Don't Wait to Generate Labeling for Your Lab's LDTs; Early Efforts Can Help Improve Tests, Assist with Later Marketing Submissions

Clinical laboratories with lab-developed tests (LDTs) should begin working on labels for these tests now even though the compliance deadline for labeling is still a year and half away, advises Kelly Gordon, PhD, Founder of Boudicca Dx LLC, a consulting company based in Brentwood, TN. The work that goes into developing labeling now can be helpful in identifying where there may be gaps in information needed for the lab to submit a marketing submission later, says Gordon.


Kelly Gordon, PhD

"My advice is to start doing labeling now, don't wait," says Gordon. "You might find you don't have enough data for a submission, and this would give you time to generate more data. If there are a lot of gaps in your data, you might want to send a pre-submission to the FDA."

A pre-submission lays out for the FDA all the information that would support a marketing submission, allowing the lab to receive feedback from the agency before a formal marketing submission is made, explains Gordon.

Gordon also notes that beginning work on labeling now can help facilitate compliance with Stage 1 (medical device reporting, complaint files and correction and removal reporting). The compliance date for Stage 1 is May 6, 2025.

Under the final rule on Food and Drug Administration (FDA) oversight of LDTs, issued May 6, 2024, clinical laboratories must comply with labeling requirements for most in-vitro diagnostic tests by May 6, 2026. The FDA held a webinar Sept. 24, 2024, to provide information on how to comply with labeling requirements for IVDs, including LDTs.

According to the FDA, labeling provides users, healthcare providers and patients with information on the test, including its intended use, limitations and performance. Labeling must prominently display all required information and be truthful and non-misleading. An LDT without such labeling would be misbranded, says the agency.

Gordon notes that developing the type of labeling that the FDA requires is more difficult than developing labeling typically used in a CLIA laboratory. In a CLIA lab, testing information and data is more aggregated, while FDA labeling is more detailed and focused on individual test components, she explains.

"I think the biggest challenge for labs will be in making sure there are no gaps in the analytical validity and clinical validity data," she says. "CLIA tests weren't required to have clinical validity data. They were only required to have analytical validity data. So, for some labs, this will be new."

Components of a Label

Labeling accompanying an IVD, including an LDT, may include one or more of the following: package insert, test protocol, reagent and instrument specification documents, test menu and test report template. According to the FDA, each label should contain the following elements:

1. Name of product. This includes the proprietary name and common name, if any.

2. Intended use, including the type of procedure (e.g., qualitative or quantitative).

3. Summary and explanation of test. This should include a short history of the methodology, with pertinent references and a balanced statement of the special merits and limitations of the product. If the product labeling refers to any other procedures, appropriate literature citations should be included and the labeling should explain the nature of any differences from the original and their effect on the results.

4. Principles of procedure, such as chemical, physical or biological principles of the procedure. Explain concisely, with chemical reactions and techniques involved, if applicable.

5. Reagents, including a declaration of the established name, quantity, proportion of concentration of each reactive ingredient; a statement of warnings or precautions; adequate instructions for reconstituting, mixing, dilution; appropriate storage instructions; a statement of any purification of treatment required for use; physical, biological or chemical indications of instability or deterioration.

6. Instruments, including use or function; installation procedures and special requirements; principles of operation; performance characteristics and specifications; operating instructions; calibration procedures, including materials and/or equipment to be used; operational precautions and limitation; hazards; and service and maintenance information.

7. Specimen collection/preparation, including special precautions and special preparations of the patient; additives, preservatives, etc., necessary to maintain the integrity of the specimen; known interfering substances; recommended storage, handling or shipping instructions for the protection and maintenance of stability of the specimen.

8. Procedure. A step-by-step outline of recommended procedures from reception of the specimen to obtaining results. List any points that may be useful in improving precision and accuracy. This would include a list of all materials provided, materials required but not provided, a description of the amounts of reagents necessary, a statement describing the stability of the final reaction material to be measured and the time within which it shall be measured, details of calibration, and details of kinds of quality control procedures and materials required.

9. Results. Explain the procedure for calculating the value of the unknown, explain each component of the formula used for the calculation of the unknown, include a sample calculation, explaining the answer. If the test provides other than quantitative results, provide an adequate description of expected results.

10. Limitations, including known extrinsic factors or interfering substances affecting results. If further testing, either more specific or more sensitive, is indicated in all cases where certain results are obtained, the need for the additional test shall be stated.

11. Expected values. State the range of expected values as obtained with the product from studies of various populations. Indicate how the range was established and identify the population on which it was established.

12. Specific performance characteristics. Include, as appropriate, information describing such things as accuracy, precision, specificity and sensitivity. These shall be related to a generally accepted method using biological specimens from normal and abnormal populations. Include a statement summarizing the data upon which the specific performance characteristics are based.

13. Bibliography.

14. Name and place of business.

15. Date of issuance of labeling.

Don't Wait to See What Happens

Gordon advises labs not to wait to see how the courts will rule on pending challenges to the LDT final rule before beginning to develop labeling for their tests.

"If the rule is repealed or stayed, all the work you've done will only improve your LDTs," she says. "A pragmatic approach is important just in case it's repealed."

Gordon adds that an advantage of filing a pre-submission request with the FDA for a novel test is that you then set the rules for that kind of test. "When you are the first test, you become a predicate for your competitors' tests," she notes.