LDT Review: The New York Experience

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• As the New York State Department of Health’s designee, the **Wadsworth Center**, through its Clinical Laboratory Evaluation Program (CLEP), regulates and oversees clinical diagnostic laboratories that test specimens from New York State patients; this includes review of LDTs

• The **Wadsworth Center**, as New York’s Public Health Laboratory, is held to the same regulatory standards as every other laboratory in New York
Our Experience as a Regulator
New York State, under Public Health Law and Regulation, requires that

“All technical procedures employed in a laboratory are of proven reliability and generally accepted by leading authorities in the specialties of laboratory medicine and/or approved by the Department”
These provisions require that

- Laboratories establish performance specifications for accuracy, precision, reportable range, reference interval(s), analytical sensitivity and specificity (analytical validation)
- Laboratories establish the clinical sensitivity and specificity of novel assays (clinical validation)
- Laboratories submit validation data and SOPM for review in accordance with guidelines established by the Department of Health prior to the marketing and use of the test system on patient specimens
In practice that means that a laboratory planning to offer non-FDA cleared or in-house developed tests (LDT), including off-label, RUO, IUO & ASR assays must:

- Develop a detailed SOP
- Conduct validation studies to demonstrate an assay’s analytical performance, including reproducibility and precision, and accuracy.
- Demonstrate an assay’s clinical validity, through clinical studies and/or review of literature data
- Submit the entire documentation for review to CLEP
• Clinical Laboratory Evaluation Program (CLEP) staff will review for completeness

• Wadsworth Center subject matter expert scientists will review the actual data, provide a written review, and make approval/denial recommendation to CLEP

• New labs must satisfy all validation requirements first before offering a new assay, established labs can get conditional approval during the review period.

• Guidance documents can be found at http://www.wadsworth.org/labcert/TestApproval/index.htm
Obtain CQ for director and assistant director(s) (if applicable)

- Permit application
  - Meet on-site inspection requirements
    - 1st LDT submission
      - Cannot test during review
      - CLEP administrative review
    - Routed to appropriate subject matter expert scientist for review
    - Can test during review
      - After multiple approved assays w/ similar technology
      - Conditional approval
      - Review letter to lab
        - Lab response <60 days
          - Testing allowed
          - Approved
          - Denied
Submissions must include

- SOP, including
  - Background and indication(s) for testing (intended use)
  - Specimen requirements, controls, performance criteria
  - Step-by-step procedure
  - Result interpretation

- Any advertising material
Furthermore …

- Patient reports that must include
  - Actual result
  - Interpretation of the result, if possible in the context of known clinical information
  - Method used
  - Limitations of the assay and disclaimers
- Validation protocol and actual validation data, comprising summary and representative examples of actual run data
- References and relevant reprints
Summary of workload data

• Over 10,000 unique applications received and reviewed since 1996

• 6038 currently approved (as of 5/12/2015)

• 98 denied

• 2852 inactivated

• 1440 currently in progress
LDT review workload (as of Q1, 2015)

Total >10,000 unique applications, not including replies to reviews
Rare Disease and Unmet Needs Provisions

Non Permitted Laboratory process

If no approved comparable test in a permitted laboratory is available then a physician can request an exemption with appropriate justification.

Up to 50 tests may be allowed to be performed before a full submission is required.

Applies to both unapproved tests in an otherwise permitted laboratory, or to any test in a laboratory that does not hold a NYS permit.
Our Experience as a regulated Laboratory
• LDTs provide flexibility to develop new assays when they are needed that is not dependent on a traditional IVD becoming available

• All elements required for a validation package submission should be part of a good test development and validation process anyway

• But, putting together validation packages is time consuming and takes resources

• It is like writing a manuscript, all elements are there, but it takes time to organize them in a logical manner

• Being forced to submit LDTs to an oversight body ensures proper validations are performed
• Biggest concern: length of time waiting for review; may prevent laboratory from meeting legislative mandates, especially in NBS

• Conditional approval allows testing during review and reduces the impact of the time delay from the review process

• The Non-permitted Laboratory process allows testing for rare analytes, provided the assay has been validated, without the need to submit a full validation package. Limited to 50 tests
Consensus of Wadsworth laboratory directors

• Overall, the impact of LDT regulation by New York is manageable, at least in its current implementation and practice
Conclusions

• From our perspective as a regulator, we believe that expanding oversight of LDTs nationally is warranted.

• Implementation has to be carefully designed to
  ➢ Balance the benefit to the patient with the additional burden to the laboratories
  ➢ Preserve the existing public health infrastructure
  ➢ Preserve our ability to respond to public health threats

• Requires substantial initial education of laboratories

• From our perspective as a testing laboratory, LDT oversight as currently implemented by New York is manageable.