

Radiological protection - Performance criteria for laboratories using Fluorescence In Situ Hybridization (FISH) translocation assay for assessment of exposure to ionizing radiation (ISO 20046:2019)

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 20046:2021 sisaldab Euroopa standardi EN ISO 20046:2021 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 20046:2021 consists of the English text of the European standard EN ISO 20046:2021.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas	This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation.
Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 10.02.2021.	Date of Availability of the European standard is 10.02.2021.
Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest.	The standard is available from the Estonian Centre for Standardisation and Accreditation.

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile standardiosakond@evs.ee.

ICS 13.280

Standardite reprodutseerimise ja levitamise õigus kuulub Eesti Standardimis- ja Akrediteerimiskeskusele

Andmete paljundamine, taastekitamine, kopeerimine, salvestamine elektroonsesse süsteemi või edastamine ükskõik millises vormis või millisel teel ilma Eesti Standardimis- ja Akrediteerimiskeskuse kirjaliku loata on keelatud.

Kui Teil on küsimusi standardite autorikaitse kohta, võtke palun ühendust Eesti Standardimis- ja Akrediteerimiskeskusega: Koduleht www.evs.ee; telefon 605 5050; e-post info@evs.ee

The right to reproduce and distribute standards belongs to the Estonian Centre for Standardisation and Accreditation

No part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, without a written permission from the Estonian Centre for Standardisation and Accreditation.

If you have any questions about copyright, please contact Estonian Centre for Standardisation and Accreditation:

Homepage www.evs.ee; phone +372 605 5050; e-mail info@evs.ee

ICS 13.280

English Version

Radiological protection - Performance criteria for
laboratories using Fluorescence In Situ Hybridization
(FISH) translocation assay for assessment of exposure to
ionizing radiation (ISO 20046:2019)

Radioprotection - Critères de performance pour les
laboratoires utilisant l'analyse des translocations
visualisées par hybridation in situ fluorescente (FISH)
pour évaluer l'exposition aux rayonnements ionisants
(ISO 20046:2019)

Strahlenschutz - Leistungskriterien für Laboratorien,
die den Fluoreszenz-in-situ-Hybridisierungs-(FISH)-
Translokationstest zur Bewertung der Exposition
gegenüber ionisierender Strahlung verwenden (ISO
20046:2019)

This European Standard was approved by CEN on 18 January 2021.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.



EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

European foreword

The text of ISO 20046:2019 has been prepared by Technical Committee ISO/TC 85 "Nuclear energy, nuclear technologies, and radiological protection" of the International Organization for Standardization (ISO) and has been taken over as EN ISO 20046:2021 by Technical Committee CEN/TC 430 "Nuclear energy, nuclear technologies, and radiological protection" the secretariat of which is held by AFNOR.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by August 2021, and conflicting national standards shall be withdrawn at the latest by August 2021.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 20046:2019 has been approved by CEN as EN ISO 20046:2021 without any modification.

Contents

	Page
Foreword	v
Introduction	vi
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Translocation assay by FISH	5
4.1 General.....	5
4.2 Culturing and fixation.....	5
4.3 Types of staining.....	5
4.4 Scoring.....	6
4.5 General requirement of the laboratory.....	6
5 Responsibility of the customer	6
6 Responsibility of the laboratory	7
6.1 Setup and sustainment of the QA program.....	7
6.2 Responsibility during service.....	7
7 Confidentiality of personal information	8
7.1 Overview.....	8
7.2 Applications of the principle of confidentiality.....	8
7.2.1 Delegation of responsibilities within the laboratory.....	8
7.2.2 Requests for analysis.....	9
7.2.3 Transmission of confidential information.....	9
7.2.4 Anonymity of samples.....	9
7.2.5 Reporting of results.....	9
7.2.6 Storage of data and results.....	9
8 Laboratory safety requirements	9
8.1 Overview.....	9
8.2 Microbiological safety requirements.....	10
8.3 Chemical safety requirements.....	10
8.4 Optical safety requirements.....	11
8.5 Safety plan.....	11
9 Sample processing	11
9.1 Culturing and staining.....	11
9.2 Scoring.....	12
9.2.1 Criteria for scoring.....	12
9.2.2 Conversion of translocation frequencies to genome equivalence.....	12
10 Background levels of translocations	13
11 Calibration curves	14
11.1 Calibration source(s).....	14
11.2 Establishment of calibration curve(s).....	14
12 Criteria for converting a measured aberration frequency into an estimate of absorbed dose	16
12.1 Determination of estimated whole-body absorbed dose and confidence limits.....	16
12.1.1 General.....	16
12.1.2 Comparison with the background level: Characterisation of the minimum detectable dose.....	16
12.1.3 Confidence limits on the number of translocations.....	19
12.1.4 Adjustment for background yield.....	20
12.1.5 Calculation of absorbed dose.....	21
12.1.6 Calculation of uncertainty on absorbed dose.....	22

12.1.7	Acute and non-acute exposure cases.....	22
12.1.8	Other exposure scenarios	23
13	Reporting of results.....	23
13.1	General.....	23
13.2	Content of the report (see Annex C for an example of a standard form).....	23
13.3	Interpretation of the results.....	24
14	Quality assurance and quality control.....	24
14.1	Overview.....	24
14.2	Specific requirements.....	24
14.2.1	General.....	24
14.2.2	Performance checks by inter-laboratory comparisons.....	24
14.2.3	Performance check of scorer qualification.....	25
14.2.4	Performance checks of sample transport integrity.....	25
14.2.5	Performance checks of sample integrity by service laboratory.....	26
14.2.6	Performance checks of instrumentation.....	26
14.2.7	Performance checks of sample protocol.....	26
14.2.8	Performance checks of sample scoring.....	26
14.2.9	Performance checks of result report generation.....	26
Annex A	(informative) Sample instructions for customer.....	27
Annex B	(informative) Sample questionnaire.....	29
Annex C	(informative) Sample of report.....	31
Annex D	(informative) Sample data sheets for recording painted aberrations.....	32
Annex E	(informative) Fitting of the dose response-curve by the method of maximum likelihood and calculating the uncertainty of the absorbed dose estimate.....	34
Annex F	(informative) Process for dose estimation.....	35
Bibliography	40

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 85, *Nuclear energy, nuclear technologies and radiological protection*, Subcommittee SC 2, *Radiological protection*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

The purpose of this document is to define the use of fluorescent in situ hybridization (FISH) for chromosome translocation analysis on human peripheral blood lymphocytes for biological dosimetry of exposure to ionizing radiation. Biological dosimetry, based on the study of chromosomal aberrations, mainly the dicentric assay, has become a routine component of accidental dose assessment. Dicentric aberrations, however, disappear with time after exposure, making this assay useful only in the short term after exposure. Translocations, however, are more stable, allowing dose estimates to be made long times after exposure or after protracted exposures.

This document provides a guideline for performing the translocation assay by FISH for dose assessment using documented and validated procedures. The minimum requirements for testing translocation yield in peripheral blood lymphocytes, by precisely defining the technical aspects of staining chromosomes (number of chromosomes and types of painting), selecting types of aberrations and cells, scoring aberrations, converting aberration yield to dose, statistical considerations, problems related to heterogeneous, chronic or delayed exposures and extrapolation to full genome are described. Dose assessment using the FISH assay has relevance in medical management, radiation-protection management, record keeping, and medical/legal requirements.

A part of the information in this document 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 document expands and standardizes the quality assurance and quality control and the evaluation of performance.

Radiological protection — Performance criteria for laboratories using Fluorescence In Situ Hybridization (FISH) translocation assay for assessment of exposure to ionizing radiation

1 Scope

The purpose of this document is to provide criteria for quality assurance (QA), quality control (QC) and evaluation of the performance of biological dosimetry by cytogenetic service laboratories.

This document addresses:

- a) the responsibilities of both the customer and the laboratory;
- b) the confidentiality of personal information, for the customer and the laboratory;
- c) the laboratory safety requirements;
- d) sample processing; culturing, staining and scoring, including the criteria for scoring for translocation analysis by FISH;
- e) the calibration sources and calibration dose ranges useful for establishing the reference dose-response curves that contribute to the dose estimation from chromosome aberration frequency and the detection limit;
- f) the scoring procedure for translocations stained by FISH used for evaluation of exposure;
- g) the criteria for converting a measured aberration frequency into an estimate of absorbed dose (also appears as “dose”);
- h) the reporting of results;
- i) the QA and QC;
- j) [Annexes A](#) to [F](#) containing sample instructions for the customer, sample questionnaire, sample datasheet for recording aberrations, sample of report and fitting of the low dose-response curve by the method of maximum likelihood and calculating the uncertainty of dose estimate.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

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

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <https://www.electropedia.org/>