



Consistent accuracy: a goal for thrombosis and hemostasis testing is accomplished using an external quality assurance program

Richard A. Marlar¹, Piet Meijer², Ian Jennings³, John Olson⁴; on behalf of EQATH (External Quality Assurance in Thrombosis and Hemostasis)

¹Department of Pathology, University of New Mexico, TriCore Reference Laboratories, Albuquerque, NM, USA; ²ECAT Foundation, Voorschoten, The Netherlands; ³NEQAS for Blood Coagulation, Sheffield, UK; ⁴Department of Pathology and Laboratory Medicine, University of Texas Health, San Antonio, TX, USA

Correspondence to: Richard A. Marlar, PhD. Department of Pathology, University of New Mexico, TriCore Reference Laboratories, Albuquerque, NM 87131, USA. Email: RMarlar@salud.unm.edu.

Received: 29 October 2019. Accepted: 23 March 2020; Published: 30 June 2020.

doi: 10.21037/aob.2020.03.02

View this article at: <http://dx.doi.org/10.21037/aob.2020.03.02>

Accuracy of laboratory testing used in the diagnosis and management of thrombotic and hemostatic disorders can be very troublesome. Hemostatic testing has many pitfalls that are common to all sections of the laboratory, as well as a number of issues unique to hemostasis testing that are not seen in other laboratory disciplines (1,2). All aspects of laboratory testing have issues associated with analytical and post-analytical variables but hemostasis has many more issues pertaining to the preanalytical aspects of sample procurement and processing. Another major complexity is in the actual measurement of the end-product (a fibrin clot) which can be ascertained using different analytical endpoints, calculations and technical methods, thus generating different criteria for the clotting endpoint (3). The process of forming a clot includes many enzymatic reactions and potential interfering components that can contribute to an inaccurate result (3). In addition, the results are usually based on arbitrary endpoint units such as time (seconds) or a percent of a local population that can differ in various countries or even regions of a country (3,4). Many results are determined based on secondary endpoints that can also contribute to the cause of a significant error. With all of these variables taken together, it becomes more difficult to assess the result accuracy by individual laboratories with nothing to compare with their result and must assume a consistent and accurate diagnostic and therapeutic result to care for their patient. The lack of

internationally accepted reference methods for most tests of hemostasis compounds this difficulty.

Since thrombosis and hemostasis testing is a very difficult arena for the clinical laboratory to maintain consistently accurate results, it requires a concerted effort to maintain a long-term and quality individual laboratory program. Individual laboratories must band together regionally or nationally to ensure their results accurately assess the diagnosis and management of their patients (4). External quality assessment [EQA; or proficiency testing (PT)] portion of a quality laboratory program is directed toward the accuracy of the test result (4-6). Having a good EQA program in thrombosis and hemostasis is paramount to ensuring consistent and accurate results allowing for appropriate diagnosis and treatment of patients. It is extremely important that an External Quality Assessment Scheme (EQAS) be in-place at least regionally (but better if national or even international) to evaluate all of the assays performed in the thrombosis and hemostasis laboratory (7). An EQA program must be available for all laboratories to guarantee the accurate result for the correct diagnosis. If an EQAS program is not available to the local/regional thrombosis and hemostasis laboratories, then developing, implementing and maintaining an EQAS program must be considered.

Developing a new EQAS system in thrombosis and hemostasis can be daunting especially if done from the

Table 1 Reference organizations involved in the development of the guidance document

-
1. External Quality Assurance in Thrombosis and Hemostasis (EQATH): EQATH.org
 2. North American Specialized Coagulation Laboratory Association (NASCOLA): NASCOLA.com
 3. External quality Control of diagnostic Assays and Tests (ECAT): ECAT.nl
 4. UK National External Quality Assessment Scheme for Blood Coagulation (NEQASCoag): NEQASCOAG.org
 5. Royal College of Pathologists of Australasia Haematology Quality Assurance Program (RCPAQAP)
 6. Institute for Quality Management in Healthcare (IQMH)
 7. College of American Pathologists (CAP)
 8. Laboratorio de Evaluacion Externa de la Calidad en Hematologia (LEECH)
 9. Indian Society of Haematology and Transfusion Medicine—Christian Medical College EQAS (ISHTM-CMC)
 10. Association ProBioqual (The English version of this page is still being developed) ProBioQual
 11. Institute for Standardization and Documentation in Medical Laboratories e.V., ehemals Haemometerprüfstelle INSTAND e.V.
-

ground up. Currently the only guidance documents for establishing an EQAS program are general EQA guidance documents that are not specific for the unique issues associated with thrombosis and hemostasis (7,8). Therefore, since a guidance document for development and implementation of an EQAS program for thrombosis and hemostasis was not available, the External Quality Assessment in Thrombosis and Hemostasis (EQATH) organization has developed one such guidance document specific for clinical laboratory testing in thrombosis and hemostasis (9). The objective of this document is to provide guidance for implementing and operating a regional or national EQAS program specifically for thrombosis and hemostasis testing. This Thrombosis and Hemostasis guidance document is presented as a freestanding article in this journal (9), and can also be found as an internet link embedded in other EQAS organizations specific for thrombosis and hemostasis (see *Table 1*—reference organizations below). The guidance document outlines the major requirements for an EQAS program in thrombosis and hemostasis testing. Specific elements of this EQA Guidance document include: (I) setting up the EQA program; (II) preparation of samples, including plasma selection, pre-testing, aliquoting and packaging; (III) specimen distribution; (IV) data collection; (V) initial analysis of data for quality; (VI) data analysis for acceptability or failure of the participating laboratory's results; and (VII) final report with follow up support and education. Also included in the document are the major components necessary for the operation of the program

(personnel, equipment and methods for obtaining and processing samples) and basic methods of data evaluation and result reporting.

The EQATH sub-committee members listed in the document wrote the bulk of the document. Each committee member brings expertise to the document from the perspective of actually overseeing EQA programs while other users are very involved in EQA program utilization or operation. The document was written in alignment with the Clinical Laboratory and Standards Institute (CLSI) and International Standards Organization (ISO) documents with deviations added specific to thrombosis and hemostasis testing (*Table 2*). The document was also reviewed with the opportunity to comment on by numerous other EQA organizations and individuals (*Table 1*).

Regional or national groups interested in starting a thrombosis and hemostasis EQA program can use this document as the basis for establishing a new program. Individuals with questions, issues or needing further help in establishing a program can contact the authors of this commentary or any of the different EQA programs listed in *Table 1*.

Accurate results in clinical testing for thrombosis and hemostasis analytes can be a difficult goal; here, ensuring accuracy of testing relies on a good EQAS. Having access to a reliable program may not be readily available to all laboratories that perform thrombosis and hemostasis testing. As well, accreditation organizations and government regulations may require participation at various levels in an EQAS program. If an EQAS program does not exist or is

Table 2 A summary of other consolatory processes undertaken for development of the guidance document

| Document number | Document title |
|---------------------|---------------------------------------------------------------------|
| ISO 9000: 2015 | Quality management systems—fundamentals and vocabulary |
| ISO 15189:2012C | Medical laboratories—requirements for quality and competence. |
| ISO/IEC 17043: 2010 | Conformity assessment—general requirements for PT |
| ISO 13528: 2015 | Statistical methods for use in PT by interlaboratory comparison |
| GP27-A | Using PT to improve the clinical laboratory; approved guideline |
| MM14-A | Proficiency testing (EQA) for molecular methods; approved guideline |

PT, proficiency testing; EQA, external quality assessment.

not available to the laboratories in a region or country, then one may need to be developed. This guidance document (9) provides the background to develop and implement such a program.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Emmanuel J Favaloro) for the series “External Quality Assurance” published in *Annals of Blood*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/aob.2020.03.02>). The series “External Quality Assurance” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the

original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

- Gosselin RC, Marlar RA. Preanalytical variables in coagulation testing: setting the stage for accurate results. *Semin Thromb Hemost* 2019;45:433-48.
- Clinical and Laboratory Standards Institute (CLSI). Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays: Approved Guideline. 5th ed. CLSI Document H-21-A5 2008;28:1-48.
- Hollensead SC, Krishnan J, Kottke-Merchant K. Coagulation Testing. In: Kottke-Merchant K. editor. *An Algorithmic Approach to Hemostasis Testing*. 2nd ed. Northfield: CAP Press, 2016.
- Olson JD, Jennings I, Meijer P, et al. Lack of grading agreement among international hemostasis external quality assessment programs. *Blood Coagul Fibrinolysis* 2018;29:111-9.
- Favaloro EJ, Jennings I, Olson J, et al. Towards harmonization of external quality assessment/proficiency testing in hemostasis. *Clin Chem Lab Med* 2018;57:115-26.
- Smock KJ, Moser KA. What have we learned from coagulation laboratory participation in external quality programs? *Int J Lab Hematol* 2019;41 Suppl 1:49-55.
- International Organization for Standardization. ISO/IEC 17043: Conformity assessment-General requirements for proficiency testing. Geneva: ISO, 2010.
- World Health Organization. WHO manual for organizing a national external quality assessment programme for health laboratories and other testing sites. Geneva:

- WHO, 2016.
9. Marlar RA, Meijer P, Jennings I, et al. Guidance on the establishment, implementation and performance

for proficiency testing programs for thrombosis and hemostasis. *Ann Blood* 2020. doi: 10.21037/aob.2020.02.01.

doi: 10.21037/aob.2020.03.02

Cite this article as: Marlar RA, Meijer P, Jennings I, Olson J; on behalf of EQATH (External Quality Assurance in Thrombosis and Hemostasis). Consistent accuracy: a goal for thrombosis and hemostasis testing is accomplished using an external quality assurance program. *Ann Blood* 2020;5:11.