# TIERED EVALUATION OF LABORATORY DEVELOPED TESTS POLICY

NYSDOH Wadsworth Center's Clinical Laboratory Evaluation Program (CLEP) and its Clinical Laboratory Reference System's (CLRS) scientific staff adopted a three-tiered model for the risk-based review and approval of laboratory-developed tests (LDT) beginning November 14, 2016.

***Update: Effective November 7, 2023, CLEP and CLRS revised the policy to address LDTs that the Department has opted not to evaluate for analytical and clinical validity. This revised policy applies to all laboratories applying for or holding a New York State clinical laboratory permit and all assays that require submission as indicated on the Test Approval webpage, which can be found at*** http://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval.

LDTs that were conditionally approved prior to the date of implementation of this revised policy will continue to hold conditional approval.

LDTs proposed by laboratories that do **not** currently hold a NYS clinical laboratory permit or do not hold the appropriate permit category for the testing proposed will continue to require submission and approval before testing on NYS specimens may commence. Conditional approval is not available for such assays. Approval can only be granted when the laboratory has met all requirements and a permit (initial) or permit amendment (new categories) has been issued. Please refer to the Clinical Laboratory Evaluation Program Guide to Requirements and Services available on our website at http://www.wadsworth.org/regulatory/clep/clinical-labs.

## FEATURES OF THE TIERED EVALUATION PROCESS

1. All LDTs must be submitted to CLEP following the appropriate test submission guidelines or relevant form currently posted on the CLEP Test Approval webpage, and include the elements described therein. All submissions must include a **Risk Attestation Form** containing a succinct summary of the assay and responses to the questions listed on the Form; a description of each question is provided at the end of this policy document. The summary and responses to the questions will inform the assignment of the LDT to a risk classification by CLRS staff.

2. A classification assignment (**high**, **moderate**, **low**, **clinical trial**, **not evaluated**) will be made by CLRS staff as part of the existing CLEP LDT validation review and approval process described on the CLEP Test Approval webpage. Laboratories are generally notified of the risk assignment within three (3) to six (6) weeks of the submission of a complete package. Incomplete, vague, or unclear responses on the Risk Attestation Form may result in delayed review.

3. Questions about completing the Risk Attestation form can be submitted to CLEPVAL@health.ny.gov. However, the Department cannot make pre-submission risk determinations because each risk classification is determined upon the information provided in the Risk Attestation Form as assessed by the Panel based on the flow diagram below.

**CLASSIFICATIONS**

- **High risk**: LDTs assessed as **High risk** will **NOT** receive Conditional Approval and testing cannot be offered on specimens from NYS until the CLRS review has been completed and full approval has been granted. Review of LDTs assessed as **High risk** will be prioritized, however a timeline cannot be provided due to many variables. Laboratories will be required to respond to CLRS reviews within sixty (60) business days to avoid inactivation of the application but can apply for sixty (60) day extensions. Requests for extension should be made to CLEPVAL@health.ny.gov.
    - **High risk will apply to all LDT packages submitted by laboratories that are pending a permit or the appropriate permit category, unless the package qualifies for either a Clinical Trial or Not Evaluated classification, however all other applicable permit requirements must be met before testing on NYS specimens can begin. This includes laboratories engaged in a distributive testing model where either or both laboratories are pending permit or amendment.**

- **Moderate risk**: LDTs assessed as **Moderate risk** will receive Conditional Approval if the laboratory holds a permit in the appropriate category of testing. Laboratories may offer the test on NYS specimens upon notification from CLEP of the moderate risk classification and conditional approval. The department reserves the right to withhold or withdraw conditional approval at its discretion. CLRS may indefinitely defer the review of LDTs assessed as **Moderate risk** if the methodology is well-established at the laboratory and/or the result is not a key determinant or has low impact on patient safety. Only those that are reviewed may receive full approval. Laboratories will be required to respond to CLRS reviews within sixty (60) business days to avoid the rescinding of conditional approval. A sixty (60) day extension may be granted upon request. Requests must be made to CLEPVAL@health.ny.gov.

- **Low risk**: LDTs assessed as **Low risk** will receive full approval and will not be subject to review by CLRS staff, provided the laboratory holds a permit in the appropriate category of testing. Laboratories will be able to offer the test once notified by CLEP of the **Low risk** classification and approval. The Department reserves the right to withhold approval and/or require CLRS review of any LDT at its discretion.

- **Clinical Trial**: LDTs assessed as being performed **solely** for **Clinical Trial** purposes will receive notification from CLEP recognizing that the proposed test is part of a clinical trial and may be performed on specimens collected from trial participants. The clinical trial for which the LDTs are performed must be approved by the National Institutes of Health (NIH) or another relevant independent Institutional Review Board (IRB). For additional information, please visit: https://clinicaltrials.gov/ct2/manage-recs/fdaaa.

    - **If the assay is used for both diagnostic and clinical trial purposes, then this classification does not apply. If the assay qualifies for the Clinical Trial classification initially but is then proposed for diagnostic use in the future, a new comprehensive method validation package must be submitted.**

- **Not Evaluated** : Laboratories with LDTs assigned this classification will receive notification from CLEP that the test may be offered to clients with the disclaimer that it has not been evaluated by the NYS Department of Health. Relevant documentation from the method validation submission may be shared with the Centers for Medicare and Medicaid Services (CMS) for a determination on whether the proposed testing is subject to Clinical Laboratory Improvement Amendments (CLIA) regulations. If not, CLEP will make a separate, independent assessment on the necessity for a NYS clinical laboratory permit. If the assay is subject to CLIA or NYS law requiring a clinical laboratory permit, CLEP/CLRS will make an independent assessment for the determination of the Not Evaluated classification.

| Category | Submission required? | Initial Approval | Review required? | Review Priority |
|---|---|---|---|---|
| High | Yes | None | Yes | High[1] |
| Moderate | Yes | Conditional[2,3] | Yes | Medium |
| Low | Yes | Full[2,3] | No[4] | -- |
| Clinical Trial | Yes | N/A[2,4] | No[4] | -- |
| Not Evaluated | Yes | N/A[2,4] | N/A[4] | -- |

[1]Submissions for laboratories pending a permit or permit category are automatically assigned High Risk unless the package meets the conditions for Clinical Trial or Not Evaluated.

[2]Provided the laboratory holds the appropriate permit category.

[3]The department reserves the right to withhold approval at its discretion.

[4]The department reserves the right to review all applications at its discretion.

## DEFINITIONS OF TERMS USED IN FOR HIGH, MODERATE, AND LOW CLASSIFICATIONS

**Well-established**: The laboratory has demonstrated the ability to consistently submit complete and organized applications that adequately prove competence for development of LDTs with the same or similar technology and where an appropriate validation protocol is followed on a consistent basis over time; **AND** the methodology:

a. has been previously approved by FDA or NYS, or
b. has, without significant modifications, resulted in a meaningful clinical impact as described in multiple peer-reviewed publications.

**Key determinant**: The test result provides critical or essential information to

1. diagnose, and/or
2. indicate a greater likelihood of developing a disease or condition, and/or
3. indicate eligibility for a specific treatment, and/or
4. provide prognostic information that influences patient management or treatment decisions, and/or
5. provides information on treatment adherence and/or drug use.

**Impact**: The likelihood that an inaccurate test result will negatively impact a patient's condition or lead to patient morbidity/mortality. An LDT will have a high impact if an analytically or clinically inaccurate result leads to erroneous diagnosis and/or prediction of an inappropriate treatment, thereby increasing the risk of significant harm or death.

## LDT CLASSIFICATIONS (see flow diagram below)

- **High risk:**
  - An LDT that uses a methodology that is not well-established in the submitting laboratory and provides critical or essential information (key determinant) about a serious or life-threatening disease, disorder, or condition, whether the reported result, if inaccurate, could be used to support an incorrect diagnosis and/or an inappropriate clinical treatment that is likely to increase the risk of significant harm or death (high impact); or
  - An LDT that uses a methodology that is not well-established in the submitting laboratory, does not provide critical or essential information (not a key determinant) about a serious or life-threatening disease, disorder, or condition, but the reported result, if inaccurate, could be used to support an incorrect diagnosis and/or an inappropriate clinical treatment that is likely to increase the risk of significant harm or death (high impact).

- **Moderate risk:**
    - An LDT that uses a well-established methodology and provides critical or essential information (key determinant) about a serious or life-threatening disease, disorder, or condition, whether the reported result, if inaccurate, could be used to support an incorrect diagnosis and/or an inappropriate clinical treatment that is likely to increase the risk of significant harm or death (high impact); or
    - An LDT that uses a well-established methodology, does not provide critical or essential information (not a key determinant) about a serious or life-threatening disease, disorder, or condition, but the reported result, if inaccurate, could be used to support an incorrect diagnosis and/or an inappropriate clinical treatment that is likely to increase the risk of significant harm or death (high impact); or
    - An LDT that uses a methodology that is not well-established in the submitting lab, but is not considered a key determinant, and an inaccurate reported result is not likely to support an incorrect diagnosis and/or an inappropriate clinical treatment (low impact).
- **Low risk:**
    - An LDT that uses a well-established methodology, does not provide critical or essential information (not a key determinant) about a serious or life-threatening disease, disorder, or condition, and an inaccurate reported result is not likely to support an incorrect diagnosis and/or an inappropriate clinical treatment (low impact). Packages that are submitted under an approved exemption may also be classified as Low Risk. Laboratories may apply for an exemption from full method validation submission by following the instructions available at https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval.
- **Clinical Trial**:
    - An LDT that is being performed as part of clinical trial approved by NIH or another relevant independent IRB on specimens for participant enrollment or management where the results are reported and are used for clinical decision making. Examples of testing performed for participant management include those that influence enrollment (exclusion or inclusion), safety, toxicity, or dosing.
- **Not Evaluated**
    - The Department may choose not to evaluate analytical and clinical validity of an LDT when the intended use makes no clinical claims or direct reference to recognized diseases or conditions; relates to the maintenance or adoption of a general state of health or healthy activity; or relates to the widely accepted role of a healthy lifestyle in the management of certain chronic diseases or conditions. The intended use and results reported to the provider/patient cannot be used to support a treatment that is likely to increase the risk of significant harm or death. Additional information regarding the LDT may be required so the Department can ascertain the intended use claims and risk of harm to customers.

- All other statutory and regulatory requirements apply to the laboratory and the LDT, including the need for an authorized ordering source.
- Upon notification that the Department has determined not to evaluate the LDT, the laboratory may offer the LDT with a disclaimer that must be included on marketing materials and the test report indicating that the test was not evaluated by the New York State Department of Health.

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