CLINICAL AND LABORATORY STANDARDS INSTITUTE®

2nd Edition

CLSI C38™

Control of Preexamination Variation in Trace Element Determinations

CLSI C38 provides guidelines for patient preparation, specimen collection, transport, and processing for the measurement of trace elements in a variety of biological matrixes.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Control of Preexamination Variation in Trace Element Determinations

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Abstract

Clinical and Laboratory Standards Institute C38—*Control of Preexamination Variation in Trace Element Determinations* is intended for persons responsible for the collection and processing of samples used for trace, toxic, and essential metal and metalloid determinations. The guideline covers patient preparation as well as considerations for collection, transport, and processing of specimens by element. Contamination control and quality assurance programs are also discussed.

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Committee Membership

Consensus Council

The Consensus Council sets priorities for CLSI standards development and votes on Final Draft documents to confirm that process requirements have been met. Consensus Council members are listed on the CLSI website: https://clsi.org/standards-development/consensus-council/

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Contents

Contents (Continued)

Foreword

Preexamination factors are probably the most important cause of erroneous trace element reference data in biological matrixes today. Developing sensitive, specific, and accurate analytical technology at an acceptable cost has moved the determination of trace, toxic, and essential metals from research facilities into a wide range of medical laboratories. Expanding knowledge of trace element nutrition and toxicity has increased clinical demand for these assays. However, with increased sensitivity and lower limits of detection, the problem of specimen contamination with the metal of interest has been magnified greatly. It is vital that the accurately determined trace, toxic, or essential element concentration reflects the condition of the patient and not contamination introduced during collection, processing, handling, and analysis.

Earlier attempts to define reference interval data for many of the trace, toxic, and essential elements provided intervals that were far wider than what are now accepted as a population "normal." This resulted from a lack of awareness that the ubiquity of many trace elements in the environment required special precautions from preexamination processes through the actual analysis.

In this guideline, the components of specimen collection and preexamination and examination processing that can contribute to trace element contamination are covered. The trace elements most commonly tested for clinical purposes are individually listed. For each element, the optimal specimen for assessment, preexamination factors to consider in patient preparation and population reference intervals, or concentrations suggesting elevated exposures or deficiency, are described.

Overview of Changes

This guideline replaces CLSI C38-A, published in 1997. Several changes were made in this edition, including:

- Adding information on indications, patient preparations, sample selection, transport and storage, reference intervals, and conversion factors for each element
- Updating population reference intervals from the latest US National Health and Nutrition Examination Survey for most elements
- Adding a chapter on analytical instrumentation, recommended reporting units (see Appendix C) and an extensive appendix on reference interval studies (see Appendix D)

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

KEY WORDS

analytical instrumentation
contamination control
essential element
metalloid
specimen collection
trace element
toxic element

Chapter 1

Introduction

Control of Preexamination Variation in Trace Element Determinations

1 Introduction

1.1 Scope

C38 provides guidance for preexamination considerations for trace element analysis in biological matrixes (ie, body fluids, such as whole blood, urine, hair, nails, human milk, and tissues). This guidance includes applicable recommendations for patient preparation (such as diurnal variation, diet, medications including chelation therapy and mineral supplements; the use of alcohol and tobacco; time of collection relative to the above activities, including workplace schedules, and homeostasis), specimen collection (most appropriate specimen matrix for screening, diagnosis, or monitoring), use of anticoagulants and/or preservatives; good practices for collection procedures (including containers and devices), transport requirements, contamination monitoring and control (including water, reagents, and examination consumables), and specimen processing. Specific reference is made to those elements that are known to be essential or toxic for humans and are therefore likely to be measured for clinical reasons.

This guideline will benefit those in the medical, public health, and environmental laboratories as well as manufacturers and regulatory and accreditation agencies.

This guideline will not include an extensive review of examination protocols and postexamination considerations, lead (Pb) testing (see CLSI C40[1]) or content that is not consistent with current practices and guidelines.

1.2 Background

It is recognized that much of the pioneering research published in trace element literature is based on erroneously derived reference interval data.[2] The source of the problem was the lack of recognition of exogenous specimen contamination, which could have occurred at the collection, transport, processing, or examination stages. Thus, reference intervals for ultratrace elements, such as chromium (Cr), or acceptable blood concentrations for toxic elements, such as aluminum (Al), have decreased severalfold over the past two decades.

The use of increasingly sensitive methods, such as electrothermal atomic absorption spectrometry (ETAAS) or inductively coupled plasma mass spectrometry (ICP-MS); increasing interest in ultratrace elements; and the need for precise and accurate analyses for elements such as Pb, at extremely low levels, have accentuated the problems of examination and preexamination contamination.[3]

The intent of this guideline is to develop an awareness of the factors that affect the determination of trace elements in a variety of specimen types, foster communication between the laboratorian performing the test and those responsible for collecting the specimen, and provide suggested protocols for eliminating preexamination variability.

1.3 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