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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

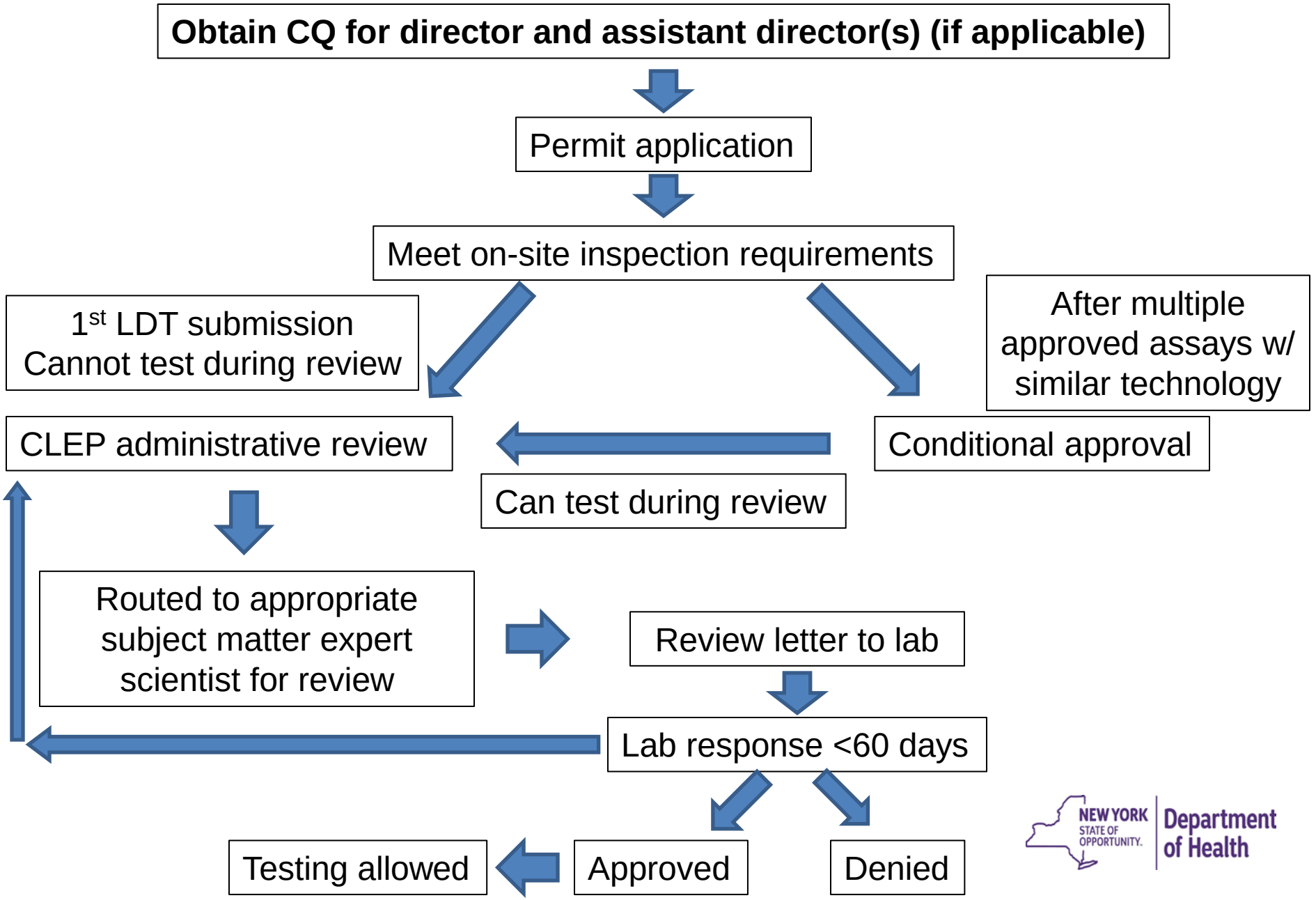
non-FDA cleared or in-house developed tests (LDT), including off-label, RUO, IUO & ASR assays

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



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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

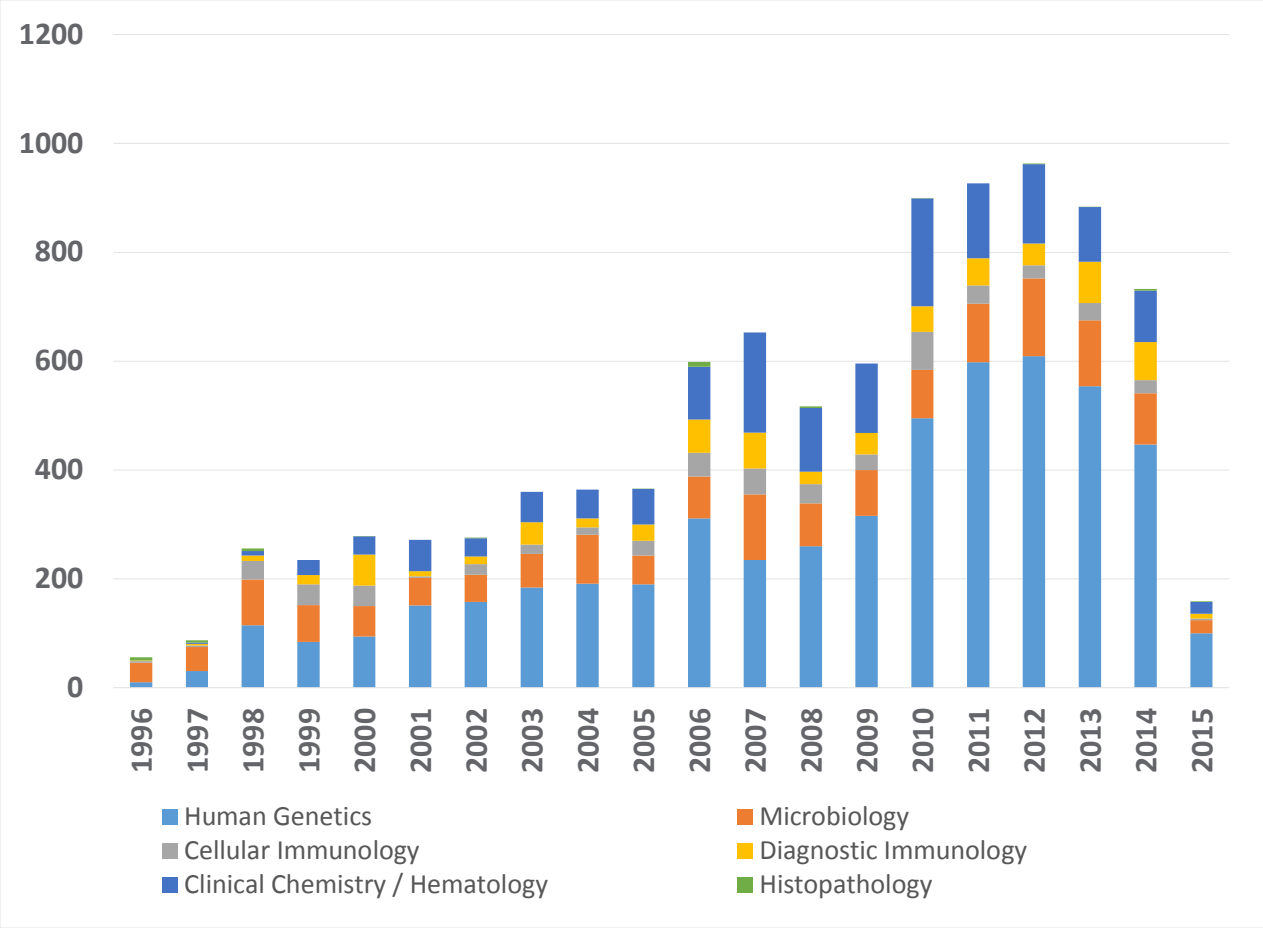
Furthermore …

- 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

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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.