101 TOPICS FOR CLINICAL MICROBIOLOGY LABORATORY LEADERS

ACCREDITATION, VERIFICATION, QUALITY SYSTEMS, AND MORE

REBEKAH M. MARTIN

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For Ben
Life with you is my favorite adventure
xxx

Excellence, then, is not an act but a habit.
—Will Durant (1926) *The Story of Philosophy: The Lives and Opinions of the World's Greatest Philosophers* (often misattributed to Aristotle)

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Foreword

As I settle into the later phase of my career in diagnostic and medical microbiology, I occasionally reflect on my activities, which I hope have had a special impact on or significance to the field. Two notable examples that stand out are mentoring the next generation of laboratory medicine leaders and serving as a subject matter expert on the topic of verification and validation of laboratory tests. (I fondly remember being referred to by colleagues as the "V and V guy.") In these areas, I have had the pleasure of collaborating with Rebekah Martin, coauthoring manuscripts on the verification and validation of laboratory tests. Martin has demonstrated a deep knowledge and understanding of this complex subject, for which written regulations are relatively sparse. This often leaves details open to interpretation and forces laboratorians to consult supplemental materials authored by subject matter experts.

In this book, Martin provides a concise overview and practical guidance for several topics that are important responsibilities of laboratory leaders. These topics include laboratory accreditation, verification and validation of laboratory tests (of course), and essential elements of a laboratory quality management system—such as personnel qualifications, competency assessments, equipment maintenance, information management, document control, process control (including individualized quality control programs), nonconforming event investigation, and process improvement. These are challenging topics, because (as previously mentioned) the laboratory regulations often lack granularity. Much is left to the discretion and expertise of the laboratory director, whether designing a test verification study, developing a competency assessment program, investigating nonconforming events, or establishing an external quality assessment program for nonregulated analytes. While there are resources available for these topics, Martin has skillfully tied it all together in one practical, insightful, and informative guide. Concise and addressing the key points, this book serves as a pocket guide that I'm confident laboratory leaders will frequently consult. Keep it in a handy location—a hard copy will likely be well worn.

Several chapters deserve special mention. The book appropriately begins with a comprehensive description of the Clinical Laboratory Improvement Amendments (CLIA), which includes a nice description of emergency use authorization (EUA) and the important distinction between an EUA and a declared public health emergency. Martin does a great job of defining test complexity designations, and her chapter on waived testing is particularly timely given the recent explosion in point-of-care testing for infectious diseases, driven largely by COVID-19, as well as sexually transmitted infections, hepatitis C virus, and others. Most point-of-care testing in the United States is performed with CLIA-waived tests, and this chapter addresses some key considerations such as personnel qualifications and training requirements.

A chapter near and dear to my heart is the one on verification and validation, which provides important definitions for ambiguous concepts such as a test system and what

represents a test modification. Martin also helps to sort out an ongoing source of confusion: when is it necessary to perform a verification or validation study? The chapter on quality management systems (QMS) discusses each of the essential elements of a QMS and describes important resources such as the Clinical and Laboratory Standards Institute (CLSI). The chapter on personnel clearly lays out the CLIA definitions of laboratory personnel, distinguishing, for examples, between individuals who might be titled "laboratory director" by their institution but are actually usually either a technical or general supervisors under CLIA's definitions—an important distinction.

Finally, the chapter on occurrence (or error, or nonconforming event) management is essential reading. Some of these laboratory errors can lead to adverse events and patient harm and Martin does a superb job explaining the process for managing errors, including monitoring, investigating, determining root cause, and implementing corrective and preventive actions. I especially note the inclusion of a risk matrix table in this chapter that highlights the probability and risk of patient harm.

Martin's book will be extremely valuable not only for laboratory leaders—medical and technical directors, managers, supervisors—but also for trainees in laboratory medicine fellowship programs, for whom board examinations are right around the corner. As a current representative of the diagnostic device industry, I also strongly believe this book will be a great resource for my industry colleagues, helping them better understand the laboratory customer environment and the regulatory guard rails in which they operate.

Michael Loeffelholz
Vice President, Scientific Affairs
Cepheid
Sunnyvale, CA

Preface

The purpose of this book is to act as a guide for navigating some of the complexities of clinical microbiology laboratory administration. As we all know, maintaining compliance in the clinical laboratory can be challenging. Not only are regulations and requirements numerous, but they can sometimes be confusing or vague—and on occasion there may be updates or events that introduce new requirements and unfamiliar processes. Additionally, terms like "CLIA," and activities such as "verification" and "document control" are often casually referred to, but are also often unaccompanied by definitions, context, or an explanation of how to fulfill related requirements. It is therefore unsurprising that it may be daunting to develop—or even to work within—a laboratory management and administrative system when there are gaps in practical knowledge.

When I began working on this project, I wanted to create something that would help fill these gaps for laboratory administrators and employees, but that would also be something I would have actually used in the clinical laboratory. I also wanted to consolidate information into a single, digestible resource. My goal was therefore to develop an easy-to-use, accessible reference that could provide readers across experience levels with context for various requirements as well as some specific suggestions for best practices. The product of these contemplations is what you now hold in your hands.

While the focus of this text is on activities for the clinical microbiology laboratory in particular, a great deal of what is included will be applicable to or adaptable for other specialties in the clinical laboratory. It should be noted that the requirements and suggestions included throughout the book are intended for clinical laboratories based in the United States that must comply with U.S. federal and/or state requirements[1].

As a final note, this book is meant to be an aid for YOU. Whether you are a new (or seasoned!) laboratory director, a microbiology fellow or pathology resident, a laboratory manager, a medical laboratory scientist, a student, or you just happen to be interested in these topics, my hope is that you find this text useful (and perhaps even a little bit engaging) and that you come away with more knowledge than when you started.

Rebekah M. Martin
October 2024

1 This book is comprehensive but not exhaustive. Laboratory personnel both within and outside of the United States are responsible for identifying and complying with all applicable regulations and requirements.

Acknowledgments

It is perhaps cliché—but nonetheless true—to say that this book would never have happened without the support of a whole host of people. I've been incredibly lucky to have a fantastic group of colleagues, friends, and family who have assisted in getting me to this point. I wish to extend particular thanks to those listed here.

Michael J. Loeffelholz, for recommending me to write this book. When you passed the torch of expertise, I never dreamed it would lead to this!

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All the Beautiful Micro Mamas: Mel, Paige, Jocelyn, Lauren, Thess, Phyu, and Dona! For sharing wisdom, experience, frustration, and laughter. You women inspire me.

Lola, my cat, for providing all the snuggles during writing sessions.

Elisa, my sibling, for being a source of delight, encouragement, and support; both in writing and in life.

Bob and Kathy, my parents, for being interested in and proud of everything I've accomplished. And of course, thank you for regularly asking about how "the book" is going. Good news mom and dad...it's finally finished!!

Ben, my husband. As an historian and archivist, you probably care very little about the regulations governing clinical micro labs. But you care about me, and you know that I care about this. Thank you for reading every single chapter and providing feedback prior to submission, and for putting up with me while I fretted about deadlines and brooded over specific wording. You are always the first to tell me "You can do it". You encourage me to reach for my dreams—whether those dreams involve writing a book, moving across the ocean, or taking time to do absolutely nothing—and I would not have made it as far as I have without your partnership and support.

And finally, thanks to you, the reader, for taking the time to engage with this book.

About the Author

Rebekah (Bekah) M. Martin, PhD, D(ABMM), MLS(ASCP)^{CM} has enjoyed working in or adjacent to the clinical microbiology laboratory throughout a career that spans the health care, academic, and industry sectors. After graduating with a clinical laboratory science degree from Michigan State University (Go Green!), she worked as a medical laboratory scientist in the microbiology division at Henry Ford Hospital in Detroit. She then went on to receive her PhD in molecular and cellular pathology from the University of Michigan where her dissertation focused on identifying bacterial and host risk factors for clinical infection with *Klebsiella pneumoniae*. She has completed a medical microbiology fellowship at the University of Utah School of Medicine and ARUP Laboratories, worked as an associate technical director of microbiology at Labcorp, taught as an assistant professor both in the Clinical and Diagnostic Sciences department at Oakland University and in the Biomedical Laboratory Diagnostics program at Michigan State University, and is currently the regional medical affairs subject matter expert for molecular solutions at Becton, Dickinson, and Company (BD) in the Europe, Middle East, and Africa region. Bekah is certified as a Diplomate of the American Board of Medical Microbiology, and also maintains certification as a Medical Laboratory Scientist through the American Society for Clinical Pathology Board of Certification. She is passionate about good food and wine. She also enjoys traveling, spending time outdoors hiking and kayaking, and spending time indoors reading. Bekah currently lives in the East Riding of Yorkshire in the United Kingdom with her husband Ben and their cat Lola.

List of Abbreviations

Unless otherwise stated, all government regulations and bodies refer to those in the United States.

A2LA	American Association for Laboratory Accreditation
AABB	Association for the Advancement of Blood & Biotherapies (formerly the American Association of Blood Banks)
ABB	American Board of Bioanalysis
ABCC	American Board of Clinical Chemistry
ABFT	American Board of Forensic Toxicology
ABMGG	American Board of Medical Genetics and Genomics
ABMLI	American Board of Medical Laboratory Immunology
ABMM	American Board of Medical Microbiology
ACHC	Accreditation Commission for Health Care
ACHI	American College of Histocompatibility and Immunogenetics (formerly American Board of Histocompatibility and Immunogenetics [ABHI])
ACLA	American Clinical Laboratory Association
AMP	Association for Molecular Pathology
AMR	Analytical measurement range
ANAB	ANSI National Accreditation Board
ANSI	American National Standards Institute
APHL	Association of Public Health Laboratories
ASCP BOC	American Society for Clinical Pathology Board of Certification
ASHI	American Society for Histocompatibility & Immunogenetics
ASM	American Society for Microbiology
ASR	Analyte specific reagents
AST	Antimicrobial susceptibility test
BSL	Biosafety level
BLA	Biologics License Application
BV	Bacterial vaginosis
CA	Categorical agreement
CAP	College of American Pathologists
CAPA	Correction and preventive action
CDC	Centers for Disease Control and Prevention
CE	Continuing education
CFR	Code of Federal Regulations
CFU	Colony forming units