enzyme activity: ☐ Consistent with disease ☐ Normal activity (not consistent with disease) ☐ Unknown
Molecular Genetics	

Was a mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ Galactosemia ☐ Other gene:_____

	[For each gene selected] **Check the types of variants found on:** *Allele 1* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown *Allele 2* ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (Normal) ☐ Unknown

Cystic Fibrosis

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ CFTR-Related Metabolic Syndrome (CRMS)
- ☐ CFTR-Related Disease
- ☐ Typical Cystic Fibrosis (CF)
- ☐ Unknown

Diagnostic Workup	
Did the NBS result indicate an elevated IRT? ☐ Yes ☐ No ☐ Unknown	
Were CFTR mutations detected on the <u>newborn screening</u> mutation panel? ☐ Yes ☐ No ☐ Unknown *Mutations seen in patients with CF have been classified as disease-causing, neutral, or varying clinical consequences through the CFTR2 project: http://cftr2.org/browse.php. Additional information about the mutation and the association with lower sweat chlorides can also be found at CFTR2.*	*[IF YES]* *Check the type of variant found on allele 1:* ☐ Variant known to be disease causing in CFTR2 ☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides) ☐ Neutral variant ☐ Variant of varying clinical consequence in CFTR2 ☐ Wild Type (Normal) ☐ Unknown (not reported in CFTR2) *Check the type of variant found on allele 1:* ☐ Varian known to be disease causing in CFTR2 ☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides) ☐ Neutral variant ☐ Variant of varying clinical consequence in CFTR2 ☐ Wild Type (Normal) ☐ Unknown (not reported in CFTR2)
Did the child have meconium ileus? ☐ Yes ☐ No ☐ Unknown	

Was a valid sweat chloride result available? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the sweat test results (please report on the highest sweat chloride value from one sweat test)? ☐ ≥60 mmol/L (regardless of age) ☐ <30 mmol/L (if age <6 months) ☐ 30-59 mmol/L (if age < 6 months) ☐ <40mmol/L (if age ≥6 months) ☐ 40-59 mmol/L (if age ≥6 months) ☐ Quantity not Sufficient *[IF NO]* If a valid sweat test was not available, were there attempts to obtain a sweat chloride that were quantity not sufficient (QNS)? ☐ Yes ☐ No ☐ Unknown
Was a sweat chloride repeated on a separate day? *(Results from different arm on the same day should NOT be reported here)* ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What were the repeat sweat test results (please report on the highest sweat chloride value from one sweat test)? ☐ ≥60 mmol/L (regardless of age) ☐ <30 mmol/L (if age <6 months) ☐ 30-59 mmol/L (if age < 6 months) ☐ <40mmol/L (if age ≥6 months) ☐ 40-59 mmol/L (if age ≥6 months) ☐ Quantity not sufficient (QNS)

Was a CFTR mutation panel completed <u>after</u> the newborn screening mutation panel? ☐ Yes ☐ No ☐ Unknown *Mutations seen in patients with CF have been classified as disease-causing, neutral, or varying clinical consequences through the CFTR2 project: http://cftr2.org/browse.php. Additional information about the mutation and the association with lower sweat chlorides can also be found at CFTR2.*	*[IF YES]* *Check the type of variant found on allele 1:* ☐ Variant known to be disease causing in CFTR2 ☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides) ☐ Neutral variant ☐ Variant of varying clinical consequence in CFTR2 ☐ Wild Type (Normal) ☐ Unknown (not reported in CFTR2) *Check the type of variant found on allele 2:* ☐ Variant known to be disease causing in CFTR2 ☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides) ☐ Neutral variant ☐ Variant of varying clinical consequence in CFTR2 ☐ Wild Type (Normal) ☐ Unknown (not reported in CFTR2)
If the child was diagnosed after the newborn period, were clinical symptoms associated with CFTR Related Disease present? *Select NA if the child was diagnosed during the newborn period.* ☐ Present ☐ Not Present ☐ Unknown ☐ Not applicable	*[IF PRESENT]* Select all symptoms included: ☐ CBAVD ☐ Recurrent pancreatitis ☐ Nasal polyposis ☐ Infertility ☐ Focal biliary cirrhosis with portal hypertension

Summary of common variants as reported on CFTR2 (this is not an exhaustive list; please visit www.CFTR2.org for the latest updated list).

Variant name - HGVS nomenclature	Protein name	Variant legacy name	On ACMG Screening Panel	CFTR2 final call	Associated with lower sweat chloride
c.3717+12191C>T	p.Phe316LeufsX12	**1078delT**	No	CF-causing	NO
c.579+3A>G	p.Phe342HisfsX28	**1154insTC**	No	CF-causing	NO
c.3454G>C	No protein name	**1717-1G->A**	Yes	CF-causing	NO
c.3208C>T	No protein name	**1811+1.6kbA->G**	No	CF-causing	NO
c.3154T>G	No protein name	**1898+1G->A**	Yes	CF-causing	NO
c.1585-1G>A	p.Leu671X	**2143delT**	No	CF-causing	NO
c.1680-1G>A	p.Lys684SerfsX38	**2183AA->G**	No	CF-causing	NO
c.1766+1G>A	p.Lys684AsnfsX38	**2184delA**	Yes	CF-causing	NO
c.2490+1G>A	p.Gln685ThrfsX4	**2184insA**	No	CF-causing	NO
c.2988+1G>A	p.Glu726ArgfsX4	**2307insA**	No	CF-causing	NO
c.1736A>G	No protein name	**2789+5G->A**	Yes	CF-causing	NO
c.1408A>G	No protein name	**3120+1G->A**	Yes	CF-causing	NO
c.1841A>G	No protein name	**3120G->A**	No	CF-causing	NO
c.2991G>C	No protein name	**3272-26A->G**	No	CF-causing	NO
c.489+1G>T	p.Lys1177SerfsX15	**3659delC**	Yes	CF-causing	NO
c.350G>A	No protein name	**3849+10kbC->T**	Yes	CF-causing	NO
c.4242+1G>T	p.Leu1258PhefsX7	**3905insT**	No	CF-causing	NO
c.3718-1G>A	p.Leu88IlefsX22	**394delTT**	No	CF-causing	NO
c.1240C>T	No protein name	**5T**	No	Indeterminate	YES
c.2260G>A	No protein name	**621+1G->T**	Yes	CF-causing	NO
c.1727G>C	No protein name	**711+1G->T**	Yes	CF-causing	NO
c.220C>T	No protein name	**711+5G->A**	No	CF-causing	NO
c.2834C>T	p.Ala455Glu	**A455E**	Yes	CF-causing	NO
c.1675G>A	p.Ala559Thr	**A559T**	No	CF-causing	NO
c.1127_1128insA	p.Ser18ArgfsX16	**CFTRdele2,3**	No	CF-causing	NO
c.1202G>A or c.1203G>A	p.Asp1152His	**D1152H**	No	Indeterminate	YES
c.1923_1931del9insA	p.Glu60X	**E60X**	No	CF-causing	NO
c.1679G>C	p.Phe508del	**F508del**	Yes	CF-causing	NO
c.3160C>G	p.Gly1244Glu	**G1244E**	No	CF-causing	NO
c.4046G>A	p.Gly178Glu	**G178R**	No	CF-causing	NO
c.4196_4197delTC	p.Gly542X	**G542X**	Yes	CF-causing	NO
c.3731G>A	p.Gly551Asp	**G551D**	Yes	CF-causing	NO
c.3197G>A	p.Gly85Glu	**G85E**	Yes	CF-causing	NO
c.2657+2_2657+3insA	p.Ile1027Thr	**I1027T**	No	Not CF-causing	NO
c.1673T>C	p.Ile148Thr	**I148T**	No	Not CF-causing	NO

c.3763T>C	p.Ile336Lys	**I336K**	No	CF-causing	NO
c.1558G>T	p.Ile507del	**I507del**	Yes	CF-causing	NO
c.3230T>C	p.Leu1077Pro	**L1077P**	No	CF-causing	NO
c.1040G>A	p.Leu206Trp	**L206W**	No	CF-causing	NO
c.3302T>A	p.Met1101Lys	**M1101K**	No	CF-causing	NO
c.274G>A	p.Asn1303Lys	**N1303K**	Yes	CF-causing	NO
c.617T>G	p.Pro67Leu	**P67L**	No	CF-causing	NO
c.2764_2765insAG	p.Gln220X	**Q220X**	No	CF-causing	NO
c.1973_1985del13insAGAAA	p.Gln493X	**Q493X**	No	CF-causing	NO
c.3196C>T	p.Arg1066Cys	**R1066C**	No	CF-causing	NO
c.4296_4297insGA	p.Arg1158X	**R1158X**	No	CF-causing	NO
c.1692delA	p.Arg1162X	**R1162X**	Yes	CF-causing	NO
c.1055G>A	p.Arg117Cys	**R117C**	No	CF-causing	NO
c.1466C>A	p.Arg117His	**R117H**	Yes	Indeterminate	YES
c.1013C>T	p.Arg334Trp	**R334W**	Yes	CF-causing	NO
c.532G>A	p.Arg347His	**R347H**	Yes	CF-causing	NO
c.1040G>C	p.Arg347Pro	**R347P**	No	CF-causing	NO
c.2908G>C	p.Arg352Gln	**R352Q**	No	CF-causing	NO
c.2424_2425insAT	p.Arg553X	**R553X**	Yes	CF-causing	NO
c.2780T>C	p.Arg560Thr	**R560T**	Yes	CF-causing	NO
c.349C>T	p.Ser1251Asn	**S1251N**	No	CF-causing	NO
c.1000C>T	p.Ser549Asn	**S549N**	No	CF-causing	NO
c.3752G>A	p.Ser945Leu	**S945L**	No	CF-causing	NO
c.1645A>C or c.1647T>G	p.Val520Phe	**V520F**	No	CF-causing	NO
c.274G>T	p.Trp1282X	**W1282X**	Yes	CF-causing	NO
c.2128A>T	p.Tyr1092X	**Y1092X**	No	CF-causing	NO
c.2195T>G	p.Tyr122X	**Y122X**	No	CF-causing	NO

Severe Combined Immunodeficiencies (SCID)

Final diagnosis as determined by a metabolic geneticist or clinician performing follow-up:

- ☐ Classic SCID
- ☐ Leaky SCID
- ☐ Omenn Syndrome
- ☐ Unknown

Diagnostic Workup	
Was the CD3 T cell level tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the CD3 T cell level? ☐ <300 autologous T cells, undetectable or very few naïve T cells ☐ 300-1500, few naïve T cells, oligoclonal T cells, or poor T cell diversity ☐ >80% CD45RO+ ☐ Any number (not zero) ☐ Untested/Unknown
Was proliferation to PHA test done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Proliferation to PHA: ☐ <10% of normal ☐ 10-50% of normal PHA ☐ 10-30% normal PHA or Absent to Candida/TT ☐ <30% of normal ☐ Any/Unknown
Was maternal engraftment documented? ☐ Yes ☐ No ☐ Unknown	
Molecular Genetics	

Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* **Were variants detected in the genes known to be associated with SCID?** ☐ Yes ☐ No ☐ Unknown *[IF YES]* *Check the type of variant found on allele 1:* ☐ Pathogenic variant in a known SCID gene ☐ Pathogenic variant in a known SCID gene on X chromosome in a male ☐ Pathogenic variant in a known SCID gene known to be associated with leaky SCID (previously reported or in a gene previously associated with combined immunodeficiency) ☐ Wild Type (Normal) ☐ Untested/Unknown *Check the type of variant found on allele 2:* ☐ Pathogenic variant in a known SCID gene ☐ Pathogenic variant in a known SCID gene known to be associated with leaky SCID (previously reported or in a gene previously associated with immunodeficiency) ☐ Wild Type (Normal) ☐ Untested/Unknown
	[IF variants detected=YES] **Was *22q1* deletion assessed?** ☐ Yes ☐ No ☐ Unknown
	[IF variants detected=YES] **Were homozygous or compound heterozygous *FOXN1* mutations assessed?** ☐ Yes ☐ No ☐ Unknown

	[IF variants detected=YES] **Were heterozygous *TBX1* variants assessed?** ☐ Yes ☐ No ☐ Unknown

Critical Congenital Heart Disease (CCHD)

What was the final diagnosis?

- ☐ CCHD
- ☐ Non-critical CCHD
- ☐ Other
- ☐ Unknown

Diagnostic Workup	
	[IF CCHD SELECTED] ☐ Truncus Arteriosus ☐ Total Anomalous Pulmonary Venous Connection ☐ Tetralogy of fallot ☐ Pulmonary Atresia ☐ Ebstein's Anomaly ☐ Hypoplastic Left Heart Syndrome ☐ Single ventricle ☐ Tricuspid atresia ☐ Transposition of the great arteries ☐ Double outlet right ventricle ☐ Coarctation of aorta ☐ Interrupted arch ☐ Aortic valve disease If Other selected; please specify_____

Please answer the following:	If Yes, what were the results of the postnatal echocardiogram? *(select all that apply)*
Was a Postnatal Echocardiogram Completed? ☐ Yes ☐ No ☐ Unknown	**Truncus Arteriosus** ☐ Truncus arteriosus ☐ Truncus arteriosus + Interrupted aortic arch **Total Anomalous Pulmonary Venous Connection (TAPVC)** ☐ Type1 (supracardiac) ☐ Type 2 (cardiac) ☐ Type 3 (infracardiac) ☐ Type 4 (mixed)

	Tetralogy of Fallot (TOF) ☐ TOF ☐ TOF, Pulmonary stenosis ☐ TOF, AVCanal (AVSD) ☐ TOF, Absent pulmonary valve

	Pulmonary Artesia ☐ Pulmonary atresia ☐ Pulmonary atresia, IVS ☐ Pulmonary atresia, VSD (Including TOF, PA) ☐ Pulmonary atresia, VSD-MAPCA
	Ebstein's Anomaly ☐ Ebstein's anomaly
	Hypoplastic Left Heart Syndrome (HLHS) ☐ Hypoplastic left heart syndrome
	Single Ventricle ☐ Single ventricle, DILV ☐ Single ventricle, DIRV ☐ Single ventricle, Mitral atresia ☐ Single ventricle, Unbalanced AV canal ☐ Single ventricle, Heterotaxia syndrome ☐ Single ventricle, Other ☐ Single ventricle + Total anomalous pulmonary venous connection (TAPVC)
	Tricuspid Artesia ☐ Single ventricle, Tricuspid atresia
	Transposition of the Great Arteries (TGA) ☐ d-TGA, IVS ☐ d-TGA, IVS-LVOTO ☐ d-TGA, VSD ☐ d-TGA, VSD-LVOTO
	Double Outlet Right Ventricle (DORV) ☐ DORV, VSD type ☐ DORV, TOF type ☐ DORV, TGA type ☐ DORV, Remote VSD (uncommitted VSD) ☐ DORV + AVSD (AV Canal) ☐ DORV, IVS ☐ DORV, Remote VSD (uncommitted VSD)
	Coarctation of Aorta ☐ Coarctation of aorta ☐ Aortic arch hypoplasia ☐ VSD + Aortic arch hypoplasia ☐ VSD + Coarctation of aorta

	Interrupted Arch ☐ Interrupted aortic arch ☐ Interrupted aortic arch + VSD ☐ Interrupted aortic arch + AP window (aortopulmonary window)

	Aortic Valve Disease ☐ Aortic Stenosis receiving intervention in first 30 days of life ☐ Pulmonary Stenosis receiving intervention in the first 30 days of life
Was a Prenatal Echocardiogram Completed? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Did the Prenatal Echo findings suggest CCHD? ☐ Yes ☐ No ☐ Unknown

X-Linked Adrenoleukodystrophy (X-ALD)

Final diagnosis as determined by a metabolic geneticist or clinician performing following-up:

- ☐ X-Linked Adrenoleukodystrophy (in males)
- ☐ Contiguous ABCD1 DXS1357E deletion syndrome (CADDS)
- ☐ X-Linked Adrenoleukodystrophy (in females)
- ☐ Peroxisomal Disorder
- ☐ Acyl-CoA Oxidase Deficiency
- ☐ D-Bifunctional Protein Deficiency
- ☐ Dyamin-like protein 1 (DLP1)
- ☐ ABDC5
- ☐ Non-peroxisomal Disorder
- ☐ Uncertain Type/Onset
- ☐ Unknown

Diagnostic Workup	
Was plasma VLCFA tested? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the VLCFA level? ☐ Elevated ☐ Slightly elevated ☐ Normal ☐ Low ☐ Unknown *"Elevated" signifies in pathogenic range, while "slightly elevated" signifies above normal, but not in the pathogenic range*
Clinical symptoms? ☐ Present ☐ Not present ☐ Not present at birth ☐ Unknown	*Symptoms may include: neonatal hypotonia, neonatal seizures, liver disease, neonatal cholestasis, sensorineural deafness, failure to thrive, craniofacial abnormalities*
Was plasmalogen testing done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Plasmalogen level? ☐ Normal ☐ Low ☐ Unknown

Family History done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Family history results: ☐ Family history present ☐ Family VLCFA studies suggestive of X-linked ALD ☐ Family history not present ☐ Unknown
Were fibroblast studies done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Fibroblast study results: ☐ Consistent with Zellweger Spectrum Disorder ☐ Consistent with Acyl-CoA Oxidase Deficiency ☐ Consistent with D-Bifunctional Protein ☐ Consistent with DLP1 ☐ Consistent with ABCD5 ☐ Unknown
Molecular Genetics	
Was mutation analysis done? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What genes were included in the mutation analysis? (select all that apply) ☐ *ABCD1* ☐ *PEX1* ☐ *ACOX1* ☐ *HSD17B4* ☐ 1 of the 7 known genes for Aicardi-Goutières Syndrome ☐ Other gene
	[IF ABCD1] **Check the type of variations found:** ☐ Pathogenic variant ☐ Deletion/duplication identified ☐ No mutation on sequencing, deletion/duplication not done ☐ No mutation on sequencing, deletion/duplication not toned; rule out other disorders of peroxisomal beta oxidation ☐ Variant of unknown significance ☐ Deletion identified in ABCD1 and DXS1357 ☐ Unknown

	[IF PEX1] **Check the type of variations found on:** **Allele 1** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown **Allele 2** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown
	[IF ACOX1] **Check the type of variations found on:** **Allele 1** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown **Allele 2** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown

	*[IF HSD17b4]***Check the type of variations found on:** **Allele 1** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown **Allele 2** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown
	[IF 1 of the 7 known genes for Aicardi-Goutières Syndrome] **Check the type of variations found on:** **Allele 1** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown **Allele 2** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown

	[IF Other Gene Selected] **Other Gene Name**;_____ **Check the type of variations found on:** **Allele 1** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown **Allele 2** ☐ Variant known to be disease causing ☐ Variant of unknown significance ☐ Variant of unknown significance (predicted to be pathogenic) ☐ Wild Type (normal) ☐ Unknown

Spinal Muscular Atrophy (SMA)

Diagnostic Workup	
Newborn Screen Molecular Test for SMN1? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the result? ☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* ☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* - observed on two independently collected NBS specimens ☐ 2 pathogenic variants ☐ 2 pathogenic variants observed on two independently collected NBS specimens ☐ 1 pathogenic variant and 1 variant of unknown significance ☐ 2 variants of unknown significance ☐ Unknown/ Not Done/Screen Negative ** true deletion of exon 7 (or larger) or for which there has been a gene conversion of exon 7 (or*
Newborn Screen Molecular Test for SMN2? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* SMN2 Copy Number? ☐ One ☐ Two ☐ Two or more ☐ Unknown/Not Done
Post-Newborn Screen Molecular Test for SMN1? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the result? ☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* ☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* - observed on two independently collected specimens ☐ 2 pathogenic variants ☐ 2 pathogenic variants observed on two independently collected specimens ☐ 1 pathogenic variant and 1 variant of unknown significance ☐ 2 variants of unknown significance ☐ Unknown/ Not Done/Screen Negative ** true deletion of exon 7 (or larger) or for which there has been a gene conversion of exon 7 (or more)*

Post-Newborn Screen Molecular Test for SMN2? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* *SMN2* Copy Number? ☐ One ☐ Two ☐ Two or more ☐ Unknown/Not Done
Parental Molecular Testing Family History/Parental Genetic Testing? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* What was the result? ☐ Phasing is complete and confirms that variants are in trans or both parents are known to be carriers of the pathogenic variants identified ☐ Both parents are known carriers of *SMN1* deletion ☐ Unknown/Not Done
Clinical symptoms? ☐ Present ☐ Not present ☐ Unknown	*Symptoms may include: Electromyography evidence of motor neuron disease, Absent reflexes, Fasciculations, Feeding difficulty, Hypotonia, Respiratory Difficulty, Weakness*
Was treatment started? ☐ Yes ☐ No ☐ Unknown	*[IF YES]* Type of treatment? (Check all that apply) ☐ Gene Therapy ☐ Nusinersin ☐ Other: please describe_____ ☐ Unknown