NYSDOH Policy for Risk-based Evaluation of Laboratory Developed Tests (LDT)

NYSDOH Wadsworth Center's Clinical Laboratory Evaluation Program (CLEP) and its Clinical Laboratory Reference System (CLRS) scientific staff are adopting a three-tiered risk-based model for the review and approval of laboratory developed tests (LDT) to begin **November 14, 2016**. This policy applies to laboratories holding a NYS clinical laboratory permit in the appropriate category of testing, and applies to **all assays** that require submission as directed on the Test Approval webpage that can be found at http://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval.

Laboratory-developed tests that are conditionally approved, or qualify for conditional approval (i.e., a package that is considered to be complete has been received by close of business (4:30 pm E.D.T.) November 11, 2016, from a laboratory holding a permit in the relevant category), prior to the date of implementation of this policy will continue to hold such approval.

Laboratory-developed tests proposed by laboratories that do **not** currently hold a NYS clinical laboratory permit or the appropriate permit category for the testing proposed will continue to require review 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 is issued the permit (initial) or permit amendment (new categories). 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 risk based evaluation process

1. All LDTs must be submitted to CLEP following the test submission guidelines and include all the required materials. This now includes a Risk Attestation Form to include a succinct summary of the assay and responses to the four questions listed at the end of this document. The summary and answers to the questions will inform the assignment of the LDT to a risk category by CLRS staff.

2. Assignment of risk into one of three classifications, **high**, **moderate** or **low**, 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 will be notified of the risk assignment within three weeks of the submission of a complete package. If a risk assignment cannot be determined, the laboratory will be requested to provide additional information. An incomplete, vague, or unclear Risk Attestation Form will delay the review of an LDT package.

3. Pre-submission consultations will be available to discuss risk categorization concerns. Requests for a consultation must be made in writing to CLEPVAL@health.ny.gov.

4. **Low** risk LDTs will receive full approval and 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 designation. Validation will be reviewed as

part of the laboratory surveys. However, we reserve the right to withhold approval and/or require CLRS review of the test at our discretion.

5. **Moderate** risk LDTs will receive Conditional Approval if the laboratory holds a permit in the appropriate category of testing. However, we reserve the right to withhold or withdraw conditional approval at our discretion. Moderate risk LDTs still require review before full approval can be granted. Laboratories will still be required to respond to CLRS reviews within 60 business days to avoid the rescinding of conditional approval.

6. **High** risk LDTs will **NOT** receive Conditional Approval and will need to complete the CLRS review process before full approval will be granted. Review of **High** risk LDTs will be prioritized.

Risk category	Submission required	Initial Approval	Review required	Review Priority
High	Yes	None	Yes	High
Moderate	Yes	Conditional[1,2]	Yes	Medium
Low	Yes	Full[1,2]	No[3]	--

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

[2]The Department reserves the right to withhold approval at its discretion.

[3]The Department reserves the right to review all applications at its discretion.

Definitions of terms used in risk classifications

- **Well-established**: the methodology and clinical indications for use:
    a. have been previously approved by the deemed regulatory body (e.g. FDA), **and/or**
    b. have been described in multiple peer-reviewed publications without significant modifications resulting in a meaningful clinical impact, **and**
    c. it has been demonstrated to the Department that the submitting laboratory consistently designs and submits 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.

- **Key determinant**: the test result provides critical or essential information to
    a. diagnose, **and/or**
    b. indicate a greater likelihood of developing a disease or condition, **and/or**
    c. indicate eligibility for a specific treatment.

- **Impact**: the likelihood that an inaccurate test result will impact a patient's condition, and/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 Risk Classifications (see flow diagram below)

- **High Risk LDT:**
  - An LDT that uses methodology that is not well-established and provides critical or essential information (key determinant) about a serious or life-threatening disease, disorder or condition, whether or not 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 methodology that is not well-established, does not provide critical or essential information (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 LDT:**
  - 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 or not 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 methodology that is well-established, does not provide critical or essential information (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, 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).

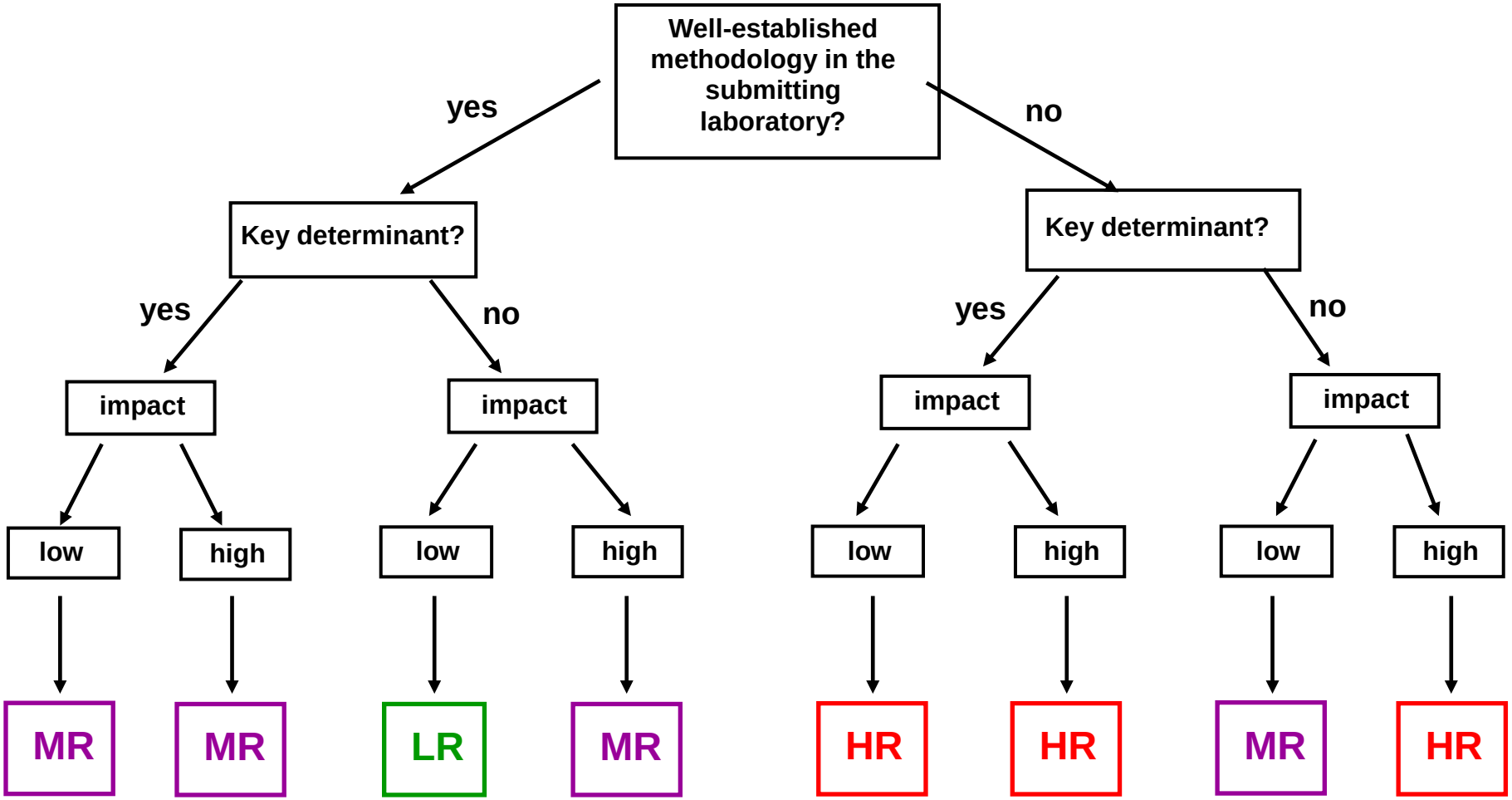
- **Low Risk LDT:**
  - An LDT that uses a well-established methodology, does not provide critical or essential information (key determinant) about a serious or life-threatening disease, disorder or condition, and an inaccurate reported result is not likely to support an incorrect diagnosis and/or an inappropriate clinical treatment (low impact).

Submission Requirements:

In addition to the appropriate submission checklist, all packages **must** be accompanied by a completed Risk Attestation Form. The form requires the following:

- **A summary of the assay**, not to exceed 400 words, specifically including the following:
  - Methodology and technology (e.g., sequencing by next generation sequencing)
  - Intended use to include target population if applicable
  - Specimen type(s)
- An indication of whether this is the laboratory's **first LDT submission for the methodology**.
- **The basis for the clinical use claim of the LDT**. Provide a listing of three key publications including the PubMedID or a reference citation that provides sufficient detail to ensure successful publication search. Relevent additional supporting publications and/or clinical or laborataory data must be included in the submission package. Indicate whether the publication is from the submitting laboratory.
- Response to the following:
  - **Does the LDT utilize a methodology that is well-established in your laboratory and generally accepted by the field?** If so, provide supporting evidence by citing at least 2 and no more than 3 relevant references (with PubMed ID or complete reference citation) or identify an available test that has FDA approval/clearance/exemption for the same methodology. Provide supporting information to demonstrate that the laboratory has consistently submitted complete and organized applications that adequately prove competence for development of LDTs with the same or similar technology and where an appropriate validation protocol has been established. Project IDs for previously approved validation package submissions should be included.
  - **Briefly explain how this LDT does, or does not, provide 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**.
  - **Briefly describe the potential impact of an inaccurate test result.**

PLEASE NOTE: Incomplete, vague or unclear responses on the Risk Attestation Form will delay review of the LDT package.


Well-established methodology in the submitting laboratory?
yes
no
Key determinant?
Key determinant?
yes
no
yes
no
impact
impact
impact
impact
low
high
low
high
low
high
low
high
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