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1st Edition

CLSI MM29™

Interpretive Framework for Heritable Disorders

Sample

CLSI MM29 provides a comprehensive overview on the expanding landscape of clinical germline genetic testing, with specific focus on good practices for result interpretation and professional communication across all clinical practitioners of medical genetics and genomics.

A CLSI report for global application.

Interpretive Framework for Heritable Disorders

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Abstract

CLSI MM29—*Interpretive Framework for Heritable Disorders* provides a structured overview on professional communication between laboratorians and clinical providers in the context of constitutional genetic and genomic testing. It is intended to facilitate more informed and effective test interpretation and clinical decision-making by medical genetics practitioners, including laboratory directors, genetic counselors, clinicians, regulatory and commercial partners, and other health care professionals. CLSI MM29 focuses on distilling the complexity of constitutional/germline genetic testing for heritable diseases with emphasis on shared understanding and professional communication, with the overarching goal of improving clinical care and patient experiences. Clinical genetic and genomic testing is an evolving area, in large part due to the rapid advances in molecular technologies that enable more accessible and comprehensive health information, which necessitates ongoing evaluation of appropriate use and good practices among health care stakeholders.

Fundamental concepts in clinical molecular and cytogenomic testing are detailed, including both diagnostic testing and predictive screening, all presented in the context of result interpretation and appropriate counseling among professionals and patients. To facilitate an effective and structured overview, separate subchapters are devoted to the following areas: medical genetic practitioners, basic genetic testing principles, spectrum of genetic/genomic technologies, and integrating genetic results into clinical care decisions.

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Foreword

Effective communication between genetic testing laboratories and clinical providers is crucial for patient care, yet it may present challenges. Communication pathways vary depending on the context, including diagnostic genetic testing for heritable disease, predictive testing, and genomic screening. For instance, while academic laboratories may have access to patient records and maintain closer relationships with clinicians, commercial laboratories often lack this access.

As genetic and genomic testing continues to gain mainstream adoption, a clear understanding of the patient's clinical picture is key to facilitating actionable test results and clinical care decisions. CLSI MM29 offers timely guidance for laboratorian and provider communication in genetic/genomic testing. The central premise of CLSI MM29 is that high-quality genetic/genomic testing alone is insufficient, because it requires effective communication between clinicians and laboratory providers throughout all aspects of the testing process for good practice clinical care, including:

- Ordering the correct test
- Making accurate classification and interpretation
- Understanding technical limitations
- Providing genetic counseling

Written by a multidisciplinary group of experts in the genetics field, CLSI MM29 focuses on the practical information that clinicians and laboratory providers must share during the genetic evaluation process. It provides an overview of key stakeholders, reviews principles of molecular genetic testing, and shows how to integrate findings into clinical care. Ultimately, CLSI MM29 fills a substantial gap by supporting communication among stakeholders to promote appropriate use of genetic testing and improve health outcomes.

NOTE: The content of CLSI MM29 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

constitutional variation

counseling

genetic testing

genetics/genomics

inherited diseases

patient/provider
communication

result interpretation

return of results

Chapter 1

Introduction

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Interpretive Framework for Heritable Disorders

1 Introduction

1.1 Scope

CLSI MM29 emphasizes the essential role of the laboratory director and/or applicable personnel to engage effectively with medical care personnel to accurately describe and convey the appropriate clinical indications for pursuing genetic testing for heritable conditions. Laboratory directors can actively create opportunities for shared decision-making with clinician colleagues to help integrate evolving technologies into clinical decisions for patient care.

CLSI MM29 also focuses on the accurate interpretation(s) of genetic test results to include the implications for patients and their relatives when relevant. Limitations of genetic testing, such as gene and/or variant content included in the analyses, are also described.

CLSI MM29 does not include detailed descriptions of genetic testing methodologies (covered in CLSI MM01¹), a catalog of genetic disorders, or how to establish a molecular genetic testing laboratory (covered in CLSI MM19²). CLSI MM29 does not cover directing or growing a laboratory, assay development/validation, or quality management (covered in CLSI MM26³).

Because there are genetic laboratories in various settings (eg, commercial or academic reference laboratories, commercial specialty genetic laboratories, and genetic laboratories within academic medical centers or hospitals),⁴ information provided in CLSI MM29 should be applied by laboratorians as appropriate based on institutional context and professional judgement.

1.2 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to “standard precautions.” Standard precautions are guidelines that combine the major features of “universal precautions and body substance isolation” practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of bloodborne pathogens. Published guidelines are available that discuss the daily operations of diagnostic medicine in humans and animals while encouraging a culture of safety in the laboratory.⁵ For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI M29.⁶

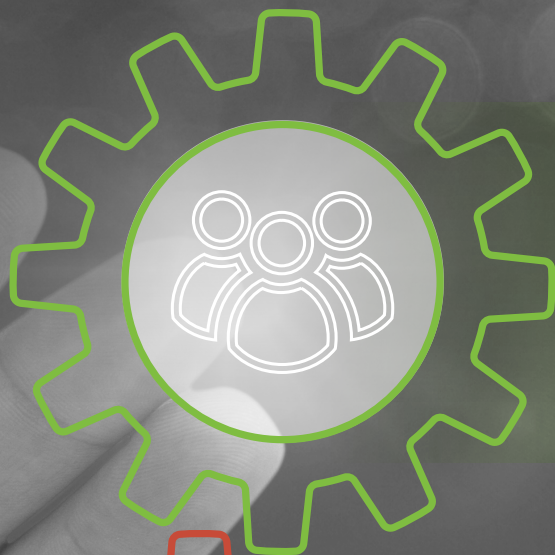
1.3 Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization whenever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in different countries and regions and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. CLSI recognizes its important role in these efforts, and its consensus process focuses on harmonization of terms to facilitate the global application of standards and guidelines. Table 1 is provided to clarify the intended interpretations of common terms.

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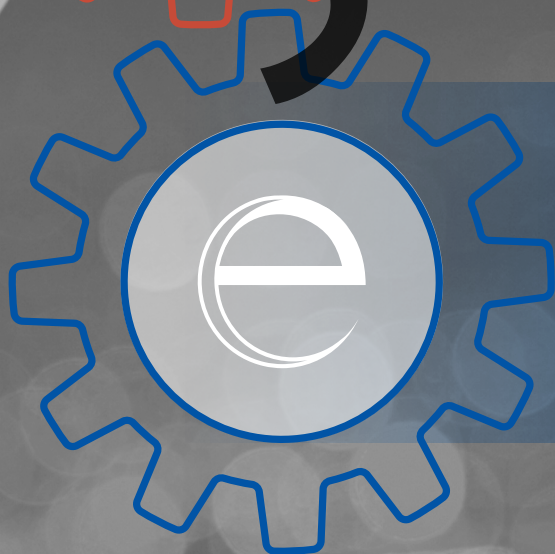
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