Diagnostic testing in clinical laboratories

This educational series describes how clinical laboratories evaluate, implement, protect, and sustain diagnostic testing. It covers laboratory-developed tests (LDTs) and *in vitro* diagnostic (IVD) tests, and explains how successful testing strategies require more than assay performance—they also depend on clinical need, validation, regulations, quality systems, intellectual property, and reimbursement. Together, the papers in the series help laboratories decide when to use standardized commercial solutions; when to develop or modify tests internally; and what operational, legal, and economic considerations should be addressed.

The key insights of the five educational papers in this series are outlined below.

1. Molecular diagnostics, LDTs, and IVDs in modern healthcare

- There are trade-offs between LDTs and IVDs (e.g., flexibility vs. standardization)
- LDTs address unmet or specialized needs in oncology, rare disease, infectious disease, pharmacogenomics (PGx), transplant, liquid biopsy, and multicancer early detection (MCED)
- IVDs support scale, consistency, inventory simplicity, technical support, cybersecurity, and manufacturer-validated workflows
- Validation increasingly includes bioinformatics, AI, privacy, cybersecurity, and data governance

2: Modern laboratory-developed tests: how labs can prepare for and implement LDTs

- Before development, evaluate the clinical need, intended use, specimen type, detection range, turnaround time, patient population, analytical targets, and workflow integration
- Keep R&D and clinical testing separated; document research use only (RUO) use and handoff
- Clinical Laboratory Improvement Amendments (CLIA) certification, state licensure, and accreditation requirements guide LDT implementation; laboratories must align quality management systems (QMS), standard operating procedures (SOPs), personnel qualifications, proficiency testing, and documentation with the assay's complexity and appropriate regulations

3: Regulation of clinical diagnostics: FDA, CMS, and emerging challenges in lab testing

- Regulatory oversight in the US is split across the FDA (commercial IVD devices), CMS Centers for Medicare & Medicaid Services (CMS)/CLIA (laboratory quality and test complexity), and accrediting bodies such as College of American Pathologists (CAP)
- The regulatory status of LDTs is in flux: the FDA asserted device authority over LDTs in 2024 and attempted to curtail enforcement discretion; however, due to successful legal challenges, the FDA rescinded this new rule and restored the regulatory text that existed prior
- CLIA focuses on lab operations and analytical validation (e.g. accuracy, precision, personnel standards), making it central for high-complexity LDTs and complex molecular assays
- Research use only (RUO), investigational use only (IUO), and emergency use authorization (EUA) are described

4: Intellectual property associated with LDTs and IVD tests

- Novel platforms, reagents, workflows, or previously unassociated biomarkers are more promising patent candidates than conventional platforms or widely known markers
- Trade secret protection is a viable alternative for some LDTs; however, regulatory filings require public disclosure and independent reverse engineering is lawful
- Freedom-to-operate (FTO) analyses and patent landscape review should happen before major investment into new test development

5: Reimbursement trends and strategies for LDTs and IVD tests in the US

- Coding, coverage, and payment are separate; a code does not guarantee reimbursement
- Payers want clinical utility, medical necessity, impactful outcomes, and economic value
- MolDX, Z-codes, PLA/CPT strategy, RAPID, and AI reimbursement all affect adoption
- Reimbursement strategy should begin early in test development, because evidence generation, coding pathway, payer engagement, and health economic data can shape whether a test is adopted after it is technically validated

Which paper should I read first?

Scenario		Focus of the paper
I need the big picture on LDTs, IVDs, and molecular testing	Paper 1	Definitions, use cases, IVD vs. LDT trade-offs, precision medicine, AI/bioinformatics, validation, and QMSR
We are thinking about launching or modifying an LDT	Paper 2	R&D vs. clinical testing separation, intended use, platform/reagent decisions, SOPs, validation, QMS, proficiency testing (PT) training, and LIS/HIS
I need to understand regulatory boundaries	Paper 3	FDA vs. CMS roles, RUO/IUO limits, EUA, CLIA certificates, high-complexity testing, software/AI oversight, and regulatory uncertainty
We have a novel biomarker, assay method, or panel	Paper 4	Patentability, Mayo/Myriad limits, trade secrets, first-to-file urgency, freedom-to-operate, invalidity opinions, and IVD visibility risk
I need to understand how to get reimbursed for our test	Paper 5	Coding, coverage, payment, CPT/PLA, MACs, CLFS, MolDX and Z-codes, health economics, RAPID, and AI reimbursement

Diagnostic test implementation

Define clinical need and intended use	• What patient population, clinical decision, specimen type, turnaround time, and unmet need justify the test? • Is there an existing FDA-cleared/approved test that meets the need? • What clinical utility must be demonstrated before development moves forward?	Papers 1 and 2
Choose test pathway	• Should the lab implement an IVD, develop an LDT, or modify an assay? • Would FDA approval or a commercial pathway be needed for broad adoption or payment? • Does the lab prioritize flexibility, customization and speed, or standardization, manufacturer support, and reimbursement clarity?	Papers 1, 3, and 5
Build business, regulatory, IP, and reimbursement plan	• What CLIA, FDA, state, and accreditation issues apply to this test? • Could the assay, biomarker, method, software, or panel create IP value or infringement risk? • What coding, coverage, payment, and outcomes evidence requirements should be considered early?	Papers 3, 4, and 5
Design or select the workflow	• What platform, specimen type, reagents, controls, calibrators, and software or bioinformatics are needed? • What report format and LIS/HIS updates will be required? • What documentation is needed to support workflow consistency and inspection readiness?	Papers 2 and 3
Develop SOPs, QC plans, and validation protocols	• What SOPs, quality control (QC) processes, validation plan, and acceptance criteria must be created? • What training, competency, and QMS records are required? • How will the lab document controls, proficiency testing alternatives, and ongoing quality expectations?	Papers 2 and 3
Verify and/or validate performance	• Does the test meet requirements for accuracy, precision, analytical sensitivity, analytical specificity, and reportable range? • Are reference intervals, clinical validity, and clinical utility supported? • Have software, bioinformatics, or algorithm-dependent components been verified?	Papers 2 and 3
Prepare for launch	• Has the validation report been signed by the laboratory director? • Are staff trained and competent, and are PT or acceptable alternatives arranged? • Are reports—LIS/HIS updates, coding, the reimbursement path, etc.— ready for launch?	Papers 2, 3, and 5
Monitor, improve, and manage changes	• How will QC, PT, CAPA, and ongoing test performance be monitored? • How will lot changes, platform changes, software updates, algorithm performance, and retraining needs be managed? • How will reimbursement denials, payer audits, documentation requests, and test changes requiring additional verification/validation be tracked?	Papers 2, 3, and 5

Learn more at **thermofisher.com/LDTeducation** and **thermofisher.com/reimbursement**

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