# Diagnostic Form Templates for

# Newborn Screening

Last Updated: November 10, 2025

# Case Information Template:
## Information Collected for ALL Cases

| Infant Demographic Information | |
|---|---|
| State Unique ID? (alphanumeric)*<br>*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)<br>*If time of birth is not available, only enter the date* | |
| Year*<br>*Year of birth is stored to calculate Quality Indicators* | *Automatically populated based on date of birth* |
| Birth Weight? (in grams) | |
| Biological Sex? | ☐ Male<br>☐ Female<br>☐ Unspecified<br>☐ Unknown |
| Race? (Select all that apply) | ☐ White<br>☐ Black or African American<br>☐ American Indian or Alaskan Native<br>☐ Asian<br>☐ Native Hawaiian or other Pacific Islander<br>☐ Not Reported<br>☐ Unknown |
| Ethnicity? | ☐ Hispanic, Latino(a) or Spanish origin<br>☐ Not of Hispanic, Latino(a), or Spanish origin<br>☐ Not Reported<br>☐ Unknown |
| Screening Information | |
| Which newborn screen result indicated this infant was at risk for the disorder? | ☐ First Screen<br>☐ Requested Subsequent Screen<br>☐ Routine Second Screen |
| Was prenatal testing done that indicated that this infant was at risk for this disorder? | ☐ Yes<br>☐ No<br>☐ Unknown |
| Was there family history that indicated that this infant was at risk for this disorder? | ☐ Yes<br>☐ No |

| | ☐ Unknown |
|---|---|
| Was this individual identified outside of the newborn screening? | ☐ Yes<br>☐ No<br>☐ Unknown |
| What was the reason the infant was missed? (IF individual was identified outside of newborn screening = Yes) | ☐ Parental Refusal<br>☐ Lost to follow-up after unsatisfactory specimen<br>☐ Biologic false negative/result within normal range<br>☐ Did not have valid screen due to error<br>☐ 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 Professional** | |
| Date of intervention by appropriate medical professional(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<br>☐ No<br>☐ 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<br>☐ No<br>☐ Unknown |

## Disorder Confirmatory Diagnosis Follow-Up

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

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

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

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

| | |
|---|---|
| **Was enzyme analysis for holocarboxylase synthetase deficiency enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme activity:<br><br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |

| Molecular Genetics | |
|---|---|
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What genes were included in the mutation analysis? (select all that apply)<br>☐ *HLCS*<br>☐ Other gene: _____ |

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br>Was 3OH Isovaleric acid level<br>☐  Elevated<br>☐  Normal<br>☐  Unknown<br><br>Was Isovaleryl glycine level<br>☐  Elevated<br>☐  Normal<br>☐  Unknown |
| **Were plasma acylcarnitines tested?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br>Was C5 -DC level<br>☐  Elevated<br>☐  Normal<br>☐  Unknown |
| **Was enzyme analysis for Glutaric Acidemia enzyme activity completed?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br>Was enzyme activity:<br>☐  Consistent with disease<br>☐  Normal activity (not consistent with disease)<br>☐  Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis done?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br>What genes were included in the mutation analysis? (select all that apply)<br>☐  *IVD*<br>☐  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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was 3OH Isovaleric acid level<br>☐ Elevated<br>☐ Normal<br>☐ Unknown<br><br>Was 3-methylcrotonyl glycine level<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Were plasma acylcarnitines tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was C5 -OH level<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was maternal 3-MCC level tested and ruled out?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Was enzyme analysis for 3-MCC enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme activity:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]* What genes were included in the mutation analysis? (select all that apply)<br>☐ *MCCC1*<br>☐ *MCCC2*<br>☐ Other gene: _____ |

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  Unknown<br><br>*Allele 2:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Please indicate which of the following metabolites were detected:<br><br>Propionyl glycine?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>Tiglyglycine?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>Methylcitrate?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>3OH Propionic acid level?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>MMA?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>Methylcrotonyl glycine?<br>☐ Yes<br>☐ No<br>☐ Unknown |

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

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

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

| Were enzyme complementation studies completed?<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Were complementation studies:<br><br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
|---|---|

| **Molecular Genetics** ||

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

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

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

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

| | |
|---|---|
| **Was total plasma homocysteine tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was total plasma homocysteine:<br><br>☐ Elevated<br>☐ Normal<br>☐ Unknown |

| | |
|---|---|
| **Were enzyme complementation studies completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Were complementation studies:<br><br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |

<div align="center" style="background-color:purple;color:white;"><strong>Molecular Genetics</strong></div>

| | |
|---|---|
| **Was mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What genes were included in the mutation analysis? (select all that apply)<br><br>☐ *MMACHC*<br>☐ *MMADHC*<br>☐ *LMBRD1*<br>☐ *ABCD4*<br>☐ *HCFC1*<br>☐ *C2ORF25*<br>☐ Other gene: _____ |
| | *[For each gene selected]*<br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was fractional excretion of free carnitine level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown<br><br>Was 3-methylcrotonyl glycine level<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Were plasma carnitine levels tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was free carnitine (C0)<br>☐ Low<br>☐ Normal<br>☐ Unknown |
| **Were other causes for carnitine loss ruled out?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Was enzyme analysis for carnitine deficiency enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme activity:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| Molecular Genetics | |
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What genes were included in the mutation analysis? (select all that apply)<br>☐ *SCL22A5*<br>☐ Other gene: _____ |

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

## Medium-chain acyl-CoA Dehydrogenase Deficiency (MCAD)

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

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

**Trifunctional Protein Deficiency (TFP)**

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

| | |
|---|---|
| **Was functional analysis of fatty acid oxidation in cultured fibroblasts performed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was functional fibroblast analysis:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |

| Molecular Genetics |
|---|

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

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

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

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

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

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

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was plasma ASA level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown<br><br>Was Citrulline level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Were plasma urine acids tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was urine ASA level?<br>☐ Elevated<br>☐ Normal<br>☐ Unknown<br><br>Was urine Citrulline level?<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was enzyme analysis for ASA enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme analysis:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |

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

| | |
|---|---|
| | *[For each gene selected]*<br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was plasma ASA level:<br>☐ Present<br>☐ Absent<br>☐ Unknown<br><br>Was Citrulline level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was blood ammonia levels tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was blood ammonia level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was enzyme analysis for Citrullinemia type 1 enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme analysis:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What genes were included in the mutation analysis? (select all that apply)<br>☐ *ASS1*<br>☐ Other gene: _____ |

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  Unknown<br><br>*Allele 2:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was Phe level:<br>☐ Elevated (>120umol/L on unrestricted diet)<br>☐ Normal<br>☐ Unknown<br><br>Was Phe/Tyr level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Were biopterin studies done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Were biopterin studies:<br>☐ Normal<br>☐ Abnormal<br>☐ Unknown |
| **Was enzyme analysis for Hyperphe (inclusive of classic PKU) enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme analysis:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What genes were included in the mutation analysis? (select all that apply)<br>☐ *PAH*<br>☐ Other gene: _____ |

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was Methionine level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was plasma Homocysteine tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was plasma Homocysteine level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was enzyme analysis for CBS enzyme activity completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was enzyme analysis:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What genes were included in the mutation analysis? (select all that apply)<br>☐ *CBS*<br>☐ Other gene: _____ |

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

## Maple Syrup Urine Disease (MSUD)

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

- ☐ Classic
- ☐ Intermediate
- ☐ Thiamine-response
- ☐ Hydroxyprolinemia
- ☐ Unclassified
- ☐ Unknown

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

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

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  Unknown<br><br>*Allele 2:*<br>☐  Variant known to be disease causing<br>☐  Variant of unknown significance<br>☐  Variant of unknown significance (predicted to be pathogenic)<br>☐  Wild Type (Normal)<br>☐  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?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br><br>Was plasma succinylacetone level:<br>☐  Elevated<br>☐  Normal<br>☐  Unknown<br><br>Was plasma tyrosine level:<br>☐  Elevated<br>☐  Normal<br>☐  Unknown |
| **Were urine organic acids tested?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br><br>Was urine succinylacetone level:<br>☐  Elevated<br>☐  Normal<br>☐  Unknown<br><br>Was urine tyrosine level:<br>☐  Elevated<br>☐  Normal<br>☐  Unknown |
| **Was enzyme analysis for fumarylacetoacetate hydrolase completed?**<br>☐  Yes<br>☐  No<br>☐  Unknown | *[IF YES]*<br>Was enzyme analysis:<br><br>☐  Consistent with disease<br>☐  Normal activity (not consistent with disease)<br>☐  Unknown |
| **Molecular Genetics** | |

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

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

# Endocrine Disorders

## Congenital Hypothyroidism (CH)

**Final Diagnosis as determined by clinician performing follow-up:**

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

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

| | |
|---|---|
| **Was Serum Free T4 tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was Serum Free T4 below the age-established reference range?<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br>Was it tested before initiation of treatment?<br>☐ Yes<br>☐ No<br>☐ Unknown |
| **Does this baby have other pituitary hormone deficiencies?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Does this baby have midline defects?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Was TBG tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was TBG below the age established reference range?<br>☐ Yes<br>☐ No<br>☐ Unknown |
| **Was T3 or T4 resin uptake tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was T3 or T4 resin uptake above the age-established reference range?<br>☐ Yes<br>☐ No<br>☐ 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**<br>☐ Male<br>☐ Female<br>☐ Unknown<br>☐ Unspecified | |
| **Was confirmatory serum 17-OHP level obtained?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Was there a value at baseline:<br>☐ >10,000 ng/dl<br>☐ 1000-10,000 ng/dl;<br>☐ < 1000 ng/dl;<br>☐ Unknown<br><br>Was it tested before initiation of treatment?<br>☐ Yes<br>☐ No<br><br>Was there a result after ACTH stimulation:<br>☐ >10,000 ng/dl<br>☐ 1000-10,000 ng/dl;<br>☐ < 1000 ng/dl;<br>☐ Unknown<br><br>Was it tested before initiation of treatment?<br>☐ Yes<br>☐ No |
| **Was tandem mass spectrometry urinary steroid profile obtained?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Were the urinary spectrometry steroid profile results:<br><br>☐ Indicative of 21-Hydroxylase Deficiency CAH<br>☐ Unknown |

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

| | |
|---|---|
| | *[For each gene selected]*<br><br>Check the types of variants found on:<br><br>*Allele 1*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ FS<br>☐ FSC<br>☐ FSA<br>☐ $FSA_2$<br>☐ $FSAA_2$<br>☐ Other; other result name_____<br>☐ Unknown |
| **Was quantitative (HPLC or electrophoresis) testing completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What were the results?<br>☐ FS<br>☐ FSC<br>☐ FS with high $A_2$<br>☐ FSA with high $A_2$<br>☐ FSA<br>☐ Other; other result name_____<br>☐ Unknown |

| | |
|---|---|
| **Was mutation analysis performed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Check the type of variant found on:<br><br>*Allele 1*<br>☐ *S*<br>☐ *C*<br>☐ *Beta + Thal*<br>☐ *Beta$^0$ + Thal*<br>☐ Other; _____<br>☐ Unknown<br><br>*Allele 2*<br>☐ *S*<br>☐ *C*<br>☐ *Beta + Thal*<br>☐ *Beta$^0$ + Thal*<br>☐ Other; other name_____<br>☐ Unknown |
| **NBS result**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What were the results?<br>☐ FS<br>☐ FSC<br>☐ FSA<br>☐ FSA$_2$<br>☐ Other<br>☐ Unknown |
| **Was a CBC performed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ Normal – high MCV<br>☐ Low MCV<br>☐ Unknown |

| | |
|---|---|
| **Were family studies (in parents) done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Maternal Status: what were the results?<br>☐ Carrier *S*<br>☐ Carrier *C*<br>☐ Carrier *Beta + Thal*<br>☐ Carrier *Beta$^0$ Thal*<br>☐ Other: _____<br>☐ Unknown<br><br>Paternal Status: what were the results?<br>☐ Carrier *S*<br>☐ Carrier *C*<br>☐ Carrier *Beta + Thal*<br>☐ Carrier *Beta$^0$ Thal*<br>☐ Other: _____<br>☐ Unknown |
| **Was there a positive family history?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Were HPLC & IEF tested on the same sample from the infant?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What were the results?<br>☐ FS<br>☐ FSC<br>☐ FSA$_2$<br>☐ FSAA$_2$<br>☐ Other<br>☐ Unknown |
| **Were Hgb tests (electrophoresis or HPLC) performed on family members?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ Positive<br>☐ Negative<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Was qualitative (IEF or HPLC) testing completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ FC<br>☐ FD<br>☐ FE<br>☐ FO$_{ARAB}$<br>☐ Other; other result name_____<br>☐ Unknown |
| **Was quantitative (HPLC or electrophoresis) testing completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ FC<br>☐ FD<br>☐ FE<br>☐ FO$_{ARAB}$<br>☐ Other; other result name_____<br>☐ Unknown |

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

| | |
|---|---|
| **Were family studies (in parents) done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | Maternal Status: what were the results?<br>☐ Carrier *C*<br>☐ Carrier *D*<br>☐ Carrier *E*<br>☐ Carrier *O$_{Arab}$*<br>☐ Carrier *Beta + Thal*<br>☐ Carrier *Beta$^0$ Thal*<br>☐ Other: _____<br>☐ Unknown<br><br>Paternal Status: what were the results?<br>☐ Carrier *C*<br>☐ Carrier *D*<br>☐ Carrier *E*<br>☐ Carrier *O$_{Arab}$*<br>☐ Carrier *Beta + Thal*<br>☐ Carrier *Beta$^0$ Thal*<br>☐ Other: _____<br>☐ Unknown |
| **Was there a positive family history?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Were Hgb tests (electrophoresis or HPLC) performed on family members?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What were the results?<br>☐ Positive<br>☐ Negative<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What was the enzyme level?<br>☐ Within lab known affected range<br>☐ Normal<br>☐ Unknown |
| **Were urine GAGS tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What was the urine GAG level?<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |

| | |
|---|---|
| **Clinical symptoms/lab findings?**<br>☐ Symptoms present and documented by specialists. Public health (PH) program continued to collect data through the development of symptoms<br>☐ 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<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Pathogenic variant and associated with SEVERE disease<br>☐ Pathogenic or likely pathogenic variant<br>☐ Variant of unknown significance<br>☐ Variant known to be associated with ATTENUATED disease.<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Pathogenic variant and associated with SEVERE disease<br>☐ Pathogenic or likely pathogenic variant<br>☐ Variant of unknown significance<br>☐ Variant known to be associated with ATTENUATED disease.<br>☐ Wild Type (Normal)<br>☐ 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)?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What was the enzyme level?<br>☐ Within lab known affected range for infantile onset (IO)<br>☐ Low (above affected range, for IO, may or may not be in late-onset (LO range), but should not be above LO range))<br>☐ Within lab known affected range for late onset (LO)<br>☐ Low (above affected range, for LO not normal)<br>☐ Unknown |
| **Was enzyme activity tested in skin/muscle?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>What was the enzyme activity?<br>☐ Positive skin or muscle biopsy<br>☐ Unknown |
| **Was there cardiac involvement consistent with Pompe?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Findings:<br>☐ Positive findings on chest X-ray/EKG/ECHO in newborn period<br>☐ Positive findings on chest X-ray/EKG/ECHO |
| **Lab findings for CK/AST/ALT/LDH/Urine Hex4?**<br>☐ Elevated<br>☐ Not Present<br>☐ Unknown<br>☐ Untested | |

| Were there any clinical findings? <br> ☐ Symptoms present after one year of age and documented by specialists. PH program continue to collect data through the development of symptoms <br> ☐ Symptoms present before one year of age, but no cardiac involvement <br> ☐ 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? | [IF YES] |
|---|---|
| <br>☐ Yes<br>☐ No<br>☐ Unknown | Check the types of variants found on:<br><br>*Allele 1:*<br>☐ Pathogenic<br>☐ Pathogenic variant and associated with infantile onset<br>☐ Novel variant that is likely pathogenic<br>☐ Pathogenic variant or likely pathogenic variant, with deletion or duplication consistent with infantile onset<br>☐ Pathogenic and associated with non-classical disease, or variant of uncertain significance<br>☐ Pathogenic or likely pathogenic variant, no other variants found; duplication/deletion testing not done or not known<br>☐ Pathogenic or likely pathogenic variant; no other variants found<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2:*<br>☐ Pathogenic<br>☐ Pathogenic variant and associated with infantile onset<br>☐ Novel variant that is likely pathogenic<br>☐ Pathogenic variant or likely pathogenic variant, with deletion or duplication consistent with infantile onset<br>☐ Pathogenic and associated with non-classical disease, or variant of uncertain significance<br>☐ Pathogenic or likely pathogenic variant, no other variants found; duplication/deletion testing not done or not known<br>☐ Pathogenic or likely pathogenic variant; no other variants found<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was enzyme activity:<br>☐ <10%<br>☐ 10-30%<br>☐ Normal<br>☐ Unknown |
| **Molecular Genetics** | |
| **Was a mutation analysis performed for biotinidase deficiency?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]* What genes were included in the mutation analysis? (select all that apply)<br>☐ BTD<br>☐ Other gene:_____ |
| | *[For all genes selected]*<br><br>**Check the types of variants found on:**<br>*Allele 1:*<br>☐ Variant known to be disease causing (Unknown)<br>☐ Variant known to be disease causing (known to be associated with profound enzyme deficiency)<br>☐ Variant known to be disease causing (known to be associated with partial enzyme deficiency ["mild" mutation (D44H)]<br>☐ Variant of unknown significance<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2*<br>☐ Variant known to be disease causing (Unknown)<br>☐ Variant known to be disease causing (known to be associated with profound enzyme deficiency)<br>☐ Variant known to be disease causing (known to be associated with partial enzyme deficiency ["mild" mutation (D44H)]<br>☐ Variant of unknown significance<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was GALT level:<br>☐ <10%<br>☐ 10-30%<br>☐ Normal<br>☐ Unknown |
| **Was Gal-1-P tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was Gal-1-P level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **Was Urine Galactitol tested?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Was Urine Galactitol level:<br>☐ Elevated<br>☐ Normal<br>☐ Unknown |
| **If Variant Galactosemia, was protein phenotyping completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown<br>☐ Not applicable | *[IF YES]*<br><br>Did result indicate:<br>☐ Phenotype consistent with variant<br>☐ Phenotype NOT consistent with variant<br>☐ Unknown |
| **If Arginase Deficiency, were enzyme studies completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown<br>☐ Not applicable | *[IF YES]*<br><br>Was enzyme activity:<br>☐ Consistent with disease<br>☐ Normal activity (not consistent with disease)<br>☐ Unknown |
| **Molecular Genetics** | |

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

| | |
|---|---|
| | *[For each gene selected]*<br><br>**Check the types of variants found on:**<br><br>*Allele 1*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ Unknown<br><br>*Allele 2*<br>☐ Variant known to be disease causing<br>☐ Variant of unknown significance<br>☐ Variant of unknown significance (predicted to be pathogenic)<br>☐ Wild Type (Normal)<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Were CFTR mutations detected on the <u>newborn screening</u> mutation panel?**<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br><br>*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]*<br><br>*Check the type of variant found on allele 1:*<br>☐ Variant known to be disease causing in CFTR2<br>☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides)<br>☐ Neutral variant<br>☐ Variant of varying clinical consequence in CFTR2<br>☐ Wild Type (Normal)<br>☐ Unknown (not reported in CFTR2)<br><br>*Check the type of variant found on allele 1:*<br>☐ Varian known to be disease causing in CFTR2<br>☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides)<br>☐ Neutral variant<br>☐ Variant of varying clinical consequence in CFTR2<br>☐ Wild Type (Normal)<br>☐ Unknown (not reported in CFTR2) |
| **Did the child have meconium ileus?**<br>☐ Yes<br>☐ No<br>☐ Unknown | |

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

| | |
|---|---|
| **Was a CFTR mutation panel completed <u>after</u> the newborn screening mutation panel?**<br>☐ Yes<br>☐ No<br>☐ Unknown<br><br><br>*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]*<br><br>*Check the type of variant found on allele 1:*<br>☐ Variant known to be disease causing in CFTR2<br>☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides)<br>☐ Neutral variant<br>☐ Variant of varying clinical consequence in CFTR2<br>☐ Wild Type (Normal)<br>☐ Unknown (not reported in CFTR2)<br><br>*Check the type of variant found on allele 2:*<br>☐ Variant known to be disease causing in CFTR2<br>☐ Variant known to be disease causing in CFTR2 (shown to be associated with lower sweat chlorides)<br>☐ Neutral variant<br>☐ Variant of varying clinical consequence in CFTR2<br>☐ Wild Type (Normal)<br>☐ 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.*<br><br>☐ Present<br>☐ Not Present<br>☐ Unknown<br>☐ Not applicable | *[IF PRESENT]*<br><br>Select all symptoms included:<br><br>☐ CBAVD<br>☐ Recurrent pancreatitis<br>☐ Nasal polyposis<br>☐ Infertility<br>☐ 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?**<br><br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What was the CD3 T cell level?<br><br>☐ <300 autologous T cells, undetectable or very few naïve T cells<br>☐ 300-1500, few naïve T cells, oligoclonal T cells, or poor T cell diversity<br>☐ >80% CD45RO+<br>☐ Any number (not zero)<br>☐ Untested/Unknown |
| **Was proliferation to PHA test done?**<br><br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Proliferation to PHA:<br><br>☐ <10% of normal<br>☐ 10-50% of normal PHA<br>☐ 10-30% normal PHA or Absent to Candida/TT<br>☐ <30% of normal<br>☐ Any/Unknown |
| **Was maternal engraftment documented?**<br><br>☐ Yes<br>☐ No<br>☐ Unknown | |
| **Molecular Genetics** | |

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

| | *[IF variants detected=YES]*<br>**Were heterozygous *TBX1* variants assessed?**<br><br>☐   Yes<br>☐   No<br>☐   Unknown |
| --- | --- |

## Critical Congenital Heart Disease (CCHD)

**What was the final diagnosis?**
- ☐ CCHD
- ☐ Non-critical CCHD
- ☐ Other
- ☐ Unknown

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

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

**Tetralogy of Fallot (TOF)**

- ☐ TOF
- ☐ TOF, Pulmonary stenosis
- ☐ TOF, AVCanal (AVSD)
- ☐ TOF, Absent pulmonary valve

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**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**<br>☐ Interrupted aortic arch<br>☐ Interrupted aortic arch + VSD<br>☐ Interrupted aortic arch + AP window (aortopulmonary window) |

| | |
|---|---|
| | **Aortic Valve Disease**<br>☐ Aortic Stenosis receiving intervention in first 30 days of life<br>☐ Pulmonary Stenosis receiving intervention in the first 30 days of life |
| **Was a Prenatal Echocardiogram Completed?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Did the Prenatal Echo findings suggest CCHD?<br>☐ Yes<br>☐ No<br>☐ 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What was the VLCFA level?<br>☐ Elevated<br>☐ Slightly elevated<br>☐ Normal<br>☐ Low<br>☐ Unknown<br><br>*"Elevated" signifies in pathogenic range, while "slightly elevated" signifies above normal, but not in the pathogenic range* |
| **Clinical symptoms?**<br>☐ Present<br>☐ Not present<br>☐ Not present at birth<br>☐ Unknown | *Symptoms may include: neonatal hypotonia, neonatal seizures, liver disease, neonatal cholestasis, sensorineural deafness, failure to thrive, craniofacial abnormalities* |
| **Was plasmalogen testing done?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br><br>Plasmalogen level?<br>☐ Normal<br>☐ Low<br>☐ Unknown |

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

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

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

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

## Spinal Muscular Atrophy (SMA)

| Diagnostic Workup | |
|---|---|
| **Newborn Screen Molecular Test for SMN1?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What was the result?<br>☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)*<br>☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* - observed on two independently collected NBS specimens<br>☐ 2 pathogenic variants<br>☐ 2 pathogenic variants observed on two independently collected NBS specimens<br>☐ 1 pathogenic variant and 1 variant of unknown significance<br>☐ 2 variants of unknown significance<br>☐ Unknown/ Not Done/Screen Negative<br><br>*\* 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>SMN2 Copy Number?<br>☐ One<br>☐ Two<br>☐ Two or more<br>☐ Unknown/Not Done |
| **Post-Newborn Screen Molecular Test for SMN1?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What was the result?<br>☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)*<br>☐ Zero copies of *SMN1* (presumed homozygous deletion/conversion)* - observed on two independently collected specimens<br>☐ 2 pathogenic variants<br>☐ 2 pathogenic variants observed on two independently collected specimens<br>☐ 1 pathogenic variant and 1 variant of unknown significance<br>☐ 2 variants of unknown significance<br>☐ Unknown/ Not Done/Screen Negative<br><br>*\* 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?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>*SMN2* Copy Number?<br>☐ One<br>☐ Two<br>☐ Two or more<br>☐ Unknown/Not Done |
| **Parental Molecular Testing Family History/Parental Genetic Testing?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>What was the result?<br>☐ Phasing is complete and confirms that variants are in trans or both parents are known to be carriers of the pathogenic variants identified<br>☐ Both parents are known carriers of *SMN1* deletion<br>☐ Unknown/Not Done |
| **Clinical symptoms?**<br>☐ Present<br>☐ Not present<br>☐ Unknown | *Symptoms may include: Electromyography evidence of motor neuron disease, Absent reflexes, Fasciculations, Feeding difficulty, Hypotonia, Respiratory Difficulty, Weakness* |
| **Was treatment started?**<br>☐ Yes<br>☐ No<br>☐ Unknown | *[IF YES]*<br>Type of treatment? (Check all that apply)<br>☐ Gene Therapy<br>☐ Nusinersin<br>☐ Other: please describe_____<br>☐ Unknown |