CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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Maternal Serum Screening

This document addresses the steps required to provide reliable screening and reporting using examples of serum markers currently in common use (AFP, hCG, uE3, inhibin A, PAPP-A). Emphasized is first-trimester screening, in which serum markers used are PAPP-A and hCGβ, and the main ultrasound marker is nuchal translucency. Outcome evaluation, information management, and calculation of risk are also emphasized.

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

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Maternal Serum Screening; Approved Standard—Second Edition

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Abstract

Clinical and Laboratory Standards Institute document I/LA25-A2—*Maternal Serum Screening; Approved Standard—Second Edition* is written for clinical laboratorians who participate in prenatal screening for open neural tube defects and trisomy 21 (Down syndrome) involving alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3), inhibin A, and/or pregnancy-associated plasma protein-A (PAPP-A) measurements, as well as for clinicians and manufacturers who have a direct interest in the tests. First-trimester screening (including nuchal and ultrasound measurements) and integrated first- and second-trimester screening are emphasized. The standard is intended to present necessary considerations: preanalytical, analytical, and postanalytical (preexamination, examination, and postexamination); and to ensure the reliability of the tests, including the risk calculation, the outcome evaluation, and the accuracy of the information management. If properly applied, the five biochemical determinations and the risk calculations can contribute constructively to the field of prenatal screening and to the welfare of pregnant women and the fetus.

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Foreword

This document updates, extends, and replaces I/LA25-A to provide recommendations on maternal serum screening techniques. Many new options are available since publication of I/LA25-A, including testing in the first trimester, in the second trimester, and testing that combines both the first and second trimester.

At this time, the principles of serum screening remain similar regardless of which assay(s) is/are used as part of the evaluative service. The standard addresses the steps required to provide reliable screening and reporting using examples of serum markers currently in common use (alpha-fetoprotein [AFP], human chorionic gonadotropin [hCG], unconjugated estriol [uE3], inhibin A, pregnancy-associated plasma protein-A [PAPP-A]). It is recognized that the list of assays and methods of pregnancy screening will continue to change. First-trimester screening relies on, in addition to the biochemical markers hCG or hCGβ and PAPP-A, a nuchal translucency (NT) measurement that requires the expertise of experienced ultrasonographers. Outcome evaluation, information management, and risk calculation are also emphasized in this standard. Screening for trisomy 21 (Down syndrome) also includes the incidental detection of trisomy 18 (Edwards syndrome) in both the first and second trimester, along with trisomy 13 (Patau syndrome) and monosomy X (Turner syndrome) in the first trimester.

Key Words

Alpha-fetoprotein, amniotic fluid, chromosomal abnormalities, human chorionic gonadotropin, inhibin A, monosomy X (Turner Syndrome), nuchal translucency, open neural tube defects, pregnancy-associated plasma protein A, prenatal diagnosis, trisomy 13 (Patau Syndrome), trisomy 18 (Edwards Syndrome), trisomy 21 (Down syndrome), unconjugated estriol

Maternal Serum Screening; Approved Standard—Second Edition

1 Scope

This standard specifies requirements and recommendations for maternal serum aspects of prenatal screening for neural tube defects (NTDs) and trisomy 21 (T21) (Down syndrome [DS]) and incorporates ultrasound measurements to ensure that screening methods and quality control procedures are carried out to a high standard. It offers guidance that may be used by manufacturers and clinical laboratories that provide prenatal screening services. This document also addresses the standards that should be maintained by manufacturers and by laboratories and clinicians when providing screening services used to evaluate pregnancies and risks of fetal disease.

This document intends to strike a balance between being sufficiently specific to be clear but not too prescriptive, allowing laboratory directors to use their professional judgment in setting policy.

The intended users of this standard are manufacturers, diagnostic laboratories, regulatory agencies, and public health authorities involved in providing or regulating prenatal screening services used to evaluate pregnancies and risks of fetal disease.

2 Introduction

Prenatal screening for serious fetal abnormalities has made significant advances since the 1970s, when maternal serum alpha-fetoprotein (MSAFP) started to be used as a screening test for open NTDs. Additional maternal serum measurements have been shown to be useful, for example, in screening for T21. Laboratories have not only had to extend the number of measurands they offer but also become proficient in risk assessment calculations based on the pattern of the results. The maternal serum screening (MSS) laboratory reports must be designed so that clinicians can inform patients of the risk of having an affected fetus.

The goal of this document is to update information on MSS for NTDs and T21, and especially introduce first-trimester and integrated screening standards.

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 blood-borne pathogens. Standard and universal precaution guidelines are available from the US Centers for Disease Control and Prevention.[1] 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 document M29.[2]

4 Terminology

4.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever 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