

WISCONSIN NEWBORN SCREENING (NBS) PROGRAM – CONDITION NOMINATION

Nomination of a Condition to the Wisconsin Newborn Screening Panel

Date of Nomination

August 21, 2025

NOMINATOR

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CO-SPONSORING ORGANIZATION #1 (as appropriate, additional sponsors may be included on page 5)

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Condition	STATEMENT
Nominated Condition	Gaucher disease
Description of Disorder	Lysosomal Storage Disorder
Screening Method	Dried Blood Spot
Gene	GBA 1
OMIM or other names for condition	None
Case Definition	Gaucher disease is an autosomal recessive inborn error of metabolism characterized by the toxic accumulation of glucocerebroside lipids within multiple organs. Gaucher disease results from mutations in the GBA1 gene, leading to deficient glucocerebrosidase activity within lysosomes. Clinical manifestations, including hepatosplenomegaly, pancytopenia, osteoporosis, and avascular necrosis, vary in severity depending on the disease type.

NOTE: Please reference each statement/answer with the corresponding reference number listed in **Key References**.

CRITERION

Criterion 1: Mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.

Timing of Clinical Onset	<i>Relevance of the timing of newborn screening to onset of clinical manifestations. Must cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.</i> Gaucher disease is a heterogeneous disease that is classified as non-neuronopathic type 1 (GD1) and neuronopathic types 2 and 3 (GD2, GD3). Clinical heterogeneity and progressive onset of symptoms lead to misdiagnosis and substantial diagnostic delays for many patients. Patients with GD1 (about 85%-90% of cases) may develop symptoms during childhood or later in life or remain asymptomatic throughout life [Stirnemann 2017, Rasmussen 2025] #1,2. Symptoms of GD1 can range from mild and moderate to life threatening, in rare cases. About half of patients with GD1 are diagnosed before 10 years of age (37%) or at 10–18 years of age (12%) (Mehta et al., 2017)#3. Diagnoses are usually made within 1 year of first seeing a doctor (73%) but can take 7 years or longer (14%). The diagnosis of neuronopathic GD is challenging due to heterogeneous clinical presentation and symptoms that can overlap between GD2 and GD3 (Goker-Alpan & Ivanova, 2024)#4. Patients with GD2 (5%-10% of cases) develop severe neurological impairment and symptoms in infancy (Goker-Alpan & Ivanova, 2024; Rasmussen, 2025; Stirnemann et al., 2017). Neurological deficits appear within 6 months of life and progress rapidly: the mean survival age is 11.7 months (Schiffmann et al., 2020; Stirnemann et al., 2017)#5. Early recognition of GD2 is therefore critical for clinical decision-making and family counseling. In patients with GD3 (5% of all cases), neurological symptoms usually appear later than in GD2, but early onset at 4–6 months of age can also occur (Goker-Alpan & Ivanova, 2024; Rasmussen, 2025; Stirnemann et al., 2017). GD3 often has a more protracted disease course than GD2. The more severe symptoms of GD3 include progressive myoclonus epilepsy, cerebellar ataxia or spasticity, and dementia. Behavioral changes and unexpected death have also been reported. Early identification of Gaucher disease offers substantial benefits, including: • Eliminating diagnostic delays: Diagnostic delays can lead to complications such as avascular necrosis, severe bleeding, chronic bone pain, life-threatening sepsis, pathologic fractures, growth failure, and chronic liver disease. • Timely initiation of treatment: Gaucher disease is a progressive condition; both disease stage at the time of treatment initiation and treatment adherence over time influence outcomes. Enzyme replacement therapy (ERT), which is approved by the US Food and Drug Administration (FDA) for symptomatic adults and children with GD1, has been shown to normalize hemoglobin and platelet counts, reduce organomegaly, minimize irreversible complications like bone deformities, and reduce risk of avascular necrosis (Goker-Alpan & Ivanova, 2024; Stirnemann et al., 2017). The greatest effects of ERT on bone mineral density are observed in children and young adults, likely because of the changes in bone mineral density that naturally occur in childhood. • Monitoring asymptomatic cases: For infants with late-onset variants, early identification enables regular monitoring to prevent disease progression and optimize health outcomes. Patients with asymptomatic disease can access infrastructure that includes support from genetic counselors and physicians familiar with Gaucher disease.
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Criterion 2: For each condition, there should be information about the incidence, morbidity and mortality, and the natural history of the disorder.

Incidence	<i>Determined by what method(s): pilot screening or clinical identification?</i> Data from a French disease registry indicate that the incidence of Gaucher disease in the general population is about 1:50,000 births (Stirnemann et al., 2017)#6. Incidence is higher among the Ashkenazi Jewish population (1:350 to 1:1200; based on a literature review) (Aviner et al., 2009; Weinreb et al., 2022)#7,8. Orphanet estimates the incidence of Gaucher disease at 1.7:100,000 (Orphanet, 2024)#9. Pilot screening programs in four US states have produced incidence rates ranging from 1:4374 to 1:43,995. The highest incidence was reported in New York, at 1:4374 (15 of 65,605 infants) (Wasserstein et al., 2019)#10; Weinreb et al. have suggested that the incidence of Gaucher disease might be relatively high in New York due to a relatively high proportion of infants of Ashkenazi Jewish descent (Weinreb et al., 2022). In New Jersey, the incidence was 1:24,362 (18 of 438,515 infants) (Menello et al., 2025)#11. In Illinois, the incidence rate was 1:43,959 (5 of 219,973 infants) (Burton et al., 2017)#12. In a report of a pilot study in Washington state, the estimated incidence was 1:44,485 (Elliott et al., 2016)#13.
Severity of Disease	<i>Morbidity, disability, mortality, spectrum of severity, natural history.</i> There is a huge range of severity of GD. In Europe and North America, 90%-95% of cases are non-neuronopathic GD1 (Stirnemann et al., 2017)#14. GD 1 symptoms include growth retardation, splenomegaly, hepatomegaly, bleeding phenomena, and acute or chronic bone pain. One study of symptomatic GD1 patients found that 56% experienced symptoms before age 20, and 48% of these were diagnosed before age 6. Patients with GD2 and GD3 exhibit neurological symptoms. Patients with GD2 (<5% of all cases) have early, severe neurological impairment and symptoms that manifest in infancy (Goker-Alpan & Ivanova, 2024; Stirnemann et al., 2017)#15. Signs and symptoms include systemic involvement with hepatosplenomegaly, opisthotonus, bulbar signs, oculomotor paralysis, apnea and laryngeal spasms, altered psychomotor development, and myoclonic epilepsy. In patients with GD3 (5% of all cases), neurological symptoms often appear before age 2 and can include progressive myoclonus epilepsy, cerebellar ataxia or spasticity, and dementia. Behavioral changes and unexpected death have been reported (Goker-Alpan & Ivanova, 2024; Stirnemann et al., 2017). Differentiating between GD2 and GD3 can be challenging for physicians and has implications for clinical decision-making and family counseling (Weinreb et al., 2022)#16. For patients with GD3, treatment with ERT may address visceral and hematologic manifestations, improve quality of life, and increase longevity.

Criterion 3: Conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences.

Urgency	How soon after birth must treatment be initiated to be effective? For patients with GD3, treatment must be initiated immediately after birth to provide the best possible outcome for the baby. ERT is standard of care treatment for symptomatic patients with GD1, and is used off-label for patients with GD2 and GD3 (Rasmussen, 2025)#17. Three recombinant human enzymes are approved by the US FDA for the treatment of adult and pediatric patients with GD1: imiglucerase (Cerezyme®; Sanofi), velaglucerase alfa (VPRIV®; Takeda), and taliglucerase alfa (Elelyso; Pfizer). Treatment urgency depends on disease subtype (GD1, GD2, GD3), type and severity of disease manifestations, and the genetic alterations involved. Once ERT is initiated, treatment is lifelong (though ERT dose may be reduced in adults with GD1) (Weinreb et al., 2022)#18. Because Gaucher disease is a progressive condition, disease stage at the time of treatment initiation can affect clinical outcomes. Timely intervention aims to return patients to an asymptomatic state and slow disease progression (van Dussen, Biegstraaten, Hollak, & Dijkgraaf, 2014)#19. Following 8 years of newborn screening in Illinois, treatment was recommended for 8 of 21 (38%) cases of Gaucher disease, including 5 (28%) cases of GD1, 2 (100%) cases of GD2, and 1 (100%) case of GD3 (Rasmussen, 2025). Five of the 8 patients were 3 years or younger. At the time of treatment recommendation, patients with GD1 had a mean spleen volume 6.9-fold normal and mean liver volume 1.6-fold normal. A prospective study of 33 patients with GD1 and two analyses of the International Collaborative Gaucher Group (ICGG) Gaucher Registry have demonstrated benefits of ERT on bone mineral density (Weinreb et al., 2022). Early intervention with ERT is particularly important for children, whose bone mineral density increases more rapidly and consistently than adults (Goker-Alpan & Ivanova, 2024)#20. Bone pain, bone crises, and bone marrow infiltration typically improve within 1-2 years of ERT. Bone mineral density improves after several years of treatment.
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Efficacy (Benefits)	Extent of prevention of mortality, morbidity, disability. Treatment limitations, such as difficulty with acceptance or adherence. The efficacy of ERT in pediatric patients with Gaucher disease has been summarized by Weinreb et al. (Weinreb et al., 2022). In brief, data from clinical trials and real-world registries support that children treated with ERT have reduced spleen and liver volumes, normalized height and bone mineral density, reduced bone crises, increased hemoglobin levels and platelet counts, and stabilized disease. Long-term treatment with ERT reduces the need for splenectomy, reduces frequency of bone complications, and likely reduces the risk of developing malignancies. As a result of somatic improvements, patients also report improved quality of life. ERT does not reverse chronic bone lesions such as bone marrow infarcts and osteonecrosis which is why early treatment before these manifestations occur is crucial. Eliglustat, a substrate reduction therapy, is approved in the US for ages 18 and above and in the EU for ages 6 and above. Many children in the US are prescribed Eliglustat for off label usage. The cost of SRT and ERT in the United States is currently approximately the same as there are no generics or biosimilars available. Adjunctive and Emerging Therapies: Brain-penetrant substrate reduction agents (e.g., venglustat) and pharmacological chaperones (e.g., ambroxol) show early promise in addressing neurological disease, highlighting the importance of diagnosing affected infants early enough to qualify for emerging therapies. In a Phase 2 trial with venglustat and imiglucerase on 11 GD3 patients, notable reductions in plasma and cerebrospinal fluid levels of disease biomarkers, an increase in brain volume, and ataxia improvements were observed. LEAP2mono trial is now assessing the effectiveness and safety of venglustat in comparison to imiglucerase in patients aged 12 years and older with GD3 (Clinicaltrials.gov, NCT05222906). Among other potential treatments for nGD are pharmacological chaperones (PCs). PC is orally administered small molecules that refold the mutated proteins, preventing ERAD and proteasomal degradation. Ambroxol hydrochloride is a pH-dependent GCase activator and inhibitor. Ambroxol has been shown to improve lysosomal functions and the enzymatic activity. In studies, Ambroxol was found safe and arrested the neurological manifestations. On high doses, seizures and myoclonus decreased, with improved neurocognitive functions. These early trials underscore the importance of early diagnostic measures like Newborn Screening. This is vital for grasping the actual prevalence and progression of nGD in newborns and infants, which in turn is critical for making decisions which could be life saving. Efficacy generally of any treatment for GD Types 2,3. GD3: Prior to enzyme replacement therapy (ERT), patients with GD3 frequently underwent splenectomy for cytopenias, resulting in increased skeletal complications and reduced survival. With the advent of ERT, the natural history has been transformed, and now these individuals, if diagnosed timely, are expected to live their natural life span. Initiation of therapy in early childhood results in dramatic decreases in hepatosplenomegaly, normalization of hematological parameters, stabilization of growth, and marked reductions in biomarkers such as Lyso-Gb1. These systemic benefits alleviate pain, fatigue, and abdominal discomfort, prevent irreversible complications, and extend survival. ERT therefore provides a life-saving intervention for patients diagnosed early. GD2: While ERT does not alter the inevitable neurological progression in GD2, treatment significantly improves palliative outcomes. Reduction in organomegaly, correction of anemia and thrombocytopenia, and improved nutrition and energy directly enhance quality of life, and ease caregiving. In a Phase IV single-center study of 11 Type 2 and 3 infants and young children (many identified by newborn screening), ERT led to rapid normalization of hematological values and significant reductions in organ volumes within six months, with no drug-related
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	adverse events. Beyond visceral and hematologic control, ERT reduces systemic inflammation, which may indirectly influence neuroinflammatory processes that contribute to neuronal injury in GD2 and GD3. Thus, even in the acute GD2 phenotype, ERT offers tangible benefits to patients and families. Moreover, indirect effects of systemic disease control may include a reduction in the inflammatory milieu. Given that neuroinflammation is a key contributor to neuronal injury in neuronopathic GD, it is plausible that sustained ERT could exert a secondary, favorable influence on neurological progression, even if incompletely.
Potential Harms	Potential medical or other ill effects from treatment. The labels for taliglucerase alfa and velaglucerase alfa carry boxed warnings, which state that anaphylaxis has occurred during the early course of ERT and after extended duration of therapy. The imiglucerase label has a warning for hypersensitivity and infusion-associated reactions. For imiglucerase, the most common adverse reactions are back pain, chills, dizziness, fatigue, headache, hypersensitivity reactions, nausea, pyrexia, and vomiting. Adverse reactions are similar for pediatric and adult patients. In a 12-month clinical trial of taliglucerase alfa in 9 treatment-naïve pediatric patients (2-13 years old) with GD1, who received treatment at 50% the recommended dose (30 U/kg; n=4) or the full dose (60 U/kg every other week; n=5), adverse reactions included vomiting (n=4), hypersensitivity reaction (n=2), severe vomiting and gastrointestinal inflammation (n=1), and mild throat irritation and chest discomfort (n=1). In a 9-month trial conducted in 31 patients with GD1 (including 5 pediatric patients) who switched from imiglucerase to taliglucerase alfa, the most common adverse reactions were arthralgia (13%), headache (13%), and pain in extremity (10%). For adults and children with GD1 who receive velaglucerase alfa, the most common adverse reactions include hypersensitivity reaction (treatment naïve patients, 52%; switched from imiglucerase, 23%), headache (35% and 30%), dizziness (22% and 8%), pyrexia (22% and 13%), abdominal pain (19% and 15%), back pain (17% and 18%), joint pain (15% and 8%), asthenia/fatigue (15% and 13%), and prolonged activated partial thromboplastin time (aPTT; 11% and 5%). The safety profile for velaglucerase alfa is similar for children as for adults; adverse reactions that occur more commonly in children include rash, prolonged aPTT, and pyrexia (>10% difference). The development of IgG antibodies has been reported for all three ERTs. With imiglucerase, 46% of patients with detectable IgG antidrug antibodies (ADA) experienced hypersensitivity. With taliglucerase alfa, hypersensitivity reactions occurred in 36% of patients with ADA and 15% without ADA. With velaglucerase alfa, hypersensitivity reactions occurred in 52% of treatment-naïve patients and 23% of patients who switched from imiglucerase, and was not associated with the development of ADA.
Criterion 4: The interventions should be reasonably available to affected newborns.	
Modality	<i>Drug(s), diet, replacement therapy, transplant, surgery, other. Include information regarding regulatory status of treatment.</i> The US FDA-approved ERTs imiglucerase, taliglucerase alfa, and velaglucerase alfa are administered via intravenous infusion. The typical dosage is 60 U/kg administered every two weeks.
Availability	<i>Describe scope of availability and note any limitations.</i> Imiglucerase, taliglucerase alfa, and velaglucerase alfa are each widely available throughout the United States. The Gaucher Community Alliance (GCA), in partnership with industry partners, supports all patients who desire access to these treatments by identifying local infusion sites and supporting local providers. Many patients transition to home infusions over time. Coverage of treatments is widely accepted by all payors, private and governmental, throughout the country.
Criterion 5: Appropriate follow-up should be available for newborns that have a false positive newborn screen.	

Follow-up for False Positives	<i>Define the follow-up process.</i> GCA recommends second-tier testing, which greatly reduces the number of false positives at screening. For infants with decreased glucocerebrosidase activity, confirmatory testing of β -glucosidase activity, lyso-Gb1 levels, and GBA status will rule out false positives at the initial evaluation following the positive screen.
Criterion 6: The characteristics of mandated tests in the newborn population should be known, including specificity, sensitivity, and predictive value.	
Screening test(s) to be used	<i>Description of the high volume method, instrumentation and if available as part of multi-analyte platform.</i> Newborn screening for Gaucher disease can be performed by measuring GBA1 enzyme activity in dried blood spots on filter paper (DBS) via tandem mass spectrometry (MS/MS) using a commercially available assay kit (Burton et al., 2017; Elliott et al., 2016; Menello et al., 2025) #21,22,23. Measuring enzyme activity using MS/MS is considered the method of choice rather than fluorimetry. In mass spectrometric approaches, the marker for Gaucher disease is decreased activity of the glucocerebrosidase (GBA). In the MS/MS assay, the enzymatic reaction is first performed in the “pre-MS/MS” step before injection into the mass spectrometer to detect enzymatic products. This is done in an assay cocktail of enzymatic substrates, internal standards, inhibitors of non-lysosomal storage disorder (non-LSD) enzymes, and a reaction buffer, which is added directly onto a well or test tube with the DBS punch. This method of measuring enzymatic activity is generally aligned with the high throughput workflow of newborn screening laboratories. The approach of measuring enzyme activity is like that of other lysosomal storage disorders (eg, MPS I, Pompe disease). Revvity (PerkinElmer) has developed a 6-plex LSD MS/MS assay that is FDA approved and commercially available. The assay measures enzymatic activity to detect Gaucher, Pompe, Krabbe, MPS-I, Niemann-Pick, and Fabry diseases and is currently the most commonly used assay in most states to screen for LSDs (Elliott et al., 2016; Wasserstein et al., 2019)#24.
Modality of Screening	<i>Dried blood spot, physical or physiologic assessment, other</i> Dried Blood Spot

Does the screening algorithm include a second tier test? If so, what type of test and availability?	<i>Dried blood spot, physical or physiologic assessment, other</i> In Missouri and Illinois, second-tier screens are performed free of charge to the family following a positive primary test. Second-tier screens are tests run on the same DBS sample but typically with different target analytes and different assays. A promising tool to reduce false-positive rates, as well as to identify cases where a second-tier screen is necessary, is the post-analytical multivariate pattern recognition software, Collaborative Library Integrative Reports by Mayo (CLIR; found at https://clir.mayo.edu/).¹⁶ This was developed to be used in conjunction with the primary or secondary screens to either provide a diagnostic result or to differentiate differential diagnoses of two different disorders. It is a free collaborative software for users that contributes positive reference data to allow for the constant expansion of the library. CLIR allows users to input newborn demographic data, such as birth weight and age at DBS collection, along with at least three enzyme activity values, to adjust screen results to ensure that disease marker cutoffs are based on the individual, instead of using a universal cutoff for all newborns. It has been integrated since February 2016 in newborn screens for Krabbe, Pompe, and MPS I. Upon detection of decreased glucocerebrosidase in the primary and optional secondary screens, two tests are performed to confirm a diagnosis of GD. The measurement of glucocerebrosidase enzymatic activity in leukocytes (Mayo ID: GBAW) and liquid chromatography–MS/MS (LC-MS/MS) to detect elevated concentrations of plasma glucosylsphingosine (Lyso-GL1) (Mayo ID: GPSY and GPSYW). If decreased glucocerebrosidase activity is determined but Lyso-GL1 levels are not elevated, total gene sequencing of the GBA1 gene is required for a definitive diagnosis of Gaucher disease (Mayo ID: GBAZ). Mayo Clinic offers LGB1 analysis in DBS incl. for 2nd tier testing. In those regions of Italy where Gaucher is part of NBS, LGB1 is used as a 2nd tier test and based on publications like this, it works well:https://pmc.ncbi.nlm.nih.gov/articles/PMC10801488/ Both Revvity and the Greenwood Genetic Center also offer LGB1 in DBS. Oregon and New Mexico perform 2nd tier testing. The other states: IL, NJ, MO, and TN do not do 2nd tier testing currently. The ACMG's Newborn Screening ACT Sheet and Algorithm for Gaucher disease can be found here :https://www.acmg.net/PDFLibrary/Gaucher-Algorithm.pdf Genetic testing is done as part of confirmatory testing only, not by the NBS lab.
Clinical Validation	<i>Location, duration, size, preliminary results of past/ongoing pilot study for clinical validation, positive predictive value, false positive rate, analytical specificity, sensitivity.</i> Missouri has the most extensive and continuous population-wide Gaucher screening program. The Missouri State Public Health Laboratory has used a fluorimetric enzyme activity test on a digital microfluidic (DMF) platform to screen all samples from newborns that were received since January 11, 2013, for Pompe, MPS I, Gaucher, and Fabry disorders. Enzyme activity was measured from DBS using a 4-plex DMF approach with the artificial 4-methyl-umbelliferyl-β-d-glucopyranoside substrate at a pH of 5.2. Out of the 133 newborns who were confirmed through diagnostic testing results 5 were confirmed to have Gaucher disease. Illinois piloted their LSD screen in 2014 and expanded it to a state-wide screen in 2015. From November 2014 to August 2016, they performed a 5-plex LSD screen for Gaucher, Pompe, Fabry, MPS I, and Niemann-Pick diseases. Within that timeframe, they screened 219,973 infants with a reported incidence for GD of 1:43,995 (n = 5) (Burton et al., 2017). They used the UPLC-MS/MS method with a conservative cutoff of ≤ 17 $\mu\text{mol/L/h}$ to avoid false-negatives. Cutoff values were determined by comparing enzymatic activity from DBS of normal infants versus infants with Gaucher disease. The pilot screening programs in New York and Washington state used similar technology.

Analytic Validation	<i>Limit of detection/quantitation, detection rate, reportable range of test results, reference range. Include regulatory status of test, information about reference samples and controls required for testing and availability of or potential for external quality assurance system, e.g., QC and PT for both screening and confirmatory tests.</i> Both the MS/MS and DMF assays are part of FDA-approved in vitro diagnostic tests and can be assumed to have sufficient analytical validation for newborn screening of Gaucher disease. In the pilot study for the MS/MS assay, the cutoff was 10% of mean enzyme activity (12.69 μ mol/h/L) (Elliott et al., 2016). For the DMF assay, the cutoff was about 30% of the mean (Sista et al., 2013)#25. For both assays the limit of detection and quantification were below the cutoff values, and both assays showed acceptable linearity of response with incubation time. Quality control DBS materials for both platforms are available from the CDC. PerkinElmer also provides quality control DBS samples for the MS/MS assay (Elliott et al., 2016).
Potential Secondary Findings	<i>May other disorders be identified by the screening test for the nominated condition?</i> ☐ Yes ☒ No If yes: • <i>How should that identification be handled—should those screening results be disclosed to the physicians or parents?</i> • <i>Would that disorder(s) meet the outlined criteria?</i> ☐ Yes ☐ No ○ <i>If yes, please prepare a separate nomination form for the secondary disorder(s)</i> ○ <i>If no, what criteria does it not meet?</i>

Summary of Population-based Pilot Study(ies)

Location of Prospective Pilot	Illinois, Missouri, New Jersey, Tennessee, New Mexico and Oregon currently screen for Gaucher, some in excess of 10 years. New York's pilot program has also been operating for 10 years.
Number of Newborns Screened	Illinois: 219,973 (Burton et al., 2017) Missouri: 43,701 (Hopkins et al., 2015) #26 New Jersey: 438,515 (Menello et al., 2025) New York: 65,605 (Wasserstein et al., 2019) Washington: 44,485 (Elliott et al., 2016)
Number of Positive Results	<i>Positive by primary test versus 2nd tier test if applicable.</i> Illinois: 1:43,995 (n=5) (Burton et al., 2017) Missouri: 1:43,701 (n=1) (Hopkins et al., 2015) New Jersey: 1:27,407 (n=16) Of 60 screen-positive cases, authors reported 18 true positives, 24 false positives, and 19 cases that did not undergo confirmatory testing (Menello et al., 2025). New York: 1:4374 (n=15) Of 17 screen-positive cases, authors reported 15 true positives and 2 false positives (normal acid α -glucosidase on confirmatory testing (Wasserstein et al., 2019). Washington: 1:43,000 (n=1) Of 3 screen-positive cases, authors reported 1 true positive, 1 false positive, and 1 carrier for the common mutation p.N370S (Elliott et al., 2016).
False Positive Rate; False Negative Rate (if known)	<i>False positive by primary test versus 2nd tier test if applicable.</i> Reports on pilot screenings describe false positive rates in the primary test of 12% (2/17) in New York (Wasserstein et al., 2019). False positive results have not been reported for Illinois (Burton et al., 2017; Rasmussen, 2025).
Number of Infants Confirmed with Diagnosis	<i>How are diagnosis confirmed [clinical, biochemical, molecular]?</i> Diagnosis is confirmed molecularly.

Criterion 7: If a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.	
Is this a new sample collection system?	<i>If yes, demonstrate reliability and timeliness of sample collection process, including data collection, analysis, and reporting of new results.</i> This test can be completed using existing testing platforms that currently use MS/MS on DBS samples
Criterion 8: Before a test is added to the panel, the details of reporting, follow-up, and management must be completely delineated, including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region.	
Considerations of Screening and Diagnostic Testing	<i>False positives, carrier detection, invasiveness of method, other</i> In the pilot screening programs, false positive results vary depending on the cutoff number used and the method of testing. Using second-tier testing and a more conservative cutoff reduces the number of false positives. One carrier was detected in the pilot screening program for Washington state (Elliott et al., 2016)#27; none of the other programs reported carriers. The test is not invasive, and no additional blood would be needed, as Wisconsin already uses the LSD panel.
Is test FDA cleared/approved	<i>Include availability of information, sole source manufacturer, etc.</i> The Revvity Neo-LSD kit test is FDA approved and is used for multiple other disorders
List all CLIA or CAP certified labs offering testing in the US	<i>Link to GeneTests, and Genetic Test Reference if applicable.</i> The following laboratories measure glucocerebrosidase enzyme activity or sequence the entire GBA gene. Some were identified in Genetic Test Reference. Others are known to experts on Gaucher disease but are not listed in the Genetic Test Reference Database. Glucocerebrosidase enzyme assay Thomas Jefferson University Lysosomal Diseases Testing Laboratory, Philadelphia, PA, CLIA number 39D0948425 Mayo Clinic Laboratories, Rochester, MN, CLIA number 24D0404292 Greenwood Genetic Center, Greenwood, SC, CLIA number 42D0689473 PerkinElmer Genomics, Pittsburgh, PA, CLIA number 39D0673919 Biochemical Genetics Laboratory, University of Illinois Medical Center, Chicago, IL; CLIA number 14D0664392 GBA Sequencing Tests Blueprint Genetics, Seattle, WA, CLIA number 99D2092375 Center for Human Genetics, Inc., Cambridge, MA, CLIA number 22D0650242 Fulgent Genetics, Temple City, CA, CLIA number 05D2043189 Gene by Gene, Houston, TX, CLIA number 45D1102202 GeneDx, Gaithersburg, MD, CLIA number 21D0969951 Greenwood Genetic Center, Greenwood, SC, CLIA number 42D0689473 PreventionGenetics, Marshfield, WI, CLIA number 52D2065132 PerkinElmer Genomics, Pittsburgh, PA, CLIA number 39D0673919 Johns Hopkins Medical Institutions Pathology Laboratory, Baltimore, MD, CLIA number 21D0709511 Invitae Corporation, San Francisco, CA, CLIA number 06D2084040

Follow-up and management process	<i>Development of standard instructions, identification of consultants, identification of appropriate referral centers throughout the state/region, follow-up for results, management of ongoing care, education, and outreach.</i> GCA is a national patient advocacy organization with a professional advisory board and volunteer families in almost every state. All newly diagnosed patients have access to resources and meet with a staff member to discuss the best path forward for education. The GCA has identified Comprehensive Care Centers across the country that have the resources and experience to provide the comprehensive care recommended by the international consensus guidelines (Kishnani et al., 2022)#28. In addition, GCA and its industry partners have resources and people dedicated to the education of families and providers so patients can receive the best possible care close to home. The GCA remains active in providing support to patients and families throughout their patient journey, including counseling and referral for financial assistance programs as appropriate. In the State of Wisconsin there are two major academic institutions that provide comprehensive care for Gaucher disease: Children’s Wisconsin/Medical College of Wisconsin in Milwaukee and University of Wisconsin Hospitals and Clinics in Madison. Both centers currently treat patients with Gaucher disease and offer multidisciplinary care including genetic counseling as well as specialists in biochemical genetics, hematology, and neurology. Additionally, both institutions are experienced in providing disease-specific therapies for Gaucher disease, such as enzyme replacement therapy and substrate reduction therapy, in accordance with current clinical standards. The IWGGD is currently finalizing pediatric and adult treatment guidelines and will be published late 2025 or 2026. The draft guidelines are out for review. While not treatment guidelines, the IWGGD’s care guidelines for non-neuronopathic GD children were published in 2023 and can be found here: https://iwggd.com/wp-content/uploads/2023/10/Pediatric-supportive-care.pdf
Criterion 9: Recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives. The mechanism of funding those costs should be identified. Expertise in economic factors should be available to those responsible for recommendations and decisions.	
Screening test	There will be minimal additional cost for the Wisconsin state lab if they are already using either the GelbChem or Revvity platforms to screen for Pompe disease, as glucocerebrosidase is part of that platform.
Confirmatory testing	Given the precision of the screening test demonstrated in Illinois, Missouri, New Jersey, New York, and Washington, the cost of confirmatory screening with serum enzyme measurement and DNA sequencing is anticipated to be low compared to other disorders that are currently screened for.
Treatment	Treatment is covered widely by all payors, private and public. GCA and industry partners assist families with enrolling in patient support programs to cover financial costs that are not covered by insurance. Families should not have to forgo treatment and suffer due to financial barriers.
Counseling	The GCA supports families in accessing local services like counseling. GCA annual meetings include in-person networking and support groups for siblings and caregivers. GCA also schedules multiple virtual "Community Chats" throughout the year that allow families to connect in real time; these meetings are sub-divided by topic to provide targeted support (teen group, neuronopathic GD group, caregivers, etc.). GCA also hosts several social media platforms that allow patients and families the opportunity to communicate and connect.
False positives	It is reasonable to hope that a false positive rate will approach zero with the testing process outlined above.

Mechanism of funding	Testing thorough the current infrastructure can be implemented without significant financial burden on the system because of the excellent performance of the test. For each patient, an earlier diagnosis will result in significant cost savings for the patient and the system.
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Key References to support each criterion. Please list and attach as PDF(s). If mailing, include hard copies.	
#	Criterion 1
1	PLEASE SEE ATTACHED PAGE
2	
	Criterion 2
3	
4	
	Criterion 3
5	
	Criterion 4
	Criterion 5
	Criterion 6
	Criterion 7
	Criterion 8
	Criterion 9

Additional Co-sponsoring Organizations

CO-SPONSORING ORGANIZATION #2	
Name	Organization
Aviva Rosenberg, JD	Gaucher Community Alliance
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Patient Advocacy Group	
Address	
5255 Fair Oaks St, Pittsburgh, PA 15217	
Email Address	Telephone Number
aviva@gauchercommunity.org	504-782-2057
CO-SPONSORING ORGANIZATION #3	
Name	Organization
Ozlem-Goker Alpan, MD	LDRTC
Affiliation (i.e., health professional, researcher, clinician, advocate)	
HCP, Researcher, Clinician	
Address	
3702 Pender Drive, Suite 170, Fairfax, VA 22030	
Email Address	Telephone Number
ogoker-alpan@ldrtc.org	703-261-6220
CO-SPONSORING ORGANIZATION #4	
Name	Organization
Carlos Prada, MD	Lurie Children's Hospital of Chicago
Affiliation (i.e., health professional, researcher, clinician, advocate)	
HCP, Researcher, Clinician	
Address	
225 E. Chicago Ave. Chicago, Illinois 60611	
Email Address	Telephone Number
cprada@luriechildrens.org	312.227.6763
CO-SPONSORING ORGANIZATION #5	
Name	Organization
Affiliation (i.e., health professional, researcher, clinician, advocate)	
Address	
Email Address	Telephone Number

Submission Checklist	
☒	Nomination form
☒	Conflict of Interest Forms completed by Nominator and all Co-Sponsoring Organizations
☒	PDF(s) or hard copies of references
Contact information of Nominator: Sheldon Garrison PhD, sheldon.garrison@rogersbh.org and Michael Finkel, DO, mfinkel@mcw.edu	

Submit Nominations to: DHSWICongenitalDisorders@wisconsin.gov

Or mail to:

WI Division of Public Health
Newborn Screening Program
1 West Wilson Street – Room 233
Madison, WI 53703