

**Appendix III**  
**DCLOT Algorithm for Determining Level of Validation Required for Endpoints Assays**

Effective Date:09/10/19

Document No.:APP-A-OD-003.01

**I. SCOPE**

Applies to any laboratory developed test (LDT) used for endpoint determination that may be submitted to the FDA in support of licensure or used to advance a product to subsequent clinical trial phases.

**II. APPENDIX**

Notes on the use of this algorithm:

1. This algorithm is separate from CLIA certification [1] or GCLP compliance of a laboratory [2]. If CLIA or GCLP is required for testing, the laboratories would also need to be in compliance with those requirements in addition to the requirements described in the algorithm.
2. In the “fit-for-purpose” concept, the required performance characteristics of the assay are first determined for the study [3]. Will the assay need to be qualitative or quantitative? Are positivity criteria developed for a qualitative assay? If quantitative, what range is needed? What level of precision is needed for the study? Is there a “gold standard” assay that measures the same analyte for assessing accuracy? What level of sensitivity and specificity? After the required performance characteristics are determined and pass/fail criteria set, the assay is performed with controls to confirm whether the assay meets pre-specified criteria. If one or more of the assay parameters do not meet the acceptance criteria, the assay cannot be accepted as fit-for-purpose and cannot be used for testing clinical trial samples. Additional assay optimization work is required so the assay meets all acceptance criteria before being used to test clinical trial samples.
3. The algorithm employs the “fit-for-purpose” concept which means:
  - The level of validation should be appropriate for the intended purpose of the study.
  - If data from the assay in question will be submitted to a regulatory agency for decision making for approval, safety or labeling, then full validation is required according to the FDA Guidance on Biomedical Method Validation.
  - If the endpoint is considered exploratory and the data would not be submitted for decision-making, then less stringent approaches (standardization or qualification) demonstrating that the assay can provide the desired results (i.e., it is fit-for-purpose) may be sufficient.

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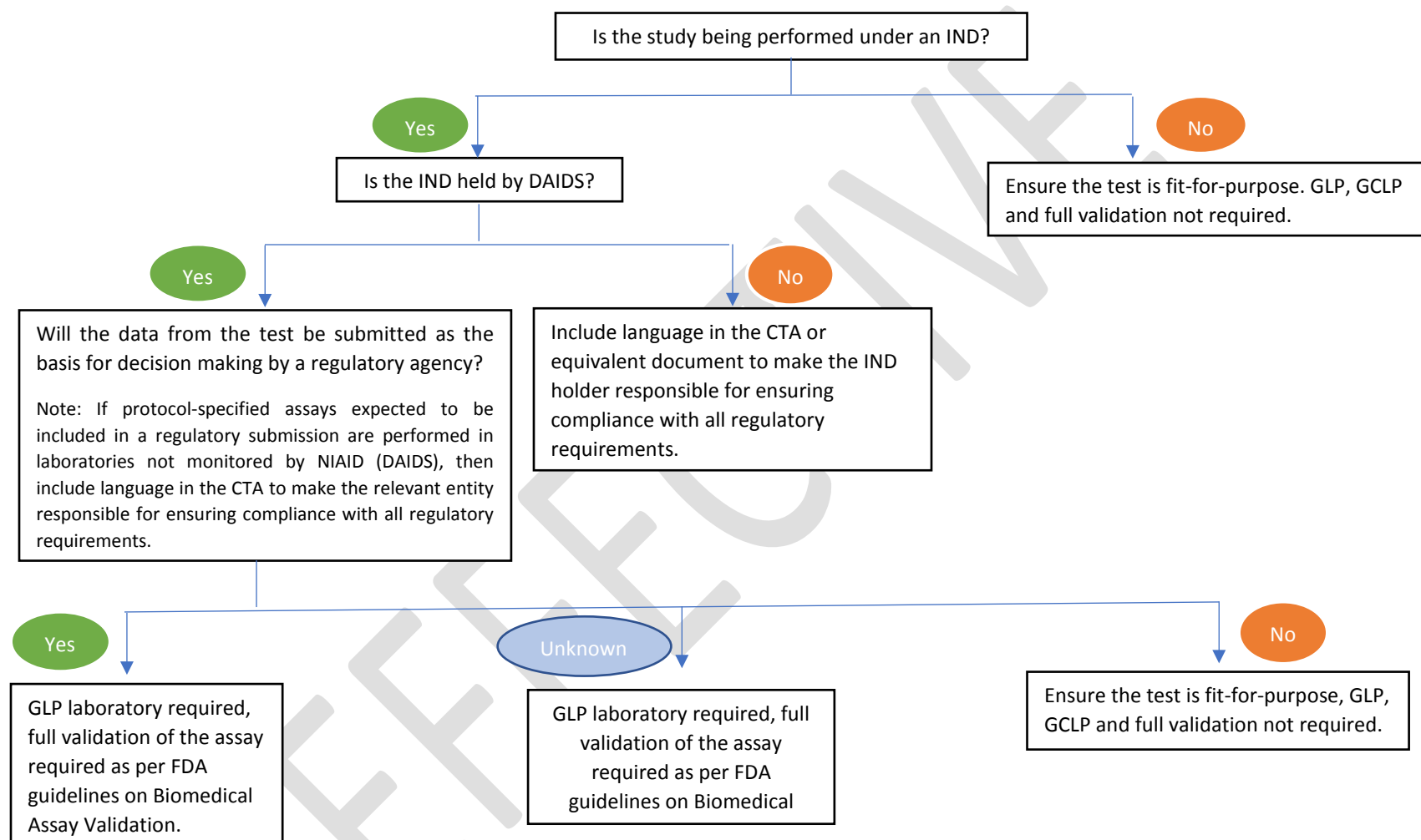
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- For exploratory research, the methods should be documented to be fit-for-purpose, since the LDT are being used to evaluate responses to interventions given to research participants, which may expose the participants to some level of risk.
- The final report should include, data on the sensitivity and specificity of qualitative methods, and data on the accuracy, precision, linear range, sensitivity and specificity of quantitative methods. The report must be signed by the lab director and kept at the lab and provided to the trial sponsor if requested.

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**III. REFERENCES**

1. [Clinical Laboratory Improvement Amendments \(CLIA\)](#)
2. [DAIDS Guidelines for Good Clinical Laboratory Practice Standards](#)
3. [U.S. Code of Federal Regulations, Title 21, Parts 11 and 58](#)
4. [U.S. Food and Drug Administration, Guidance for industry: bioanalytical method validation, 2018](#)

**IV. REVISION HISTORY**

APP-A-OD-003.00 is the initial version of Appendix III DCLOT Algorithm for Determining Level of Validation Required for Endpoints Assays Requirements for DAIDS Supported and/or Sponsored Laboratories in Clinical Trials Policy submitted to the DAIDS QMS.

APP-A-OD-003.01 was revised on 06/27/19 to include the following changes:

The main change from the previous version of Appendix III submitted to the QMS includes deletion of a typographical error and addition of the CLIA reference. Also update of algorithm to remove reference to whether study expected to impact clinical guidelines