Biochemical and Molecular Confirmation Testing for Newborn Screening

Specifications

Confirmatory testing for dried blood spot specimens with abnormal results identified by Newborn Screening.

Definitions:

a) ABCD1 also known as Adrenoleukodystrophy protein gene is affected in X-linked Adrenoleukodystrophy.
b) ACADVL is very long-chain acyl-CoA dehydrogenase gene is affected in very long chain acyl Co-A dehydrogenase deficiency.
c) Biochemical Testing is performed on newborn screening specimens that had a positive result to rule in or rule out a particular disease or disorder. Testing is performed using specific chemicals that identify markers specific to a particular disease or disorder.
d) CLIA is a licensing organization that inspects laboratories in the US and certifies them as approved to perform testing on patient samples. CLIA stands for Clinical Laboratory Improvement Amendment.
e) DNA means deoxyribonucliec acid. DNA encodes genetic information.
f) Fabry is a hereditary disorder of fat metabolism resulting from defects in the GLA gene.
g) False positive test means the test gave a positive result, but the individual does not have disease.
h) GAA also known as Acid Alpha Glucosidase gene is implicated in Pompe Disease.
i) GALC also known as Galactosylceramide beta-galactosidase gene is implicated in Krabbe Disease.
j) Gaucher disease is a rare inherited metabolic disorder resulting from changes or mutations in the GBA gene.
k) GBA also known as Beta-glucocerebrosidase gene is implicated in Gaucher disease.
l) GLA also known as Alpha-galactosidase A gene is affected in Fabry disease.
m) IDUA also known as Alpha-L-iduronidase is affected in Mucopolysaccharidosis I
n) KB means Kilobase. These relate to the length of nucleic acid molecules. In the case of the GALC gene a homozygous 30 KB deletion is positive for Krabbe disease.
o) Krabbe is a hereditary disease affecting the nervous system resulting from pathogenic variants in the GALC gene.

p) Lysosomal Disorders are inherited metabolic diseases that are characterized by abnormal accumulation of various toxic materials in cells resulting from enzyme deficiencies. These include the following gene defects: GAA, GALC, GBA, GLA, and IDUA.
q) Molecular tests target a specific gene to determine whether disease causing mutations and or deletions exist in the gene.
r) MPS I means Mucopolysaccharidosis I
s) Mucopolysaccharidosis I is a hereditary metabolic disease resulting from pathogenic variants in the IDUA gene.
t) Pompe Disease is a rare multisystem disorder caused by pathogenic variations in the GAA gene.
u) Second tier biochemical test is a test used to further differentiate a true positive test from a false positive test.
v) SMA means Spinal Muscular Atrophy.
w) Spinal Muscular Atrophy is a group of inherited disorders characterized by loss of motor neurons or anterior horn cells in the spinal cord.
x) SMN2 means Spinal Muscular Neuron 2.
y) SMN2 copy number indicates disease severity for Spinal muscular atrophy.
z) VLCAD means Very long chain acyl Co-A dehydrogenase deficiency
aa) XALD means X-linked Adrenoleukodystrophy

Minimum Requirements:

1) Supplier shall provide Biochemical Tests on dried blood spots for Lysosomal Disorders as indicated in the table below with the following testing volumes and maximum acceptable time frames for reporting.

Disorder	**Biochemical Test**	**Estimated Volume per year**	**Acceptable Time frame for reporting**
Mucopolysaccharidosis I	Heparan, Dermatan, Total Keratan Sulfate	45	No later than four (4) business days
Pompe Disease	Creatine/Creatinine/ GAA ratio	20	No later than four (4) business days
Gaucher	Glucopsychosine	8	No later than four (4) business days
Krabbe	Psychosine	20	No later than four (4) business days

2) Supplier must be a CLIA approved laboratory and maintain CLIA certification throughout the length of the contract and must provide a copy of their most recent CLIA certificate to the

State. Proof of certification is needed as this a requirement of CLIA for all reference laboratories.

3) When Biochemical Tests are positive for Mucopolysaccharidosis I or for Gaucher Disease the supplier should perform molecular sequencing for the IDUA gene or the GBA gene respectively. Sequencing should not be performed unless Biochemical Tests are positive.

4) Regarding Pompe Disease, Biochemical Tests and Molecular tests should be performed at the same time.

5) For Krabbe Disease, Psychosine should be performed first and if positive above the supplier reference value, the supplier should proceed with Molecular testing according to their testing algorithm.

6) Supplier shall provide DNA Molecular Sequencing on dried blood spots for the disorders named below and provide results within the below time frames of receiving the sample for the following disorders and gene targets with the testing volumes as indicated in the table below:

Disorder	**Target**	**Estimated Volume per year**	**Acceptable Time frame for reporting**
Mucopolysaccharidosis I	IDUA gene	15	No later than fourteen (14) business days
Pompe Disease	GAA gene	10	No later than four (4) business days
Gaucher	GBA gene	5	No later than fourteen (14) business days
Fabry	GLA gene	10	No later than fourteen (14) business days
XALD	ABCD1 gene	36	No later than fourteen (14) business days
Spinal Muscular Atrophy	SMN2 copy number	15	No later than fourteen (14) business days

Very Long Chain Acyl CoA Dehydrogenase Deficiency	ACADVL gene	15	No later than thirty (30) business days
Galactosemia	Mutation panel	15	No later than fourteen (14) business days
Krabbe	GALC gene	20	No later than fourteen (14) business days

7) Any additional Biochemical or Molecular Tests for the aforementioned disorders may be ordered by the State as needed based online item contract pricing.

8) Supplier must report results of testing to the State no later than four (4) business days for Biochemical Tests and no later than fourteen (14) business days for all molecular tests with the exception of VLCAD which should be no later than thirty (30) business days.

9) Supplier must provide a toll-free number for the State to call for results or questions between 8 a.m. to 4:30 p.m. Central Standard Time (CST) Monday to Friday except for State holidays.

10) Patient Biochemical and or Molecular results must be accessible to the State through a secure web portal that is password protected.

11) The web portal must alert user or give visual notification to user upon log-in that newly reported results are available for review, download, or printing.

12) The web portal must have functionality to search and access historical patient results using patient name, lab number or date of birth.

13) The supplier must have a web accessible test menu that allows selection of test(s) to be must outline or an alternative test ordering process if web ordering is not available such as through email request.

14) Supplier must notify the State of positive Biochemical and or Molecular results via email, fax, or phone call to laboratory management Monday – Friday between 8 a.m. – 4:30 p.m. CST treating these as urgent.

15) Individual patient results must be downloadable as a PDF.

16) Format for PDF reporting should include at minimum the laboratory performing the test, patient demographic information (Name, Date of Birth, Date of Specimen Collection), specimen accession number, test results, test cutoffs, and interpretation of the test results.