# Clinical pathology selected abstracts

*Editor: Deborah Sesok-Pizzini, MD, MBA, professor, Department of Clinical Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and chief, Division of Transfusion Medicine, Children's Hospital of Philadelphia.*

## Preparing for passage of regulatory requirements for laboratory-developed tests

November 2018—The FDA has raised concerns, in recent years, about several high-risk laboratory-developed tests (LDTs), including a concern that patients may undergo unnecessary treatment or delay or forego treatment due to the inaccuracy of such tests. Other agencies have also challenged the validity, accuracy, oversight, and safety of LDTs, a subset of IVDs that are intended for clinical use and designed, manufactured, and used within a single laboratory. A 2014 FDA draft guidance, titled "Framework for Regulatory Oversight of Laboratory Developed Tests," proposes regulations regarding laboratory oversight of such testing. The FDA recommends that all IVDs intended for use in drug or biologic therapeutic decision-making be held to the same scientific and regulatory standards as medical devices developed by medical device firms. The agency has proposed that laboratories adopt a formal risk-based classification and approval process, quality system regulation (QSR), and formalized design control structure, as described in the 2014 draft guidance. However, laboratories continue to struggle to understand their responsibility to comply should the guidance become policy. Therefore, the authors introduced regulatory definitions and discussed the QSR proposed in the guidance, as well as the regulatory and quality oversight required to design, develop, and validate LDTs. The intent of the article is to educate laboratory professionals about LDTs and serve as a proactive call to action on addressing FDA concerns about the use of LDTs. The investigators performed nine interviews with laboratory professionals to explore concerns and challenges regarding the FDA draft guidance. They then translated the results into operational factors and surveyed professionals to test the factors they would use to create a regulatory quality management system (QMS) framework. The authors found that the nine interviewees and 35 survey respondents showed concerns about risk classification, process validation, patient safety, and general ambiguity regarding the proposed requirements for developing LDTs. However, the respondents all agreed with statements relevant to the design of a QMS based on the needs and gaps expressed by laboratory professionals. The authors concluded that research is needed to design an agile, robust QMS that will incorporate the suggested factors of leadership commitment, training, pre-assessment, design control, document control, and development of a QMS framework. They stated that the translation and method for design control in a clinical laboratory does not exist. Laboratories are taking a wait-and-see approach to the FDA's final guidance because many will be required to change business strategies and outsource or terminate some tests if the FDA proposal becomes policy.

D'Angelo R, Weiss R, Wolfe D, et al. Facing the inevitable: Being prepared for regulatory requirements for laboratory developed tests. *Am J Clin Pathol.* 2018;149:484–498.

Correspondence: Dr. Rita D'Angelo at dangeloadvantage@gmail.com

## A risk-based decision-making approach to assessing risk of Babesia in U.S. blood supply

Due to the increasing threat of transfusion-transmitted babesiosis to the U.S. blood supply, the AABB tasked the Ad Hoc *Babesia* Policy Working Group with using the Alliance of Blood Operators' risk-based decision-making framework to assess the risks and benefits of performing *Babesia* testing on the nation's blood supply. The assessment considered patient safety, product availability, sector sustainability, and technology availability. The working group assessed safety risk, economic and operational impact, reimbursement equity, and ethical considerations and stakeholder feedback from two consultations and concluded that a regional approach to donor

screening for *Babesia* in endemic states was the most appropriate. Furthermore, it concluded that nucleic acid testing using a ribosomal RNA template was the recommended platform for donor testing because it was the most cost-effective, resulted in no wasted units, and identified a similar number of infections as antibody plus DNA-based PCR. The working group also recommended that the AABB collect data to further identify risks in endemic states. It suggested that it is necessary to periodically re-evaluate which states receive "endemic" status since the geographic area affected by *Babesia microti* is likely to expand. In conclusion, the working group reported that public awareness of the Babesia threat is the first line of defense for the nation's blood supply, and the AABB should work with the appropriate agencies to provide general education about the health risks from *B. microti.*

Ward SJ, Stramer SL, Szczepiorkowski ZM, et al. Assessing the risk of *Babesia* to the United States blood supply using a risk-based decision-making approach: Report of AABB's Ad Hoc *Babesia* Policy Working Group (original report). *Transfusion.* 2018;58:1916–1923.

Correspondence: Dr. Susan L. Stramer at susan.stramer@redcross.org