

Principles for Oversight of Laboratory Developed Procedures (LDPs)

Desired Outcomes:

- Patients receive the most appropriate test(s) for their clinical condition.
- Laboratory tests are accurate and reliable.
- Health care professionals are able to provide professional services and practice medicine without undue restrictions.
- Regulatory oversight does not slow innovation, constrain flexibility and adaptability, or limit a test's sustainability as a result of being unduly burdensome and overly expensive.

Principles:

- ✓ Any proposed regulation should i) be able to clearly define the problem to be solved through regulatory action, ii) be able to quantitatively assess the problem, iii) be able to show that the proposed regulatory action will effectively address the problem, and iv) demonstrate that the regulatory burden is appropriate to the societal costs imposed by the problem.¹
- ✓ **Laboratory developed procedures (LDPs), also known as laboratory developed tests (LDTs), are not medical devices.** Because the technologies underlying many LDPs are rapidly advancing, LDP oversight requires great flexibility to accommodate continual evolution and improvements of these procedures. There is no evidence of systemic problems with LDPs or laboratory testing generally in the United States.
- ✓ **LDPs are distinct from boxed and shipped laboratory test kits** that are distributed in interstate commerce to laboratory customers of varying skill levels and over whom the manufacturer has no control. Independent regulatory approaches are necessary to accommodate the very different risks posed by these disparate activities.
- ✓ LDPs are a medical service throughout the design, validation, performance, monitoring, improvement, interpretation, and communication of the results. LDPs are not designed and developed by "laboratories" but by board-certified professionals who perform these procedures as a part of their professional practice. The central role of the medical professional throughout the entire test process minimizes the risks of LDPs and ensures their safe and effective use. It is the laboratory director's legal and professional responsibility to assure the safety, accuracy and appropriateness of all laboratory tests. **Regulation of professional practice should be by relevant licensure and credentialing bodies.**
- ✓ Laboratory professionals promote patient safety through the use of professional judgment at every stage of the LDP process. **Therefore, FDA oversight is not warranted for the vast majority of LDPs.**
- ✓ The single test, single drug paradigm as described by term "companion diagnostic," is rapidly becoming obsolete as new technologies allow for the testing of multiple analytes simultaneously with greatly

¹ O'Leary et al. (2014) Regulating Laboratory Developed Tests. *Journal of Molecular Diagnostics* 16, 595-598

reduced per-analyte costs. **The term “companion diagnostic” should not be included in any legislation or regulatory policy. For the same reason, drug labels should not specify the brand name of diagnostic tests.**

- ✓ **Any new regulatory framework should not be duplicative of already existing regulations.**
- ✓ **Any proposed regulation should not shift product liability from the manufacturers to medical professionals or their laboratories.**
- ✓ **The CLIA program should be modernized to reflect changes in technology, continue to ensure analytically and clinically valid laboratory testing, and updated to require laboratories have ready access to a mechanism for ordering physicians to report possibly erroneous results.** Examples of CLIA modernization could include enhanced proficiency testing requirements, more explicit requirements and standards for clinical validity of tests, provision for CMS' periodic expansion of the list of analytes for which proficiency testing is required, and modification of proficiency testing mediation/enforcement requirements.
- ✓ **Any regulatory framework should allow appropriately qualified professionals to modify an FDA approved or cleared test to better suit the needs of the patient or the laboratory.** In almost all cases, third party pre-market review is unnecessary when technical modifications or alternative specimen types are validated.
- ✓ LDPs are continually improved as a result of emerging medical knowledge. To facilitate rapid improvements to patient care, **advancements of existing LDPs should require only notification to the oversight agency rather than re-submission.**
- ✓ Any federal office or center responsible for establishing the regulations for and overseeing the review of molecular tests should have in its top leadership a board-certified professional who has served as a laboratory director in a clinical molecular diagnostics laboratory, and thus understands the special considerations of complex LDPs.
- ✓ **Medicare administrative contractors should be prohibited from regulating laboratory test performance.** All CMS regulation of laboratory tests should reside within the CLIA program.
- ✓ Laboratory professionals are equipped with the necessary information to ensure that the most appropriate test is ordered. Information about tests should be readily available and mechanisms encouraged that will **enhance communication between laboratory professionals and ordering/ treating physicians as well as patients.**
- ✓ Many laboratories perform testing using well-validated technologies and methods, the accuracy and reliability of which have been broadly demonstrated and the knowledge of limitations well-established. To prevent impeding necessary improvements to tests, **validation of such methods should not have to be repeatedly reproved in different tests.** Once, for example, sequencing is established as a platform, there is no further need to demonstrate performance characteristics of the platform for each analyte. This is consistent with the standard in Europe.
- ✓ **Drug developers should provide or fund the development of standard reference materials, where relevant, to harmonize testing across technologies and platforms** and ensure the continued availability of the therapy as testing technologies advance.