Market Access and Reimbursement

Navigating the Molecular Diagnostics Reimbursement Process

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Since the earliest map of the human genome was first completed, in 2003, applications of genetic testing have increased exponentially in both research and clinical settings. A 2018 study funded by the National Human Genome Research Institute estimated that there were then approximately 75,000 genetic tests in existence, representing roughly 10,000 distinct types of tests, with new tests entering the market at the rate of about 10 per day.[1] Of that estimated total, roughly 86% were single-gene tests and 14% were panel tests, including 9,311 multianalyte assays with algorithmic analyses, 873 whole-genome sequencing tests, 122 whole-exome sequencing tests, and 85 noninvasive prenatal tests (NIPTs). The researchers found that the highest percent of spending was for prenatal tests, followed by hereditary cancer tests.

Such a flood of new genetic tests entering the market has raised a corresponding need to address a wide range of health policy, regulatory, and reimbursement issues. Among the many genetic tests now on the market, only a handful have been submitted to FDA for authorization under the agency's premarket approval (PMA) process for in vitro diagnostics (IVDs). FDA granted its first premarket notification (510(k)) clearance for a genetic test in 2013, when the TruSight cystic fibrosis test by Illumina (San Diego) was cleared to run on the company's MiSeqDx high-throughput sequencing system.[2] Since then, FDA has cleared only a handful of genetic tests, meaning that the vast majority of such tests are being developed, validated, and performed as laboratory-developed tests (LDTs) in facilities licensed under the terms of the Clinical Laboratory Improvement Amendments of 1988 (CLIA).[3]

According to the Centers for Medicare and Medicaid Services (CMS), there are approximately 320,000 CLIA-certified laboratories in the United States. The category includes all hospital, reference, and physician-owned laboratories (POLs) that are permitted to perform various types of FDA-authorized and laboratory-developed tests, and to submit reimbursement claims to CMS.

CLIA certification is overseen by CMS with the objective of ensuring quality laboratory testing. Although certification does not impose

any direct Medicare or Medicaid program responsibilities on clinical laboratories, all labs seeking to submit claims and receive payments from Medicare or Medicaid must be properly certified and have their own CLIA number.[4]

While the primary function of clinical laboratories is to ensure that patients have access to testing that can lead to better health outcomes, laboratories in all healthcare settings have struggled to keep up with the ever-changing science needed to support submissions for reimbursement coverage and payment claims. The system has been especially overburdened by the rapid increase in genetic testing, creating a need for better methods of evaluating the clinical and economic benefits of such tests.

MACs and MolDx

CMS is responsible for overseeing the healthcare of more than 100 million Americans.[5] In light of the enormity of this task, the agency relies on a network of Medicare Administrative Contractors (MACs) to serve as the primary operational contacts between CMS offices and the healthcare providers enrolled in the program. There are 12 MACs with assigned geographical jurisdictions covering the United States (Table I). The MACs are each independently responsible for administrating both Medicare Part A and Medicare Part B claims in their respective jurisdictions.[6]

A prominent member of the group is Palmetto GBA (Columbia, SC), one of the nation's largest providers of high-volume claims and transactions processing, contact center operations, and technical services to the federal government and other commercial customers.[7]

After the initial mapping of the human genome, rapidly increasing use of molecular diagnostics—and the corresponding claims for reimbursement—created a need for better administration of such tests. In 2011, Palmetto GBA created the Molecular Diagnostic Services (MolDx) program, assigning it the task of establishing reimbursement policies for covering molecular diagnostic testing.

Palmetto uses the MolDx program to determine coverage, coding, and pricing for molecular diagnostic tests and other molecular pathology services administered through the MolDx program.[8] The MolDx program currently provides uniform policies for 28 states, across four Medicare Administrative Contractors (MACs).[9] Because of its prominence in so many jurisdictions, MolDx often influences the policies of other MACs. A successful MolDx submission will progress through three phases: test registration and ID assignment; technical assessment; and coverage determination and reimbursement.[10]

Test Registration

Test registration begins by connecting with Palmetto GBA's Diagnostics Exchange (DEX) Registry, a molecular diagnostic test identification and policy management solution that connects labs and payors. Laboratories seeking reimbursement from Palmetto must first register their molecular diagnostic tests online with DEX. In return, the laboratory will receive a DEX Z-Code Identifier—Palmetto's unique and proprietary five-character alphanumeric code assigned within DEX.[11] The DEX system uniquely identifies and catalogs each registered molecular diagnostic.

The remaining steps in the process of registering with DEX are straightforward. The applicant is asked to register as either a laboratory or hospital (the option to register as a manufacturer is available for organizations with an FDA-authorized molecular diagnostic

MAC Jurisdiction	Processes Part A & Part B Claims for the following states/territories:	MAC
DME A	Connecticut, Delaware, District of Columbia, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont	Noridian Healthcare Solutions, LLC
DME B	Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio, Wisconsin	CGS Administrators, LLC
DME C	Alabama, Arkansas, Colorado, Florida, Georgia, Louisiana, Mississippi, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia, Puerto Rico, U.S. Virgin Islands	CGS Administrators, LLC
DME D	Alaska, Arizona, California, Hawaii, Idaho, Iowa, Kansas, Missouri, Montana, Nebraska, Nevada, North Dakota, Oregon, South Dakota, Utah, Washington, Wyoming, American Samoa, Guam, Northern Mariana Islands	Noridian Healthcare Solutions, LLC
5	Iowa, Kansas, Missouri, Nebraska	Wisconsin Physicians Service Government Health Administrators
6	Illinois, Minnesota, Wisconsin **HH + H for the following states: Alaska, American Samoa, Arizona, California, Guam, Hawaii, Idaho, Michigan, Minnesota, Nevada, New Jersey, New York, Northern Mariana Islands, Oregon, Puerto Rico, US Virgin Islands, Wisconsin and Washington	National Government Services, Inc.
8	Indiana, Michigan	Wisconsin Physicians Service Government Health Administrators
15	Kentucky, Ohio **HH + H for the following states: Delaware, District of Columbia, Colorado, Iowa, Kansas, Maryland, Missouri, Montana, Nebraska, North Dakota, Pennsylvania, South Dakota, Utah, Virginia, West Virginia, and Wyoming	CGS Administrators, LLC
E	California, Hawaii, Nevada, American Samoa, Guam, Northern Mariana Islands	Noridian Healthcare Solutions, LLC
F	Alaska, Arizona, Idaho, Montana, North Dakota, Oregon, South Dakota, Utah, Washington, Wyoming	Novitas Solutions, Inc.
H	Arkansas, Colorado, New Mexico, Oklahoma, Texas, Louisiana, Mississippi	Novitas Solutions, Inc.
J	Alabama, Georgia, Tennessee	Palmetto GBA, LLC
K	Connecticut, New York, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont **HH + H for the following states: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont	National Government Services, Inc.
L	Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania (includes Part B for counties of Arlington and Fairfax in Virginia and the city of Alexandria in Virginia)	Novitas Solutions, Inc.
M	North Carolina, South Carolina, Virginia, West Virginia (excludes Part B for the counties of Arlington and Fairfax in Virginia and the city of Alexandria in Virginia) **HH + H for the following states: Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, Ohio, Oklahoma, South Carolina, Tennessee, and Texas	Palmetto GBA, LLC
N	Florida, Puerto Rico, U.S. Virgin Islands	First Coast Service Options, Inc.

Table I. Medicare administrative contractors (MACs) by state, as of June 2021. Table courtesy centers for Medicare and Medicaid Services.

for which a Z-Code is applicable). When the DEX team has reviewed the laboratory's registration information, the lab will receive a welcome e-mail with a link to set up and log in to a DEX account. Within a few weeks, the lab will receive an e-mail confirming that a unique Z-Code has been successfully assigned.

However, assignment of a Z-Code is not sufficient for submitting claims until the DEX clinical team has reviewed the test application to determine coverage and assign a 'common procedural terminology' (CPT) code. The lab will receive an e-mail from DEX when its test has been updated with the assigned CPT code and coverage in the DEX Registry.[12]

Technical Assessment

In some instances, the DEX review team may notify the lab that a determination of coverage requires additional forms and documentation as part of a technical assessment. Such technical assessments are often required for laboratory-developed molecular diagnostics, assays that employ next-generation sequencing (NGS) or other novel technologies, or assays that lack a defined or proven clinical utility.

To carry out their technical assessment, laboratories must complete a submission form and questionnaire, together with several other documents. To be considered, all of the documents needed as part of the assessment dossier must be completed.[13]

The central questionnaire of a DEX technology assessment is based on the ACCE model developed by the Centers for Disease Control and Prevention (CDC) for evaluating scientific data about emerging genetic tests.[14] The model takes its name from the four main criteria used in evaluating a genetic test:

- Analytical validity: The test's ability to accurately detect the variant of interest.
- Clinical validity: How well a positive test result correlates with the risk of disease.
- Clinical utility: Whether the test results in a measurable improvement in the patient's health or improves management of the patient.
- Ethical, legal, and social implications.

The technical assessment process can be slow and frustrating, especially if novel questions arise—as they frequently do. Establishing clinical utility is often the obstacle that companies trip over, particularly when a panel test is involved. Consider the following example.

MolDx has recently issued a local coverage determination (LCD), *Molecular Syndromic Panels for Infectious Disease Pathogen Identification Testing*, which seeks to define what constitutes a syndromic panel for infectious disease testing.[15] The LCD makes it very clear that panels "cannot be unbundled and billed as individual components, regardless of the fact that the test reports multiple individual pathogens and/or targets."[16]

The requirement of treating a syndromic panel as a single entity is a nightmare scenario for researchers seeking to demonstrate the clinical utility of a panel test. Demonstrating clinical utility for a single-analyte test is difficult enough. Doing so for an entire panel with scores of analytes would be unmanageably complex. Naturally, the published literature satisfying this requirement is virtually nonexistent. Nevertheless, Palmetto expects that laboratories will be able to support their clinical utility claims with published studies specific to each of the pathogens detected by their test.

Recognizing laboratories' frustration with its requirements, Palmetto has issued repeated updates of its frequently asked questions about molecular syndromic panels for infectious

disease testing.[16] But it is far from clear that such publications are sufficient for guiding laboratories through this process.

One company's technical assessment submission for a urinary tract infection (UTI) panel test has been repeatedly turned away for inadequate demonstration of clinical utility.

Palmetto's approach to helping laboratories through this complex process has been to issue a list of publications that "have been reviewed and have NOT adequately met the clinical validity and clinical utility criteria of the policy for urinary tract infection (UTI) panels."[17]

But Palmetto's list is far from exhaustive, and labs can readily be turned away for using a source that is only after the fact determined to be inadequate.

To prepare for the possibility that they may be required to undergo a technical assessment, labs may want to familiarize themselves with the information that will be required, with special attention to data that support the clinical utility of their test.

Coverage Determination & Reimbursement

In the past, laboratories seeking to optimize their reimbursement payments often adopted the strategy of 'code-stacking'—submitting a test under multiple appropriate CPT codes, with an expectation of reimbursement for each submitted code. But given the sheer volume of codes submitted, MACs simply didn't have enough time to review and approve each code on the basis of medical necessity.

MolDx was created to register and provide identification for molecular tests, to determine whether Palmetto GBA should cover the tests, and to determine appropriate reimbursement.

Unfortunately, the final steps in obtaining Medicare coverage and reimbursement have the potential to be the most frustrating of all. Not only is the process time-consuming—one company's submission took three years—it's also a 'black hole' where applicants rarely know much about the progress of their application.

The MolDx team is responsible for reviewing submissions, and may request additional evidence as necessary. Some such requests can become problematic for laboratories whose pockets aren't too deep. Supplying data from a head-to-head comparison with another test, for instance, could easily add a year—and significant costs—to a laboratory's already significant burden.

The longer it takes to get a final coverage determination from Medicare, the more revenue the laboratory will forego, and the more money it will have to invest in the MolDx process. In the meantime, any claims submitted by the lab will be denied as noncovered, until such time as the test's coverage is approved, and appropriate billing and coding guidelines are published to the provider community.[18]

Final Thoughts

The MAC jurisdiction for most laboratories is based on the state where the laboratory testing is performed (Table I). However, in some instances—such as reference laboratories with multiple locations—the MAC jurisdiction is based on the state where the billing takes place.[18]

The MolDx program, operated Palmetto GBA, currently provides services on behalf of four MACs (CGS Administrators, Noridian, Palmetto GBA, and Wisconsin Physicians Service).[19] Notably, each of these MACs has its own coverage policies, as reflected in their separate websites dedicated to the MolDx

program. Laboratories located in one of these jurisdictions should refer to their MAC's website for more information.

Although Palmetto's MolDx program has no official role in administrating claims submitted to commercial payors, a MolDx submission is often the first stop for laboratories seeking coverage from such payors. Both regional and national carriers have come to expect that laboratories will apply for a coverage determination from MolDx first, submitting their dossiers to commercial carriers only after they have a positive coverage determination in hand.

About The Deerborne Group

The Deerborne Group is a management consulting firm that focuses exclusively on the global in-vitro diagnostics and life sciences industries. The group's primary focus is advising corporations, venture capital, and private equity firms on commercial, operations, and corporate strategies, helping them to identify opportunities, minimize risks, and overcome management challenges.

Readers are encouraged to share this paper among their friends and colleagues. For further information, visit **The Deerborne Group** or follow the group on **Facebook**, **LinkedIn**, or **Twitter**.

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