SLOVENSKI STANDARD
oSIST prEN ISO 17099:2017

01-junij-2017

Radiološka zaščita - Merila za delovanje laboratorijev, ki za biološko dozimetrijo uporabljajo analizo tvorjenja mikrojeder s citokinetskim blokom v perifernih krvnih limfocitih (ISO 17099:2014)

Radiological protection - Performance criteria for laboratories using the cytokinesis block micronucleus (CBMN) assay in peripheral blood lymphocytes for biological dosimetry (ISO 17099:2014)

Radioprotection - Critères de performance pour les laboratoires pratiquant la dosimétrie biologique par le test des micronoyaux avec blocage de la cytodiérèse (CBMN) dans les lymphocytes du sang périphérique (ISO 17099:2014)

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13.280	Varstvo pred sevanjem	Radiation protection
17.240	Merjenje sevanja	Radiation measurements

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INTERNATIONAL STANDARD

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Radiological protection — Performance criteria for laboratories using the cytokinesis block micronucleus (CBMN) assay in peripheral blood lymphocytes for biological dosimetry

Radioprotection — Critères de performance pour les laboratoires pratiquant la dosimétrie biologique par analyse des micronoyaux par blocage de la cytokinèse (CBMN) dans les lymphocytes du sang périphérique

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT), see the following URL: Foreword — Supplementary information.

The committee responsible for this document is ISO/TC 85, *Nuclear energy, nuclear technologies, and radiological protection*, Subcommittee SC 2, *Radiological protection*.

Introduction

The purpose of this International Standard is to define the use of the cytokinesis block micronucleus (CBMN) assay with human peripheral blood lymphocytes for biological dosimetry of exposure to ionizing radiation. This assay is intended to be applied for accidental or malevolent exposures involving a) up to a few casualties to provide individual full dose estimates or b) in a triage mode to populations to provide interim dose estimates for individuals.

The CBMN assay is an alternative cytogenetic technique, which is possibly simpler and faster to perform than the dicentric assay (ISO 19238:2014, ISO 21243:2008). It is also routinely used to demonstrate exposure to genotoxic agents, other than ionizing radiation, which is not covered in this International Standard. Although culture of the blood samples is slightly longer than for dicentrics, the scoring of micronuclei in binucleated lymphocytes is easier.

As was done with the dicentric assay, the CBMN assay has been adapted for the emergency triage of large-scale multi casualty radiation accidents. The blood volume required for sufficient number of scorable binucleated cells is similar than required for the dicentric assay. Again, the faster counting speed for micronuclei compensates for the extended culture time. In addition, the CBMN assay can be performed in an automated mode.

This International Standard provides a guideline on how to perform the CBMN assay for dose assessment using documented and validated procedures. Dose assessment using the CBMN assay has relevance in medical management, radiation-protection management, record keeping, and medical/legal requirements. This International Standard is divided into two parts, according to the use of CBMN assay: radiation exposure of a few individuals or population triage in a large radiological event.

A part of the information in this International Standard is contained in other international guidelines and scientific publications, primarily in the International Atomic Energy Agency's (IAEA) technical reports series on biological dosimetry. However, this International Standard expands and standardizes the quality assurance and quality control, the criteria of accreditation and the evaluation of performance. This International Standard is generally compliant with ISO/IEC 17025 "*General requirements for the competence of testing and calibration laboratories*" with particular consideration given to the specific needs of biological dosimetry. The expression of uncertainties in dose estimations given in this International Standard complies with the "ISO-guide for the expression of uncertainty in measurement" (former GUM) and the ISO 5725-all parts.

Radiological protection — Performance criteria for laboratories using the cytokinesis block micronucleus (CBMN) assay in peripheral blood lymphocytes for biological dosimetry

1 Scope

This International Standard addresses the following:

a) confidentiality of personal information for the customer and the laboratory;

b) laboratory safety requirements;

c) radiation sources, dose rates, and ranges used for establishing the calibration reference dose-effect curves allowing the dose estimation from CBMN assay yields and the minimum resolvable dose;

d) performance of blood collection, culturing, harvesting, and sample preparation for CBMN assay scoring;

e) scoring criteria;

f) conversion of micronucleus frequency in binucleated cells into an estimate of absorbed dose;

g) reporting of results;

h) quality assurance and quality control;

i) informative annexes containing examples of a questionnaire, instructions for customers, a microscope scoring data sheet, a sample report and advice on strengths and limitations of current automated systems for automated micronucleus scoring.

2 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

2.1
acentric
chromosome fragment of varying size

Note 1 to entry: When it is formed independently of a dicentric or centric ring chromosome aberration, it is usually referred to as an excess acentric.

2.2
background level
spontaneous yield (or number) of micronuclei recorded in control samples or individuals

2.3
bias
statistical sampling or testing error caused by systematically favouring some outcomes over others

2.4
binucleated cells
cells that have completed one nuclear division after mitogen stimulation and cell type in which micronuclei are scored

Note 1 to entry: These cells are accumulated in culture using cytochalasin-B which is an inhibitor of cytokinesis.

2.5
CBMN laboratory
laboratory performing biological dosimetry measurements using the CBMN assay

2.6
centric ring
aberrant circular chromosome resulting from the joining of two breaks on separate arms of the same chromosome, generally accompanied by one acentric fragment

2.7
centromere
specialized constricted region of a chromosome that appears during mitosis joining together the two sister chromatids

2.8
chromosome
structure that carries genetic information

Note 1 to entry: Normally, 46 such structures are contained in the human cell nucleus. During nuclear division, they condense to form characteristically-shaped bodies.

2.9
chromatid
either of the two strands of a duplicated chromosome that are joined by a single centromere

Note 1 to entry: Chromatids separate during mitosis to become individual chromosomes.

2.10
confidence interval
statistical range about an estimated quantity within which the value of the quantity is expected to occur, with a specified probability

2.11
cytochalasin-B
Cyto-B
reagent used to block cytokinesis in dividing cells allowing once-divided cells to be identified as binucleated cells

Note 1 to entry: The binucleated cells are the cells in which micronuclei are specifically scored.

2.12
dicentric
aberrant chromosome bearing two centromeres derived from the joining of parts from two broken chromosomes, generally accompanied by an acentric fragment

2.13
fluorescence in situ hybridization
FISH
technique that uses specific sequences of DNA as probes to particular parts of the genome, allowing the chromosomal regions to be highlighted or “painted” in different colours by attachment of various fluorochromes

Note 1 to entry: This technique permits the detection of damage involving exchanges between differently painted pieces of DNA (usually whole chromosomes).

2.14
interphase
period of the cell cycle between the mitotic divisions

2.15
linear energy transfer
LET
quotient of dE/dl, as defined by the International Commission on Radiation Units and Measurements (ICRU), where dE is the average energy locally imparted to the medium by a charged particle of specific energy in traversing a distance of dl

2.16
metaphase
second stage of mitosis when the nuclear membrane is dissolved, the chromatids are condensed to their minimum lengths and are aligned for division at the metaphase plate

2.17
micronucleus or micronuclei
MN
small nucleus that arises from lagging acentric chromosome fragments or whole chromosomes during nuclear division and chromosome segregation at mitosis during anaphase/telophase

Note 1 to entry: More that 90 % of the micronuclei induced by ionizing radiation arise from lagging acentric chromosome fragments.

2.18
minimum detection level
MDL
smallest measurable amount (e.g. yield or dose) that is detected with a probability β of non-detection (Type II error) while accepting probability α of erroneously deciding that a positive (non-zero) quantity is present in an appropriate background sample (Type I error)

2.19
minimum resolvable dose
lowest additional dose for which the lower 95 % poisson confidence limit is greater than 0, so that there is a 97,5 % chance that the dose received in excess of normal background is greater than 0

2.20
nuclear division index
index in the CBMN assay that is calculated from the relative frequencies of mononucleated, binucleated, and multinucleated cells

Note 1 to entry: This index provides a measure of inhibition of nuclear division.

2.21
precision
dispersion of measurements with respect to a measure of location or central tendency

2.22
quality assurance
planned and systematic actions necessary to provide adequate confidence that a process, measurement, or service has satisfied given requirements for quality

EXAMPLE Dose specified in a licence.

2.23
quality control
part of quality assurance intended to verify that systems and components correspond to pre-determined requirements