December 4, 2023

Office of the Center Director
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Ave, Bldg. 66
Silver Spring, MD 20993

Re: Comments to Docket: FDA-2023-N-2177, Medical Devices, Laboratory Developed Tests Proposed Rule

On behalf of the Association of Public Health Laboratories (APHL), please accept the following comments concerning the Medical Devices, Laboratory Developed Tests (LDT) Proposed Rule, Docket No. FDA-2023-N-2177.

APHL strongly believes in accurate and quality testing and agrees that the Food and Drug Administration (FDA) has a role in oversight of LDTs to ensure they are producing reliable results for patients and providers; however, the proposed rule and any associated guidance must be carefully crafted and consider all possible impacts to avoid unintended consequences that could limit access to certain tests and place an undue burden on the public health system.

Public health laboratories (PHLs) utilize LDTs to support public health, promote health equity, prevent the spread of disease, conduct surveillance, develop disease treatment and prevention guidelines, and respond to public health emergencies effectively and efficiently. PHLs fulfill these inherently governmental functions by offering LDTs for newborn screening (NBS), infectious diseases, foodborne diseases, emergency preparedness and response, and chemical exposure assessment.

The Medical Devices, Laboratory Developed Tests Proposed Rule has the potential to reduce or eliminate access to specific testing that provides important public health benefits. As the FDA considers input from comments, it is critical to the nation's public health that PHLs continue to operate and fulfill their unique mission under the final rule. APHL has several concerns about the proposed rule language, and we ask that these concerns be addressed in the development of the final rule and any associated guidance.

Concerns

PHLs make extensive use of LDTs, and the proposed rule would hinder their ability to respond to public health outbreaks, conduct surveillance activities, and prepare and respond to public health emergencies. A subset of LDTs of public health significance conducted by high-complexity, Clinical Laboratory Improvement Amendments (CLIA)-certified PHLs is appended to this letter.

1. **The Medical Devices, Laboratory Developed Tests Proposed Rule has the unintended consequence of decreasing or limiting access to tests of public health concern.**

   PHLs utilize LDTs to protect public health and respond effectively to health threats and emergencies.
   PHL LDTs have been developed for rare pathogens of high consequence, such as multi-drug resistant *Mycobacterium tuberculosis* (MTB) and Lassa Fever, often utilizing automated high-throughput steps optimized to test for multiple pathogens to allow for rapid response not possible under the proposed framework. In urgent scenarios, like pandemics, novel infections, or biological or chemical threat agents, it is potentially harmful to patient populations and communities to prohibit or delay the use of these validated LDTs, jeopardizing the mitigation of further spread of highly infectious diseases or chemical exposure reduction efforts and medical treatment. It may also complicate the effort to improve the National Laboratory System.

   Infectious Disease Testing – Although the guidance document for public health emergencies referenced on page 50 may be helpful to PHLs during large outbreaks, it should be expanded to include more limited situations as well. An example is the importance of the LDT mpox assay created by the San Francisco PHL, which is not a Laboratory Response Network (LRN) laboratory, to the national mpox public health response. As is often the case with emerging infectious diseases, an LDT was the first assay available, and its fast implementation was critical to outbreak response and disease mitigation.

   Biological and Chemical Threat Response – PHLs use LDTs to maintain the capability for low-incidence, high-priority threats such as biological or chemical agents. These assays provide definitive results for the basis of critical public health decisions. They include the LRN for Chemical Threats (LRN-C) methods for cyanide, volatile organic compounds, toxic metals, and warfare agents and the LRN for Biological Threats (LRN-B) methods for *Francisella tularensis*, Ebola virus, and *Yersinia pestis*. PHLs serve as reference laboratories that perform testing for high-risk clinical specimens, and these LDTs are crucial to our nation's ability to respond to threats. To maintain national and local preparedness for biological and chemical emergencies, any regulatory reviews of these specialized LTDs should be allowed to be phased in over a period of time and not face excessive documentation requirements.

   PHLs utilize LDTs when an FDA-approved test is not available or when the FDA-approved tests that are available are insufficient.
   The proposed rule would have a detrimental impact on public health, where essential testing is often only offered as LDTs. Many LDTs for rare agents and diseases have a high cost and low demand; there is low likelihood that conventional manufacturers will seek FDA approval because the production of

the tests does not have a sufficient economic benefit. PHLs need continued enforcement discretion for tests of public health significance so public access to this testing is not limited or eliminated. PHLs do not profit from LDTs, and the net expense associated with them makes it unlikely the testing would be conducted elsewhere; PHLs perform LDTs for the sole benefit of protecting public health.

Newborn Screening – PHL NBS programs assess millions of babies each year for congenital or heritable disorders that cause serious health consequences or death. State governments mandate the tests infants are screened with based on the Recommended Uniform Screening Panel (RUSP); disorders are added to the RUSP by the Secretary for Health and Human Services after advisement from the Advisory Committee on Heritable Disorders in Newborns and Children. The suggested disorders are based on evidence that includes data from laboratory screening, confirmatory testing, and pilot studies; however, it is not uncommon for tests to be added to the RUSP without the availability of an FDA-approved assay, which recently occurred with mucopolysaccharidosis type II (MPS II) and guanidinoacetate methyltransferase deficiency (GAMT). PHLs must then validate and implement LDTs for these disorders within the timeframe required by their state governments. At least one state NBS program performs testing without any FDA-approved NBS assays.

LDTs give PHLs more flexibility with their NBS panels, allowing them to make modifications such as multiplexing the targets into one assay or utilizing instruments they already have at their laboratory when space, funding, and time is limited. There are many state variations in NBS panels, and it will be difficult to have FDA-approved tests that cover all permutations. The proposed changes will impact the speed at which newly added conditions will be implemented at PHLs, thus negatively impacting the health and well-being of infants and children.

Some NBS LDTs are more sensitive than the FDA-approved alternatives, such as the multiplexed severe combined immunodeficiency and spinal muscular atrophy (SCID/SMA) LDT offered by the Missouri PHL. The FDA-approved NeoBase 2 assay has a high false positivity rate for X-linked adrenoleukodystrophy (X-ALD) and requires an LDT for second-tier testing. To reduce the burden of follow-up and stress on families, the Missouri PHL utilizes the X-ALD LDT as their first-tier assay.

Sexually Transmitted Infection (STI) Testing – FDA-approved confirmatory tests do not exist for some STIs of public health significance, and where screening tests exist, they are sometimes of poor quality. The available herpes simplex virus (HSV) FDA-approved tests have poor specificity and confirmatory testing is needed. The HSV LDT Western blot confirmatory assay developed by the University of Washington is significantly more specific (99% specificity) at differentiating between HSV-1 and HSV-2 antibodies; if FDA approval for this assay is not pursued (such as due to staff, budgetary, or resource limitations), then the resulting removal of the assay will deny patients access to a more reliable test.

Infectious Disease Testing – LDTs are important to communicable disease control. The Wisconsin PHL offers two measles polymerase chain reaction (PCR) assays that determine (1) whether a patient has an infection and (2) whether that infection is from the measles vaccine or the wild-type virus. The results drive follow-up protocols: a vaccine-induced infection would not require a public health

response, whereas a patient with a naturally acquired infection would be isolated, and in-depth contact tracing would ensue with quarantine of close contacts and a public vaccination campaign. Other equally important infectious disease LDTs include MTB PCR for the rapid identification of MTB from specimens to guide patient care and public health response and *Neisseria meningitidis* serogrouping PCR to determine which vaccine should be used to control outbreaks. Please refer to the appendix for additional examples; delaying or eliminating this testing would lead to a significant risk to the treatment and control of these diseases.

Biomonitoring/Chemical Exposure Assessment – All PHL and many hospital laboratory toxicological confirmatory tests are LDTs, and some are critically important to the health of vulnerable populations, such as pediatric blood lead testing. Lead testing identifies children needing specialized medical treatment (such as chelation therapy or iron supplementation) and public health interventions like case investigation, environmental testing, and exposure reduction. The only FDA-approved assay for blood lead is a point-of-care test for capillary blood (a screening assay) that is less sensitive and less specific than the PHL LDTs. The results are also not appropriate to inform medical or public health intervention.

Chemical exposures disproportionately impact minority and low-income populations, and PHL toxicological LDTs that measure concentrations of toxic metals in clinical specimens, such as arsenic, mercury, and cadmium, are important in identifying exposure sources and treatment options. Mass spectrometry-based LDTs are the only available tests for the quantitative measurement of toxic pesticides, polychlorinated biphenyls, per- and polyfluoroalkyl substances (PFAS), and other organic toxicants; they enable medical management and/or exposure assessment for the affected patients.

PHLs utilize LDTs when the FDA-approved test does not meet all population, specimen type, or testing volume needs.

Newborn Screening – The proposed rule states some LDTs do not include enough representation of minority populations; however, neither do some FDA-approved assays. Most approved panels for cystic fibrosis mutation analysis include few cystic fibrosis disease-causing variants commonly found in African Americans, Hispanics, and Native Americans. Additionally, detection of a specific disease-causing variant of the CPT1a gene found to be highly prevalent in indigenous populations of Alaska (and associated with sudden infant death when found to be homozygous) can only be performed by an LDT. An FDA-approved test for this gene does not currently exist and is unlikely to be developed, given that it affects a very specific population.

Sexually Transmitted Infection (STI) Testing – PHLs utilize chlamydia and gonorrhea (CT/GC) LDTs to expand the list of acceptable specimen sources or population age ranges. FDA-approved assays for CT/GC are often limited to vaginal swabs and urine specimens that are self-collected under the supervision of a physician or at a clinic; however, expanded specimen source and at-home collection for STIs has high acceptability and user uptake. A reduction in testing from the removal of these LDTs may reduce testing rates and could result in increased STI incidence. PHLs also utilize CT/GC LDTs to

broaden the acceptable population age range for testing, such as testing in those less than 16 years old. Removing access to those LDTs would increase the burden of supporting child sexual assault victims and impede public health efforts acknowledging that teenagers are sexually active.

Infectious Disease Testing – PHLs often modify FDA-approved assays to increase the time from collection to testing or expand acceptable temperature or humidity ranges. For many PHLs, unaffordable building enhancements would be needed to keep humidity at the level specified by the assay manufacturer during the winter. Quality testing is assured by meeting the performance specifications mandated by CLIA regulation 42 CFR §493.1253(b)(2) before testing patient specimens. This includes showing the accuracy, precision, sensitivity, specificity, and reportable range of the modified assay are comparable to those established by the manufacturer.

PHLs utilize LDTs to promote health equity and protect underserved populations.

Many states also have medically underserved or rural areas where it is not possible for the specimens to arrive at the PHL site for testing within the manufacturer's specified timeframe or at the proper temperature. Creating LDTs by utilizing the manufactured assays with the expanded specimen acceptance criteria after analytical validation and sample stability studies allows for the testing of these underserved, rural, and frontier populations. PHLs are frequently the only laboratories testing for rare diseases or conditions in rural states, and the populations they serve are often uninsured or underinsured. It is important that these groups are not only offered tests of public health significance (such as STI testing) but also that the data associated with surveillance testing from these populations is included in national databases to inform public health priorities such as vaccine formulation.

Some PHLs modify sample stability requirements to allow providers to send specimens at room temperature up to seven days after collection. This is especially important in large or rural states with difficulty transporting specimens from STI clinics to the PHL within the manufacturer's limited temperature range and timeframe. Modification of the FDA-approved assay allows PHLs to continue offering testing to high STI-risk populations.

PHLs utilize LDTs to test for drug resistance and where antimicrobial susceptibility and efficacy must be determined for drugs that may be FDA-approved for a different indication.

Sexually Transmitted Infection (STI) Testing – Many LDTs are utilized for prompt diagnosis, treatment, and transmission prevention. This is especially important in cases of antimicrobial resistance or with invasive strains, such as *Mycoplasma genitalium*, *Chlamydia trachomatis* lymphogranuloma venereum, and *Neisseria gonorrhoeae*. Removing access to these LDTs could result in increased spread of resistant strains.

Infectious Disease Testing – LDTs allow PHLs to create innovative solutions to public health problems. For example, the California PHL developed an LDT that enabled rapid detection of drug-resistant MTB directly in clinical specimens, which was found to significantly improve the timeliness of diagnosis and treatment of multidrug-resistant tuberculosis. Related, PHLs perform MTB antimicrobial susceptibility testing on some drugs that are not FDA-approved for treating MTB; however, those drugs have demonstrated efficacy and serve a critical role in treating drug-resistant TB. Although the California PHL had slender resources, it was able to validate these assays successfully; adding additional steps to the test implementation process for PHLs could inhibit important developments of this kind.

PHLs utilize LDTs to provide more services and serve a greater population.

NBS programs are not for profit, and many barely break even. When FDA-approved assays are available, they are often cost-prohibitive. For example, Revvity charges approximately $2.00 per test for the biotinidase assay, whereas the Washington PHL performs a biotinidase LDT for mere pennies. Similarly, the Tennessee PHL performs a SCID/SMA LDT at less than $1.00 per specimen instead of utilizing the FDA-approved Perkin Elmer test at $6.50 per specimen. The proposed rule will severely impact programmatic costs, constraining the amount of testing and timely follow-up that can be completed and negatively impacting the lives of babies and their families.

This holds true for other public health programs. Long-term care facilities often request norovirus testing during gastrointestinal illness (GI) outbreaks, and many PHLs utilize a norovirus PCR LDT because the FDA-approved assay (the BioFire GI Panel) is vastly more expensive. With limited funding available to cover the cost of testing, utilizing the FDA-approved test could negatively influence outbreak response and create a hardship for underinsured or uninsured populations.

2. **PHLs have limited resources.**

PHLs are often tasked to fill gaps that would negatively affect public health if left unmanaged. Unfortunately, PHLs are not adequately funded or staffed, and with each PHL performing dozens to hundreds of LDTs, many of which do not have a predicate device, the cost to PHLs could be insurmountable. The majority of PHLs have never submitted premarket approval (PMA) or 510(k) documentation, and they barely have the personnel necessary to perform their daily testing obligations; many new positions would be needed to complete those applications. They are not equipped to redirect staff for filing FDA submissions and do not have the financial resources to pay user fees or hire additional staff. APHL member laboratories have indicated they will have no choice but to stop some critical testing if forced to comply with the proposed rule as written. PHLs must not have a significant burden placed on their staff or their limited operating budget.

3. **The proposed rule would have a detrimental impact on public health surveillance and outbreak monitoring activities.**

APHL appreciates the proposed rule provides for limited continued enforcement discretion of public health surveillance tests in connection with disease prevention and control where the results are not

reported to the patient or provider; however, PHLs participate in multiple disease monitoring efforts where report back is critical to the success of the program. Clinical laboratories and providers are incentivized to send specimens to PHLs for these projects because they receive the test results; eliminating that opportunity will reduce buy-in, lead to poor data collection, and limit the public health response. The Wisconsin PHL coordinates the Wisconsin Clinical Laboratory Network, a group of labs that participate in surveillance efforts such as submitting enteric pathogens that may be associated with foodborne illness outbreaks to the PHL. Submitting isolates for characterization allows the PHL to detect and respond to outbreaks quickly, preventing additional disease spread.

Recommendations

APHL recommends the following:

1. Expand the scope of enforcement discretion for public health surveillance testing to ensure representative data is collected from all populations. This includes surveillance testing where results are returned to the provider.

2. Provide enforcement discretion for LDTs PHLs have developed, validated, and used for at least two years without any reported adverse consequences.

3. Provide a less burdensome approval pathway for tests of public health significance that are designed for use on commercially available instruments using commercially available reagents. While it is understood that LDTs are in vitro diagnostics (IVDs) by regulatory definition, there are significant differences in complexity and instrumentation when comparing PHL LDTs to manufacturer-initiated IVDs. This simplified procedure would verify test performance characteristics with less documentation than the standard PMA or 510(k) process.

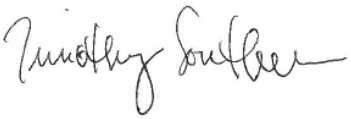
4. Continue enforcement discretion for PHL assays that are LDTs due to certain types of modifications to FDA-approved tests and clearly define what modifications to an FDA-approved protocol will not require additional review. Examples that should not require additional review include changing the supplier of an enzyme, modifying a temperature in a PCR protocol, augmenting an assay for high-throughput (such as utilizing an extraction instrument or direct load tubes), expanding the acceptable population age range, or adding specimen sources and matrices.

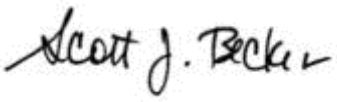
5. Expand the scope of enforcement discretion before and during public health emergencies to include assays needed for outbreaks of any size and other situations of public health significance. The final rule should not be so restrictive that it hinders test development and prevents proactive public health response to emerging issues that must be addressed quickly to mitigate morbidity and mortality.

6. Stratify the phaseout period for all LDTs by annual test volume and risk to patients, and phase out low-risk LDTs last. Regulate high-volume LDTs first due to their impact on a larger patient population. Provide risk stratification definitions and guidance on submitting PMA, 510(k), and de novo application packages. Include templates, flowcharts, standard operating protocols, and data requirements.

APHL appreciates the opportunity to provide recommendations to the FDA to help shape the Medical Devices, Laboratory Developed Tests Proposed Rule. For more information, please contact Amanda Cosser, APHL Manager of Regulatory and Public Policy, at amanda.cosser@aphl.org. APHL looks forward to continued conversations with the FDA as modifications are made to the proposed rule.

Sincerely,





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Appendix: The following table is a subset of LDTs of public health significance conducted by high-complexity, CLIA-certified PHLs.

Laboratory Developed Test Name	Description/Purpose/Justification of Use
Abrine/ricinine, urine	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by Centers for Disease Control and Prevention Laboratory Response Network for Chemical Threats (CDC LRN-C).
Acid fast bacilli (AFB) direct detection, high-performance liquid chromatography (HPLC) (sediments)	While there is an FDA approved method for direct detection of *Mycobacterium tuberculosis* complex (MTBC) there is no FDA-cleared method for direct detection of AFB. A method to detect all AFB is needed to detect other significant *Mycobacteria* species.
Acid fast bacilli (AFB) isolate identification, HPLC	
Actinomycete, HPLC	
Acylcarnitine profile, plasma	Tandem mass spectrometry (TMS)-based quantitation of acylcarnitine species for diagnostic testing and patient monitoring.
Acylcarnitine profile, serum	TMS-based quantitation of acylcarnitine species for diagnostic testing and patient monitoring.
Alcohols (methanol, ethanol, isopropanol, and acetone) in whole blood by gas chromatography/mass spectrometry (GC/MS)	There are no FDA-approved methods for these tests.
Amino acids and acylcarnitine TMS	
Amino acids, acylcarnitine	Fatty acid oxidation disorders (12); organic acidemias (12); amino acid disorders/urea cycle disorders (10).
Amino acids, dried blood spot	Ion-exchange chromatography-based quantitation of amino acids for patient monitoring. At-home testing and reduced cost compared to similar methods improve monitoring frequency and help clinical teams recognize potential adverse outcomes in a timely manner.
Amino acids, plasma	Ion-exchange chromatography-based quantitation of amino acids for diagnostic testing and patient monitoring.
Amino acids, serum	Ion-exchange chromatography-based quantitation of amino acids for diagnostic testing and patient monitoring.
Amino acids, urine	Ion-exchange chromatography-based quantitation of amino acids for diagnostic testing and patient monitoring.
Amphotericin B E test minimum inhibitory concentration (MIC) for yeast	There are no FDA-approved methods for this test.
Anaplasma phagocytophilum indirect fluorescent antibody assay (IFA)	Serves local population located in an endemic tick-borne disease area. No FDA-approved commercial alternatives available. Only research use only (RUO) kits or analyte specific reagent (ASR) components are available in the US.
Antimicrobial Resistance Laboratory Network (ARLN) yeast identification matrix assisted laser desorption ionization (MALDI)	Identification of uncommon yeast spectra not included in FDA-cleared libraries including species such as *Candida auris*.

Antimicrobial resistance polymerase chain reaction (PCR)	Identification of antibiotic resistance genes; a CDC-developed method.
Arbovirus IgM Capture ELISA: La Crosse virus, Jamestown Canyon virus, & Powassan virus	IgM testing for local arboviruses for clinical diagnosis where an FDA-cleared test does not exist.
Arbovirus IgM microsphere immunoassay (MIA): West Nile Virus/St. Louis encephalitis virus, eastern equine encephalitis virus	IgM testing for local arboviruses for clinical diagnosis where an FDA-cleared test does not exist.
ARLN: Expanded antimicrobial susceptibility testing (AST)	There are no FDA-approved methods for this test.
ARLN-CDC-CRAB broth microdilution (BMD)	Detection of carbapenem-resistant *Acinetobacter baumannii.*
ARLN-CDC-CRE BMD	Detection of carbapenem-resistant Enterobacterales.
ARLN-CDC-CRPA BMD	Detection of carbapenem-resistant *Pseudomonas aeruginosa.*
Avian flu PCR	There are no FDA-approved methods for this test.
Babesia duncani IFA	Serves local population located in an endemic tick-borne disease area. No commercial alternatives available. Only RUO kits or ASR components are available in the US.
Babesia microti IFA	Serves local population located in an endemic tick-borne disease area. No commercial alternatives available. Only RUO kits or ASR components are available in the US.
Babesia microti PCR	Molecular confirmation and species determination of positive babesia slides.
Bacillus anthracis	PCR is 510K cleared, but not the bacteriophage assay.
Bacillus anthracis nucleic acid amplification test (NAAT), direct specimen/sample	PCR assay distributed via the LRN.
BD MAX DNA-1 for *C. auris*	There are no FDA-approved methods for this test.
Biomonitoring (chemical exposure) assays: Venous blood lead testing using inductively coupled plasma mass spectrometry (ICP-MS, GFAAS); trace element analysis in blood and urine (ICP/MS) arsenic speciation using liquid chromatography-inductively coupled plasma mass spectrometry (LC-ICP-MS); organic chemical analysis such as per- and polyfluoroalkyl substances (PFAS) in serum using liquid chromatography mass spectrometry (LC/MS); chlorinated pesticides, industrial chemicals, and polychlorinated biphenyls (PCBs)	If the rule is approved, then the FDA approval process would be prohibitively resource intensive. Chemical exposures disproportionally impact minority and low-income populations; withholding individual biomonitoring information from participants would have a greater impact on these vulnerable populations.
Biotinidase	Biotinidase deficiency, newborn screening.
Biotinidase activity, serum	Spectrophotometric measurement of biotinidase enzyme activity for diagnostic testing and patient monitoring.
Blood metals (examples include Hg, Pb, and Cd) (ICP/MS)	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.

Bordetella pertussis, B. parapertussis, B. holmseii PCR	Efficient test for detection of *B. pertussis, B. parapertussis,* and B. *holmseii* for public health purposes.
Bordetella pertussis/holmesii PCR	Assay distributed by the state laboratory for rapid detection of cases and prevention of vaccine-preventable disease outbreaks at the local level.
Brucella abortus antibody	Antibody testing to aid in patient diagnoses and to assist clinical laboratories in post-exposure testing for *Brucella*, a very transmissible Select Agent.
Brucella IgG/MAT	
Brucella species detection, PCR	PCR assay distributed via the LRN for rapid detection of bioterrorism events and clinical diagnosis for clinical laboratories without biosafety level 3 (BSL3) capability.
Burkholderia mallei/pseudomallei detection, PCR	PCR assay distributed via the LRN for rapid detection of bioterrorism events and clinical diagnosis for clinical laboratories without BSL3 capability.
C. auris colonization	
C. auris real time PCR	There are no FDA-approved methods for this test.
C. pneumoniae PCR	
C26:0-Lysophosphatidylcholine	X-linked adrenoleukodystrophy (demonstration project).
CAH steroid profile	Congenital adrenal hyperplasia (second-tier).
Candida AST	Susceptibility testing of expanded panel of antifungals not in FDA-cleared panels, for national antibiotic resistance surveillance.
Candida colonization by culture	Culture-based colonization test to grow *C. auris* isolates for susceptibility testing and whole genome sequencing for outbreak detection and response.
Candida colonization by PCR	PCR-based colonization testing for rapid identification of colonized patients (results are used by infection prevention practitioners to identify and stop the spread of resistant yeast).
Carbapenemase resistance confirmation	
Carbapenemase producing enterobacteriaceae detection assay	There are no FDA-approved methods for this test.
Carbapenem-resistant enterobacteriaceae (CRE) AST	Susceptibility testing of expanded panel of antibiotics not in FDA-cleared panels, for national antibiotic resistance surveillance.
Carnitine palmitoyl transferase 1A arctic variant PCR	There are no FDA-approved methods for this test.
CFTR variant assay (second-tier)	Cystic fibrosis (CF) (second-tier).
Chikungunya virus, IgM	
Chromosomal microarray analysis (CMA), single nucleotide polymorphism (SNP)-based	The American College of Medical Genetics and Genomics (ACMG) recommends that CMA is used as a first-line test in the evaluation of individuals with multiple congenital anomalies, non-syndromic intellectual and developmental disability, and autism spectrum disorders. The American College of Obstetricians and Gynecologists recommends CMA in patients with a fetus with a structural abnormality detected by ultrasound and in cases of intrauterine fetal demise or stillbirth. Can be used to identify known familial copy number variants.

Chromosome analysis, amniotic fluid	Determination of fetal karyotype for: advanced maternal age, abnormalities observed on ultrasound examination, abnormal maternal serum screen, previous pregnancy with abnormal karyotype or parent with balanced chromosome rearrangement.
Chromosome analysis, blood	Determination of patient karyotype for: congenital anomalies, growth delays, developmental delays, syndrome identification, atypical sexual development, infertility, history of pregnancy loss, family history of chromosome abnormality, etc.
Chromosome analysis, chorionic villus sample	Determination of fetal karyotype for: advanced maternal age, abnormalities observed on ultrasound examination, abnormal maternal serum screen, previous pregnancy with abnormal karyotype or parent with balanced chromosome rearrangement.
Chromosome analysis, products of conception/tissue biopsy	Determination of fetal karyotype for: miscarriage, fetal demise, stillbirth. Skin biopsies may be used for individuals with suspected tissue mosaicism.
Clostridium botulinum toxin	
Cobas HPV	This assay is validated in-house to run on samples that have previously been processed on the Hologic T-5000.
Copy number determination for *SMN1* and *SMN2*	Spinal muscular atrophy (*SMN2* copy numbers).
COVID NGS (next generation sequencing of SARS-CoV-2)	Detection and reporting of COVID-19 variants.
Coxiella burnetii detection, PCR	PCR assay distributed via the LRN for rapid detection of bioterrorism events and clinical diagnosis for clinical laboratories without BSL3 capability.
CRE colonization	Culture-based colonization test to grow resistant bacteria isolates for susceptibility testing and whole genome sequencing (WGS) for outbreak detection and response.
Cryptosporidium subtyping	Cryptosporidiosis is a nationally notifiable disease in the United States. *Cryptosporidium* species and subtypes are generally indistinguishable using conventional diagnostic methods. Molecular characterization is important to increase knowledge about risk factors and transmission patterns and to promote community cryptosporidiosis prevention education.
Cyanide, whole blood (GC/MS)	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.
Cyclospora identification (PCR)	*Cyclospora* infection is a nationally notifiable disease in the United States. Even patients who are symptomatic might not shed enough oocysts in their stool to be readily detectable by standard stool examination. Identification of the parasite requires special laboratory tests that are not routinely done when stool is tested for parasites.
Dengue virus typing RT-PCR	Molecular identification and typing of dengue virus, for rapid identification and clinical diagnostic use.
DNA genotyping for CF	There are no FDA-approved methods for this test. The LDT is a custom-built panel from CF cases found in Washington State.
DNA SNP analysis for hemoglobin disorders and galactosemia	There are no FDA-approved methods for this test. The DNA results are a second- or third-tier screening test that helps the follow-up team know how urgent clinical care is needed.

DNA testing of CF	Second-tier newborn screening assay.
DNA testing of galactosemia	Second-tier newborn screening assay.
DNA testing of hemoglobinopathy	Second-tier newborn screening assay.
DNA testing of medium chain acyl-CoA dehydrogenase deficiency	Second-tier newborn screening assay.
DNA testing of very long chain acyl-CoA dehydrogenase deficiency	Second-tier newborn screening assay.
Dynabead enrichment	Modified package insert based on CDC recommendation. This test is part of a procedure and does not produce a final result for reporting.
E. coli stx PCR	WGS characterization of *E. coli*.
Eastern equine encephalitis/West Nile virus/St. Louis encephalitis microsphere immunoassay (EEE/WNV/SLE MIA)	This LDT is a screening test for antibodies to EEE/WNV/SLE. The commercial screening assays for arbovirus antibodies are either not available or too expensive. The approval of the proposed LDT rules would adversely affect the PHL testing capacity for arboviral diseases.
Ebola Zaire	LRN PCR assay.
Ehrlichia chaffeensis IFA	At the time of implementation, there were no FDA-approved commercial alternatives available. Only RUO kits or ASR components are available in the US.
Enterovirus, RT-PCR	For rapid detection of acute flaccid myelitis (AFM) cases at the local level.
Enzyme activity assay for biotinidase deficiency	An FDA-approved method exists, but the difference in cost between it and the LDT is substantial. The simple LDT costs pennies per specimen analyzed.
ExAST	Aztreonam-avibactam susceptibility testing for very resistant bacteria.
Exome sequencing- duo analysis	The ACMG recommends that exome sequencing be considered as a first- or second-tier test in the evaluation of individuals with congenital anomalies, developmental delay, and/or intellectual disability (PMID: 34211152). Establishing a diagnosis in individuals with a known or suspected genetic disorder for timely treatment and optimal outcomes; establishing a diagnosis in individuals with negative previous genetic testing (karyotype, chromosomal microarray analysis, single gene or gene panel testing).
Exome sequencing- proband analysis only	The ACMG recommends that exome sequencing be considered as a first- or second-tier test in the evaluation of individuals with congenital anomalies, developmental delay, and/or intellectual disability (PMID: 34211152). Establishing a diagnosis in individuals with a known or suspected genetic disorder for timely treatment and optimal outcomes; establishing a diagnosis in individuals with negative previous genetic testing (karyotype, chromosomal microarray analysis, single gene or gene panel testing).
Exome sequencing- trio analysis	The ACMG recommends that exome sequencing be considered as a first- or second-tier test in the evaluation of individuals with congenital anomalies, developmental delay, and/or intellectual disability (PMID: 34211152). Establishing a diagnosis in individuals with a known or suspected genetic disorder for timely treatment and optimal outcomes; establishing a diagnosis in individuals with negative previous genetic testing (karyotype, chromosomal microarray analysis, single gene or gene panel testing).

FISH analysis: SRY (sex determining region of Y), Yp11.3	Detection of the *SRY* gene in individuals with ambiguous genitalia or suspected sex chromosome aneuploidy disorder. May be performed in conjunction with other FISH assays, chromosome analysis or as an independent test.
FISH analysis: Stillbirth aneuploidy panel, paraffin embedded	FISH analysis of paraffin embedded placenta or fetal tissue to determine copy number of chromosomes 13, 16, 18, 21, 22, X and Y.
FISH analysis: X and Y sex chromosomes	Determination of sex chromosome complement in individuals with ambiguous genitalia or suspected sex chromosome aneuploidy disorder. Must be performed in conjunction with chromosome analysis.
FLU/SC2 with Kingfisher for extraction	Utilizing the Kingfisher for extraction of samples would be a deviation from approved extraction platforms as the Kingfisher is not included in the full FDA approval of the CDC Flu/SC2 multiplex PCR assay. This instrument allows for high throughput extraction and is sometimes the only instrument PHLs have for high throughput.
Fluorescent in situ hybridization (FISH) analysis: Deletion 22q11.2, TUPLE1	Detection of deletion 22q11.2 associated with DiGeorge/Velo-cardio-facial/Shprintzen/Conotruncal anomaly syndrome; phenotypic features include congenital heart disease, cleft palate, immune deficiency, low serum calcium levels.
Francisella tularensis antibody	Antibody testing to aid in patient diagnoses and to assist clinical laboratories in post-exposure testing for *Francisella*, a very transmissible Select Agent.
Francisella tularensis detection, PCR	PCR assay distributed via the LRN for rapid detection of bioterrorism events and clinical diagnosis for clinical laboratories without BSL3 capability.
Free and total carnitine, plasma	TMS-based quantitation of free and total carnitine for diagnostic testing and patient monitoring.
Free and total carnitine, serum	TMS-based quantitation of free and total carnitine for diagnostic testing and patient monitoring.
Full-gene variant detection for GAA	Pompe (second-tier).
Full-gene variant detection for HBB	Hemoglobinopathies (second-tier and confirmation).
GeneXpert MTB/RIF from culture broth, solid culture isolates and bronchoalveolar lavage (BAL)	Molecular identification and rifampin resistance testing of *M. tuberculosis* for rapid identification of resistant strains to immediately guide patient treatment. This modified FDA-assay allows for testing of important specimen types not FDA-approved by the manufacturer.
H. influenzae PCR	Detection of *Haemophilus influenzae* by PCR to confirm FDA-cleared test results and ensure serotyping PCR is used on the correct species.
H. influenzae serotyping PCR	Molecular serotyping to identify which serotypes are circulating, to inform future vaccine formulation and support patient care when vaccine failure is suspected.
Hantavirus IgG enzyme immunoassay (EIA)	There are no FDA-approved methods for this test.
Hantavirus IgM EIA	There are no FDA-approved methods for this test.
Hemoglobin patterns	Hemoglobinopathies (second-tier).
Hemoglobin-isoelectric focusing (IEF) assay	Newborn screening.
Hemoglobinopathy screening IEF	Newborn screening.

Hemoglobins Revvity RESOLVE Isoelectric Focusing and JB2 staining kit	Newborn screening.
Hepatitis A PCR	There are no FDA-approved methods for this test.
Herpes simplex virus 1 & 2, RT-PCR	Developed to replace cell culture assays.
HIV-1 proviral DNA PCR	Molecular identification of HIV-1 proviral DNA to determine if maternal-to-child transmission of HIV has occurred in neonates, also supports diagnosis of HIV as a part of CDC recommended algorithm. Provides a more definitive diagnosis of HIV infection post exposure in individuals taking prophylaxis.
Hologic direct load tubes	Assay is an LDT due to modification: The collection method utilizes a different collection media and is a deviation from the FDA cleared method. By utilizing direct load tubes, the PHL has decreased contamination risk, thus providing increased quality in a highly sensitive testing method.
Homocysteine	Homocystinuria (second-tier).
HSV 1 & 2/varicella zoster virus (VZV) PCR on Hologic Panther Fusion	Panther Aptima offers an FDA-approved kit for HSV 1 & 2, but it does not include VZV. Quidel offers an FDA-approved assay, but it is of poor quality.
IMP PCR	Molecular detection of IMP carbapenemase, supports culture-based isolation of resistant bacteria (colonization culture results are used by infection practitioners to identify and stop the spread of resistant bacteria).
In-house *Clostridium botulinum* toxin test, serum and stool	There are no FDA-approved methods for this test.
Ki-67	This IHC Stain was developed as an LDT before there were FDA-approved methods.
KPC/NDM-1 PCR	Molecular detection of KPC and NDM carbapenemases, supports culture-based isolation of resistant bacteria (colonization culture results are used by infection practitioners to identify and stop the spread of resistant bacteria).
LC/MS/MS analysis of C26:0 LPC for X-ALD screen	Newborn screening.
Lead, whole blood, ICP/MS, GFAAS	Definitive testing to identify lead exposed/poisoned children and adults. There is no FDA-approved test for venous blood (the required specimen type for medical management).
Legionella PCR	Detection and differentiation (*Legionella* species, *Legionella pneumophila*, and *Legionella pneumophila* serogroup 1) for clinical diagnostic and public health outbreak response; WGS for identification of *Legionella* species.
Lewisite metabolites, ICP/MS	There is no FDA approved test. Methods are consistent with those used by the LRN-C.
LRN-C assays	All human exposure assays under the Public Health Emergency Preparedness mission for the LRN-C are considered LDTs.
Lysosomal storage diseases (LSD)	Newborn screening.
M. pneumoniae PCR	
M. tuberculosis and *M. avium complex* detection by real-time PCR (NAAT/MAC)	For in-house identification of purified isolates only; NAAT replaced by FDA-approved Cepheid GeneXpert assay.

MAC PCR	Molecular identification of *M. avium* complex from many specimen types, for rapid identification of this pathogen. No FDA-cleared tests are currently available for this purpose.
MAC-ELISA testing	This is a manual three-day antibody LDT that screens for EEE, WNV, SLE, Powassan, Jamestown Canyon, and many other arboviral diseases individually. MAC-ELISA has been known to pick up new emerging arboviral disease due to cross-reactivity that can be seen. Only the CDC or some PHLs have capacity to perform the confirmatory testing using PRNT.
Malaria PCR	Molecular confirmation and species determination of positive malaria slides.
MALDI-time of flight mass spectrometry (MALDI-TOF MS)	Identification of difficult-to-identify bacteria, mycobacteria, and fungi not covered by FDA-cleared tests.
MBL Procedure	There are no FDA-approved methods for this test.
mCIM	Phenotypic detection of carbapenemase production, Clinical Laboratory & Standards Institute (CLSI) standard.
MCR-1,2 multiplex real-time PCR Assay	There are no FDA-approved methods for this test.
Measles detection, RT-PCR	RT-PCR assay distributed via the LRN for rapid detection of cases and prevention of vaccine-preventable disease outbreaks at the local level.
Measles genotyping	Molecular genotyping of measles virus which assists in molecular epidemiology of tracking measles and contributes valuable information about importation into the U.S. and toward the elimination of measles worldwide.
Measles IgG	
Measles IgM IFA	IgM antibody testing to assist in diagnosing (or ruling out) measles infection for this very consequential pathogen.
Measles vaccine PCR (MeVa)	Molecular typing to determination if a measles PCR positive result is caused by wild-type or vaccine-strain measles, which greatly impacts public health follow-up.
Measles/Mumps PCR	There are no FDA-approved methods for this test; will impact public health from responding to an emergency if access to it is eliminated.
Measles/mumps/rubella (MMR) EIA	There are no FDA-approved methods for this test.
Measurement of *SMN1*	Spinal muscular atrophy (SMA) testing.
Measurement of TRECs	Severe combined immunodeficiency (SCID) testing.
Mercury (Hg), urine	There are no FDA-approved methods for this test; the methods are consistent with what is currently recommended by CDC LRN-C.
Merifluor direct fluorescent antibody (DFA)	Detection of *Cryptosporidium* and *Giardia*.
Methylation-specific PCR, *SNRPN* gene, 15q11.2	Diagnosis of Prader Willi Syndrome or Angelman Syndrome.
Methylmalonic acid, dried blood spot	LC-MS-MS-based quantitation of methylmalonic acid for patient monitoring. At-home testing and the reduced cost compared to similar methods improve monitoring frequency and help clinical teams to recognize potential adverse outcomes in a timely manner.
Methylmalonic acid, plasma	LC-MS-MS -based quantitation of methylmalonic acid for diagnostic testing and patient monitoring.

Methylmalonic acid, serum	LC-MS-MS -based quantitation of methylmalonic acid for diagnostic testing and patient monitoring.
Methylmalonic/methylcitric acid	Propionyl CoA carboxylase deficiency and methylmalonic acidemia (second-tier).
Microbiological Sciences 183 AMD Cecret Pipeline for Analyzing Sequencing Data of SARS-CoV-2	
Middle East respiratory syndrome coronavirus (MERS-CoV) PCR	There are no FDA-approved methods for this test.
Modified carbapenem inactivation method (mCIM)	Phenotypic test to identify if a resistant bacteria has a carbapenemase, as a first step in our carbapenemase testing that also includes PCR to identify the specific enzyme, AST for susceptibility, and potentially WGS for public health purposes.
Molecular analysis, Fragile-X, genetic diagnosis	To identify expansions of the CGG repeats in the *FMR1* gene in Xq27.3 associated with *FMR1*-related disorders (fragile X syndrome, fragile X-associated tremor/ataxia syndrome (FXTAS), and *FMR1*-related primary ovarian insufficiency (POI). Carrier screening for fragile X syndrome.
mpox (BT) PCR	There are no FDA-approved methods for this test.
mpox PCR on Hologic Panther Fusion	
Mucicarmine	This special stain was developed as an LDT.
Multiplex PCR detection of *Legionella pneumophilia* sg1, *Legionella pneumophilia* sg 1-15, and *Legionella* spp.	There are no FDA-approved methods for this test.
Multiplex real-time PCR for the detection of *IMP* genes	There are no FDA-approved methods for this test.
Multiplex real-time PCR for the detection of *OXA-23*-like, *OXA-24/40*-like, and *OXA-58*-like genes	There are no FDA-approved methods for this test.
Mumps genotyping	Molecular genotyping of mumps virus which assists in molecular epidemiology of tracking mumps.
Mumps virus detection, RT-PCR	RT-PCR assay distributed via the LRN for rapid detection of cases and prevention of vaccine-preventable disease outbreaks at the local level.
Mumps, IgG	
Mycobacterium tuberculosis complex RT-PCR with rifampin	Assay is an LDT due to modification: non-sputum testing.
Mycoplasma pneumoniae NAAT	Developed as for a research project.
N. meningitidis PCR	Detection of *Neisseria meningitidis* by PCR to confirm FDA-cleared test results and ensure serogrouping PCR is used on the correct species.
N. meningitidis serogrouping PCR	Molecular serogrouping to determine which strain of *N. meningitidis* is causing disease and guide which *N. meningitidis* vaccine to be used to control outbreaks. Also used to support patient care when vaccine failure is suspected.
Neisseria gonorrhoeae (GC) AST	

Neisseria gonorrhoeae NAAT	Equity focus: Many sexually transmitted infection (STI) LDTs are validated to broaden acceptable sample collection sites to support STI testing in marginalized communities. For example, testing for GC/CT in persons < 14yo which is needed to reduce the burden for supporting child sexual assault victims and extra-genital testing (such as eye and rectal specimens) for LGBTQ populations.
Neisseria PCR	WGS serogroup determination for *Neisseria meningitidis*.
NeoLSD-Pope/MPS1 TMS	
Non-variola orthopoxvirus, RT-PCR	In response to the mpox public health emergency.
Norovirus genotyping	Molecular genotyping of norovirus which assists in the molecular epidemiology of tracking norovirus and informs future vaccine strain selection.
Norovirus PCR	This is a LDT that many long-term care facilities request for gastrointestinal illness outbreaks. The FDA-cleared test is more expensive (i.e., BioFire GI panel), and could create a hardship to underinsured or uninsured populations.
Nucleic acid amplification for *Mycobacterium tuberculosis* complex	
Organic acids, urine	GC/MS-based quantitative and qualitative assessment of organic acids for diagnostic testing and patient monitoring.
Organophosphate nerve agent metabolites (OPNA) in serum	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.
Orthopox, RT-PCR	RT-PCR assay distributed via the LRN for rapid detection of cases and prevention of vaccine-preventable disease outbreaks at the local level and rapid detection during a bioterrorism event.
OXA-23 PCR	Molecular detection of *OXA-23*-like carbapenemase, supports culture-based isolation of resistant bacteria (colonization culture results are used by infection practitioners to identify and stop the spread of resistant bacteria)
OXA-48-like PCR	Molecular detection of *OXA-48*-like carbapenemase, supports culture-based isolation of resistant bacteria (colonization culture results are used by infection practitioners to identify and stop the spread of resistant bacteria).
P16	This IHC Stain was developed as an LDT before there were FDA approved methods
P63	This IHC Stain was developed as an LDT before there were FDA approved methods.
Plasmodium PCR	Detection and characterization of *Plasmodium* species (*P. vivax, P. falciparum, P. malariae,* and P*. ovale/ovale* variant).
Quantitative analysis of ethylene glycol, blood	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by ATSDR.
Rabies DFA	There are no FDA-approved methods for this test; this is nationally-accepted protocol.
Real-time PCR for severe combined immunodeficiency and spinal muscular atrophy	Newborn screening.

Respiratory pathogen panel	Molecular identification of 21 respiratory pathogens for surveillance and outbreak response.
Rickettsia IgG IFA	
Rickettsia rickettsii IFA	At the time of implementation, there were no FDA approved commercial alternatives available. Only RUO kits or ASR components available in the US.
Rickettsia typhi IFA	At the time of implementation, there were no FDA approved commercial alternatives available. Only RUO kits or ASR components available in the US.
RT-PCR for *BCR/ABL1* fusion transcript, t(9;22)(q34;q11.2)	Detection of *BCR/ABL1* fusion transcripts associated with CML and ALL. Aids in diagnosis of hematologic disorders.
RT-PCR for *PML/RARA* fusion transcript, t(15;17)(q24;q21)	Detection of *PML/RARA* fusion transcripts associated with APL. Aids in the diagnosis and prognosis of hematologic disorders and for monitoring of disease after treatment or bone marrow transplant. May be performed in conjunction with FISH or chromosome analysis or as an independent test.
Rubella genotyping	Molecular genotyping of rubella virus which assists in the molecular epidemiology of tracking rubella virus.
Rubella PCR	Molecular identification for rapid and sensitive diagnosis of rubella infection for this very consequential pathogen.
S. pneumoniae antimicrobial susceptibility testing (AST)	Susceptibility testing of an expanded panel of antibiotics not available in FDA-cleared assays, for national antibiotic resistance surveillance.
S. pneumoniae PCR	Detection of *N. meningitidis* PCR to confirm FDA-cleared tests and ensure serotyping PCR is used on the correct species.
S. pneumoniae serotyping conventional PCR	Molecular serotyping to identify which serotypes are circulating, to inform future vaccine introduction. Also used to support patient care when vaccine failure is suspected.
Salmonella molecular serotype (SMS)	Molecular serotyping workflow part of the BioNumerics platform.
Sanger sequencing	Potential use for newborn screening confirmatory testing
SARS-CoV-2, RT-PCR	Assay is an LDT due to modification: additional specimen sources/transport media.
SARS-CoV-2/Flu/RSV	Assay is an LDT due to modification: additional specimen sources/transport media.
Schistosoma (EIA)	Schistosomiasis is considered one of the neglected tropical diseases (NTDs). The eggs tend to be passed intermittently and in small amounts and may not be detected by standard stool or urine microscopy, so it may be necessary to perform a blood (serologic) test.
SCID/SMA	Newborn screening.
SCID/SMA Multiplex qPCR	Newborn screening.
SCID-SMA Screening: PCR	Newborn screening.
Second tier CAH assay by LC/MS/MS	Newborn screening.
Second tier DNA testing for SMA through PCR analysis of *SMN2* copy number	Newborn screening.
Select Agent ELISA - 1	ELISA for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.

Select Agent PCR - 1	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 2	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 3	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 4	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 5	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 6	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 7	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 8	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 9	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
Select Agent PCR - 10	Real-time PCR for the sensitive and specific identification of a potential bioterrorism agent on the Select Agent list.
SeqStudio 16s and *rpoB* sequencing	Identification of difficult-to-identify bacteria and mycobacteria not covered by FDA-cleared tests.
Shiga toxin gene detection (STEC), PCR	Implemented because it includes an *E. coli*-specific target to confirm identification of *E. coli* instead of having to confirm *E. coli* with biochemical methods (like API 20E); used to test both enrichment broths and bacterial growth from solid media.
Shiga toxin producing *E. Coli* PCR	Using PCR or whole-genome sequence analysis to facilitate recognition of specific *E. coli* pathotypes can assist in outbreak investigations. Rapid, accurate diagnosis of STEC infection is important because early clinical management decisions can affect patient outcomes and help prevent further transmission.
Smallpox (Non-variola PCR)	
St. Louis Encephalitis (SLE), IgM EIA	
Strongyloides, IgG	
Succinylacetone	Tyrosinemia Type I.
Sudden unexplained death in the young (SUDY) exome	The evaluation of sudden, unexplained death in the young (<45 years). Positive results are used to screen family members.
Targeted variant analysis via Sanger DNA sequencing	For the detection of specific targeted DNA variants. Can be used to identify familial variants of interest.
TB auramine O staining	There are no FDA-approved methods for this test.
TB Kinyoun acid-fast staining	There are no FDA-approved methods for this test; this assay is performed in-house only to the confirm the acid-fast isolate and the results are not reported back to the submitter.

TB NAAT identification	
TB PCR	Molecular identification of *M. tuberculosis* from many specimen types, for rapid identification of this very consequential pathogen. No FDA-cleared tests are available for this critical testing.
TB plate sensitivity	There are no FDA-approved methods for this test.
Tetramine, urine	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.
Tetranitromethane metabolites	
TMS analysis for amino acids & acylcarnitines	An FDA-approved method exists, but it is of poor quality. The LDT performs better in CDC proficiency testing challenges.
TMS analysis for amino acids, acylcarnitines, X-ALD and GAMT	Newborn screening.
TMS analysis for lysosomal storage disorders (Pompe, MPS I and MPS II)	Newborn screening.
TMS analysis for X-ALD	Newborn screening.
Total homocysteine, dried blood spot	LC/MS/MS-based quantitation of total homocysteine for patient monitoring. At-home testing and the reduced cost compared to similar methods improve monitoring frequency and help clinical teams to recognize potential adverse outcomes in a timely manner.
Toxic elements in urine (urine metals)—(As, Ba, Be, Cd, Pb, Th, and U) (ICP/MS)	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.
TREC	Newborn screening.
Trek sensititre broth microdilution *GN7F*	There are no FDA-approved methods for this test.
Trek sensititre broth microdilution yeast	There are no FDA-approved methods for this test.
Trichomonas (male urine)	Molecular identification of *Trichomonas* in a patient population that doesn't have FDA-clearance on the Hologic Panther instrument.
Variant detection for *ACADM* c.985A>G	Multiple CoA carboxylase deficiency (second-tier).
Variant detection for *BCKDHA* c.1312T>A	Maple syrup urine disease (second-tier for Plain communities).
Variant detection for *GALT* c.563A>G, c.404C>T, and c.940A>G	Galactosemia (second-tier).
Variant detection for *HSD3B2* c.35G>A	Congenital adrenal hyperplasia (second-tier for Plain communities).
Variant detection for *PCCB* c.1606A>G	Propionyl CoA carboxylase deficiency (second-tier for Plain communities).
Variant detection for *RAG1* c.2974 A>G	SCID (second-tier for Plain communities).
Variant detection for *RMRP* n.71 A>G	SCID (second-tier for Plain communities).
Variant NBS hemoglobin HPLC	Newborn screening.
Varicella-zoster virus (VZV) detection, PCR	PCR assay distributed via the LRN.
VDRL, serum and cerebral spinal fluid (CSF)	Syphilis antibody test, part of CDC-recommended algorithm. No FDA-cleared test exists for CSF which is important for diagnosis of neurosyphilis and impacts treatment decisions.
Vibrio parahaemolyticus, clinical isolate, PCR	Assay adapted from the National Shellfish Sanitation Program (NSSP) to test clinical isolates.
Vibrio speciation PCR	There are no FDA-approved methods for this test.

VIM (Verona integron-encoded metallo-B-lactamase) PCR	Molecular detection of VIM carbapenemase, supports culture-based isolation of resistant bacteria (colonization culture results are used by infection practitioners to identify and stop the spread of resistant bacteria).
Volatile organic compounds (VOCs), blood and serum	There are no FDA-approved methods for this test; the method is consistent with what is currently recommended by CDC LRN-C.
VZV genotyping	Molecular genotyping of VZV which assists in the molecular epidemiology of tracking VZV.
VZV strain typing	Molecular typing for rapid determination of whether a VZV PCR positive result is caused by wild-type or vaccine-strain VZV, which greatly impacts public health follow-up.
West Nile Virus, IgM EIA	
WGS, *Campylobacter* (MS 159 AMD)	*Campylobacter jejuni* is the most frequent cause of bacterial gastroenteritis in industrialized countries worldwide. Despite the high notification rates, *Campylobacter* infections are believed to be highly underdiagnosed, and a substantial number of *Campylobacter* outbreaks may be overlooked because of a lack of routine microbiological typing of isolates by WGS.
WGS, CRO (MS 203 AMD)	
WGS, *E. coli and Shigella*	Serotyping and virulence characterization of *Escherichia* using whole genome sequence data.
WGS, GC (MS 203 AMD)	
WGS, HAI (MS 203 AMD)	
WGS, *Listeria* (MS 159 AMD)	
WGS, *Salmonella*	Identification and serotyping using whole genome sequence data.
WGS, *Vibrio* (MS 159 AMD)	
WGS for foodborne disease surveillance	There are no FDA-approved methods for this test.
X-linked adrenoleukodystrohy TMS	Newborn screening.
Yersinia pestis detection, PCR	PCR assay distributed via the LRN for rapid detection of bioterrorism events and clinical diagnosis for clinical laboratories without BSL3 capability.