~~ISO/ASTM 51939:2017(E)~~
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Standard Practice for Blood Irradiation Dosimetry[1]

This standard is issued under the fixed designation ISO/ASTM 51939; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision.

1. Scope

1.1 This practice outlines the irradiator installation qualification program and the dosimetric procedures to be followed during operational qualification and performance qualification of the irradiator. Procedures for the routine radiation processing of blood product (blood and blood components) are also given. If followed, these procedures will help ensure that blood product exposed to gamma radiation or X-radiation (bremsstrahlung) will receive absorbed doses with a specified range.

1.2 This practice covers dosimetry for the irradiation of blood product for self-contained irradiators (free-standing irradiators) utilizing radionuclides such as ^{137}Cs and ^{60}Co, or X-radiation (bremsstrahlung). The absorbed dose range for blood irradiation is typically 15 Gy to 50 Gy.

1.3 The photon energy range of X-radiation used for blood irradiation is typically from 40 keV to 300 keV.

1.4 This practice also covers the use of radiation-sensitive indicators for the visual and qualitative indication that the product has been irradiated (see ISO/ASTM Guide 51539).

1.5 This document is one of a set of standards that provides recommendations for properly implementing dosimetry in radiation processing and describes a means of achieving compliance with the requirements of ISO/ASTM Practice 52628 for dosimetry performed for blood irradiation. It is intended to be read in conjunction with ISO/ASTM Practice 52628.

1.6 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate ~~safety~~ safety, health, and ~~health~~environmental practices and ~~to~~ determine the applicability ~~or~~of regulatory limitations prior to use.*

1.7 This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.

2. Referenced documents

2.1 *ASTM Standards:*[2]
E170 Terminology Relating to Radiation Measurements and Dosimetry

[1] This practice is under the jurisdiction of ASTM Committee E61 on Radiation Processing and is the direct responsibility of Subcommittee E61.04 on Specialty Application, and is also under the jurisdiction of ISO/TC 85/WG 3.
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[2] For referenced ASTM and ISO/ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

2.2 *ISO/ASTM Standards:*[2]
51026 Practice for Using the Fricke Dosimetry System
51261 Practice for Calibration of Routine Dosimetry Systems for Radiation Processing
51275 Practice for Use of a Radiochromic Film Dosimetry System
51310 Practice for Use of a Radiochromic Optical Waveguide Dosimetry System
51539 Guide for the Use of Radiation-Sensitive Indicators
51607 Practice for Use of the Alanine-EPR Dosimetry System
51707 Guide for Estimating Uncertainties in Dosimetry for Radiation Processing
51956 Practice for Use of Thermoluminescence-Dosimetry Systems (TLD Systems) for Radiation Processing
52116 Practice for Dosimetry for a Self-Contained Dry-Storage Gamma-Ray Irradiator
52628 Practice for Dosimetry in Radiation Processing
52701 Guide for Performance Characterization of Dosimeters and Dosimetry Systems for Use in Radiation Processing

2.3 *International Commission on Radiation Units and Measurements Reports (ICRU):*[3]
ICRU 80 Dosimetry Systems for Use in Radiation Processing
ICRU 85a Fundamental Quantities and Units for Ionizing Radiation

2.4 *ISO Standards:*[4]
12749-4 Nuclear energy – Vocabulary – Part 4: Dosimetry for radiation processing

2.5 *ISO/IEC Standards:*[4]
17025 General Requirements for the Competence of Testing and Calibration Laboratories

2.6 *Guidelines on Blood Irradiation:*
Guidelines on the Use of Irradiated Blood Components (2013), Prepared by the BCSH Blood Transfusion Task Force[5]
Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products, (1993) US Food and Drug Administration[6]
Guidance for Industry, Gamma Irradiation of Blood and Blood Components: A Pilot Program for Licensing (2000) US Food and Drug Administration[6]

2.7 *Joint Committee for Guides in Metrology (JCGM) Reports:*
JCGM 100:2008 GUM 1995, with minor corrections, Evaluation of measurement data – Guide to the expression of uncertainty in measurement[7]
JCGM 200:2012 (JCGM 200:2008 with minor ~~revisions),VIM,~~revisions), VIM, International vocabulary of metrology – Basis and general concepts and associated terms[8]

3. Terminology

3.1 *Definitions:*

3.1.1 *absorbed dose (D)*—quotient of $d\bar{\varepsilon}$ by d*m*, where $d\bar{\varepsilon}$ is the mean energy imparted by ionizing radiation to matter of mass d*m* (see ICRU 85a).

$$D = d\bar{\varepsilon}/dm \tag{1}$$

3.1.1.1 *Discussion*—
The SI unit of absorbed dose is the gray (Gy), where 1 gray is equivalent to the absorption of 1 joule per kilogram of the specified material (1 Gy = 1 J/kg).

3.1.2 *absorbed-dose rate ($\dot{D}$)*—quotient of d*D* by d*t*, where d*D* is the increment of absorbed dose in the time interval d*t*, thus

$$\dot{D} = dD/dt \tag{2}$$

3.1.2.1 *Discussion*—
The SI unit is $Gy \cdot s^{-1}$. However, the absorbed-dose rate is often specified in terms of its average value over longer time intervals, for example, in units of $Gy \cdot min^{-1}$ or $Gy \cdot h^{-1}$.

[3] Available from the International Commission on Radiation Units and Measurements, 7910 Woodmont Ave., Suite 800, Bethesda, MD 20814 U.S.A.
[4] Available from International Organization for Standardization (ISO), ISO Central Secretariat, BIBC II, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, http://www.iso.org.
[5] Available from the National Blood Transfusion Service, East Anglian Blood Transfusion Centre, Long Road, Cambridge, CB2 2PT United Kingdom.
[6] Available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1488, USA.
[7] Document produced by working Group 1 of the Joint Committee for Guides in Metrology (JCGM WG1). Available free of charage at the BIPM website (http://www.bipm.org).
[8] Document produced by working Group 2 of the Joint Committee for Guides in Metrology (JCGM WG2). Available free of charge at the BIPM website (http://www.bipm.org).

3.1.3 *absorbed-dose mapping*—measurement of absorbed dose within an irradiated product to produce a one, two, or three-dimensional distribution of absorbed dose, thus rendering a map of absorbed-dose values.

3.1.3.1 *Discussion*—

For a blood canister, such a dose map is obtained using dosimeters placed at specified locations within the canister.

3.1.4 *activity (A) (of an amount of radionuclide in a particular energy state at a given time)*—quotient of –d*N* by d*t*, where d*N* is the mean change in the number of nuclei in that energy state due to spontaneous nuclear transitions in the time interval d*t* (see ICRU 85a).

$$A = -\mathrm{d}N/\mathrm{d}t \tag{3}$$

Unit: s^{-1}

The special name for the unit of activity is the becquerel (Bq). 1 Bq = 1 s^{-1}.

3.1.4.1 *Discussion*—

(1) The former special unit of activity was the curie (Ci). 1 Ci = 3.7×10^{10} s^{-1} (exactly).

(2) The 'particular energy state' is the ground state of the nuclide unless otherwise specified.

(3) The activity of an amount of radionuclide in a particular energy state is equal to the product of the decay constant, λ, for that state and the number of nuclei in that state (that is, $A=N\lambda$).

3.1.5 *approved laboratory*—laboratory that is a recognized national metrology institute; or has been formally accredited to ISO/IEC 17025; or has a quality system consistent with the requirements of ISO/IEC 17025.

3.1.5.1 *Discussion*—

A recognized national metrology institute or other calibration laboratory accredited to ISO/IEC 17025 should be used in order to ensure traceability to a national or international standard. A calibration certificate provided by a laboratory not having formal recognition or accreditation will not necessarily be proof of traceability to a national or international standard.

3.1.6 *bremsstrahlung*—broad-spectrum electromagnetic radiation emitted when an energetic charged particle is influenced by a strong electric or magnetic field, such as that in the vicinity of an atomic nucleus.

3.1.6.1 *Discussion*—

(1) In radiation processing, bremsstrahlung photons with sufficient energy to cause ionization are generated by the deceleration or deflection of energetic electrons in a target material. When an electron passes close to an atomic nucleus, the strong coulomb field causes the electron to deviate from its original motion. This interaction results in a loss of kinetic energy by the emission of electromagnetic radiation. Since such encounters are uncontrolled, they produce a continuous photon energy distribution that extends up to the maximum kinetic energy of the incident electron.

(2) The bremsstrahlung spectrum depends on the electron energy, the composition and thickness of the target, and the angle of emission with respect to the incident electron.

3.1.7 *calibration*—set of operations that establish under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards.

3.1.7.1 *Discussion*—

Calibration conditions include environmental and irradiation conditions present during irradiation, storage and measurement of the dosimeters that are used for the generation of a calibration curve.

3.1.8 *dosimeter*—device that, when irradiated, exhibits a quantifiable change that can be related to absorbed dose in a given material using appropriate measurement instruments and procedures.

3.1.9 *dosimeter batch*—quantity of dosimeters made from a specific mass of material with uniform composition, fabricated in a single production run under controlled, consistent conditions and having a unique identification code.

3.1.10 *dosimetry system*—system used for measuring absorbed dose, consisting of dosimeters, measurement instruments and their associated reference standards, and procedures for the system's use.

3.1.11 *installation qualification (IQ)*—process of obtaining and documenting evidence that equipment has been provided and installed in accordance with specifications.

3.1.12 *irradiator turntable*—device used to rotate the sample during the irradiation process so as to improve dose uniformity.

3.1.12.1 *Discussion*—

An irradiator turntable is often referred to as a turntable. Some irradiator geometries, for example with a circular array of radiation sources surrounding the product, may not need a turntable.

3.1.13 *isodose curves*—lines or surfaces of constant absorbed dose through a specified medium.

3.1.14 *measurement management system*—set of interrelated or interacting elements necessary to achieve metrological confirmation and continual control of measurement processes.

3.1.15 *operational qualification (OQ)*—process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures.

3.1.16 *performance qualification (PQ)*—process of obtaining and documenting evidence that the equipment as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product that meeting its specification.

3.1.17 *radiation-sensitive indicator*—material such as a coated or impregnated adhesive-backed substrate, ink, coating or other material which may be affixed to or printed on the product and which undergoes a visual change when exposed to ionizing radiation.

3.1.17.1 *Discussion*—

Radiation-sensitive indicators are often referred to as "indicators."

3.1.18 *reference-standard dosimetry system*—dosimetry system, generally having the highest metrological quality available at a given location or in a given organization, from which measurements made there are derived.

3.1.19 *routine dosimetry system*—dosimetry system calibrated against a reference standard dosimetry system and used for routine absorbed-dose measurements, including dose mapping and process monitoring.

3.1.20 *simulated product*—material with radiation absorption and scattering properties similar to those of the product, material or substance to be irradiated.

3.1.20.1 *Discussion*—

(1) Simulated product is used during irradiator characterization as a substitute for the actual product, material or substance to be irradiated.

(2) When used in routine production runs in order to compensate for the absence of product, simulated product is sometimes referred to as compensating dummy.

(3) When used for absorbed-dose mapping, simulated product is sometimes referred to as phantom material.

3.1.21 *timer setting*—defined time interval during which product is exposed to radiation.

3.1.22 *transfer-standard dosimetry system*—dosimetry system used as an intermediary to calibrate other dosimetry systems.

3.1.23 *transit dose*—absorbed dose delivered to a product (or a dosimeter) while it travels between the non-irradiation position and the irradiation position, or in the case of a movable source while the source moves into and out of its irradiation position.

3.1.24 *validation*—documented procedure for obtaining, recording and interpreting the results to establish that a process will consistently yield product complying with predetermined specifications.

3.1.25 *X-radiation*—ionizing electromagnetic radiation which includes both bremsstrahlung and the characteristic radiation emitted when atomic electrons make transitions to more tightly bound states.

3.1.25.1 *Discussion*—

In radiation processing applications (such as blood product irradiation), the principal X-radiation is bremmstrahlung.

3.1.26 *X-ray converter*—device for generating X-radiation (bremsstrahlung) from an electron beam, consisting of a target, means for cooling the target, and a supporting structure.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *blood product (blood and blood components)*—whole blood, red cells, frozen cells, platelet concentrates, apheresis platelets, granulocyte concentrates, and fresh or frozen plasma.

3.2.1.1 *Discussion*—
Enclosure systems for blood and blood components are commonly referred to as "bags."

3.2.2 *canister*—container used to house the blood product or blood-equivalent product during the irradiation process.

3.3 Definitions of other terms used in this standard that pertain to radiation measurement and dosimetry may be found in ISO 12749-4, ASTM Terminology E170, ICRU 85a and VIM; these documents, therefore, may be used as alternative references.

4. Significance and use

4.1 Blood and blood components are irradiated to predetermined absorbed doses to inactivate viable lymphocytes to help prevent transfusion-induced graft-versus-host disease (GVHD) in certain immunocompromised patients and those receiving related-donor products (**1**, **2**).[9]

4.2 The assurance that blood and blood components have been properly irradiated is of crucial importance for patient health. This shall be demonstrated by means of accurate absorbed-dose measurements on the product, or in simulated product.

4.3 Blood and blood components are usually irradiated using gamma radiation from ^{137}Cs or ^{60}Co sources, or X-radiation from X-ray units.

4.4 Blood irradiation specifications include a lower limit of absorbed dose, and may include an upper limit or central target dose. For a given application, any of these values may be prescribed by regulations that have been established on the basis of available scientific data (see 2.6).

4.5 For each blood irradiator, an absorbed-dose rate at a reference position within the canister is measured as part of irradiator acceptance testing using a reference-standard dosimetry system. That reference-standard measurement is used to establish operating parameters so as to deliver specified dose to blood and blood components.

4.6 Absorbed-dose measurements are performed within the blood or blood-equivalent volume for determining the absorbed-dose distribution. Such measurements are often performed using simulated product (for example, polystyrene is considered blood equivalent for ^{137}Cs photon energies).

4.7 Dosimetry is part of a measurement management system that is applied to ensure that the radiation process meets predetermined specifications (see ISO/ASTM Practice 52628).

4.8 Blood and blood components are usually irradiated in chilled or frozen condition. Care should be taken, therefore, to ensure that the dosimeters and radiation-sensitive indicators can be used under such temperature conditions.

4.9 Proper documentation and record keeping are critical components of a radiation process. Documentation and record keeping requirements may be specified by regulatory authorities or may be given in the corporation's quality policy.

4.10 Response of most dosimeters has significant energy dependence at photon energies of less than 100 keV, so proper care must be exercised when measuring absorbed dose in that energy range.

[9] The boldface numbers in parentheses refer to the bibliography at the end of this standard.

5. Type of irradiators and modes of operation

5.1 Self-contained irradiators expose samples to gamma irradiation produced by isotopes of either ^{137}Cs or ^{60}Co (**3**) (ISO/ASTM Practice 52116), or to low energy X-radiation (bremsstrahlung) produced by an X-ray tube. These irradiators house their radiation source in a protective lead shield or other appropriate high atomic number material in accordance with the safety requirements. Currently available units using low-energy X-radiation (bremsstrahlung) require less shielding than units containing gamma-emitting radioactive isotopes. Such units containing radionuclides usually have a mechanism to move the canister from the load/unload position to the irradiation position.

5.1.1 Some common methods used for improving absorbed-dose uniformity in the blood product are to either rotate the canister holding the blood product in front of the radiation source or to have multiple sources irradiating the product from different directions.

6. Radiation source characteristics

6.1 *Gamma Irradiators:*

6.1.1 The source of gamma radiation used in the irradiators considered in this practice consists of sealed ^{60}Co or ^{137}Cs radionuclides that are typically linear rods arranged in one or more planar or annular arrays.

6.1.2 Cobalt-60 emits photons with energies of approximately 1.17 and 1.33 MeV in nearly equal proportions. Cesium-137 produces photons with energies of approximately 0.662 MeV.

6.1.3 The radioactive decay half-lives for ^{60}Co and ^{137}Cs are regularly reviewed and updated. The most recent publication by the National Institute of Standards and Technology gave values of 1925.20 (±0.25) days for ^{60}Co and 11018.3 (±9.5) days for ^{137}Cs (**4**).

6.1.4 For gamma sources, the only variation in the source output is the known reduction in the activity caused by radioactive decay. This reduction in the source output and the required increase in the irradiation time to deliver the same dose may be calculated (see 10.4.2) or obtained from tables provided by the irradiator manufacturer.

6.2 *X-ray ~~Irradiators,~~Irradiators:*

6.2.1 Low energy X-ray irradiators use X-ray tubes that consist of an electron source (generally a heated wire, a filament which emits electrons), an electrostatic field to accelerate these electrons, and a converter to generate X-radiation.

6.2.2 An X-ray (bremsstrahlung) irradiator emits short-wavelength electromagnetic radiation, which is analogous to gamma radiation from radioactive sources. Although their effects on irradiated materials are generally similar, these kinds of radiation differ in their energy spectra (see 6.2.3), angular distribution, and dose rates. The physical characteristics of the X-radiation (bremsstrahlung) field depend on the design of the X-ray tube.

6.2.3 Currently available low-energy X-ray irradiators generate X-radiation with a maximum energy of 160 keV. The spectrum of the X-ray energy extends from the maximum energy to approximately 30 keV.

6.2.4 The energy of the X-radiation influences the size and shape of the canister needed to achieve the desired level of dose uniformity in the blood canister. Filters are used to reduce the low-energy components to improve dose uniformity in the canister. These filters may form part of the X-ray tube or may be material added to the irradiator or canister. Reflectors may also be used to improve the dose uniformity.

6.2.5 The absorbed-dose rate and thus time of irradiation is determined by the tube current.

7. Dosimetry systems

7.1 *Description of Dosimeters and Dosimetry Systems*—Classification of dosimeters and dosimetry systems is based on the inherent metrological dosimeter properties and the field of application of the dosimetry system (see ISO/ASTM Practice 52628). These classifications influence both the selection and calibration of dosimetry systems.

7.1.1 *Classification of Dosimeters*—Classification of dosimeters is based on their inherent metrological properties. The method of