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Guide for absorbed-dose mapping in radiation processing facilities

Guide pour la cartographie de dose absorbée du rayonnement des installations de traitement

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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.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75% of the member bodies casting a vote.

ASTM International is one of the world's largest voluntary standards development organizations with global participation from affected stakeholders. ASTM technical committees follow rigorous due process balloting procedures.

A project between ISO and ASTM International has been formed to develop and maintain a group of ISO/ASTM radiation processing dosimetry standards. Under this project, ASTM Commitee E61, Radiation Processing, is responsible for the development and maintenance of these dosimetry standards with unrestricted participation and input from appropriate ISO member bodies.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. Neither ISO nor ASTM International shall be held responsible for identifying any or all such patent rights.

International Standard ISO/ASTM 52303 was developed by ASTM Committee E61, Radiation Processing, through Subcommittee E61.03, Dosimetry Application, and by Technical Committee ISO/TC 85, Nuclear energy, nuclear technologies and radiological protection.

This first edition cancels and replaces ASTM E2303-11, which has been technically revised.

ISO/ASTM 52303:2015(E)

An American National Standard

Standard Guide for Absorbed-Dose Mapping in Radiation Processing Facilities[1]

This standard is issued under the fixed designation ISO/ASTM 52303; 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 document provides guidance in determining absorbed-dose distributions (mapping) in products, materials or substances irradiated in gamma, X-ray (bremsstrahlung) and electron beam facilities.

NOTE 1—For irradiation of food and the radiation sterilization of health care products, specific ISO and ISO/ASTM standards containing dose mapping requirements exist. See ISO/ASTM Practices 51431, 51608, 51649, 51702 and 51818 and ISO 11137-1. Regarding the radiation sterilization of health care products, in those areas covered by ISO 11137-1, that standard takes precedence.

1.2 This guide is one of a set of standards that provides recommendations for properly implementing dosimetry in radiation processing. it is intended to be read in conjunction with ISO/ASTM 52628.

1.3 Methods of analyzing the dose map data are described. Examples are provided of statistical methods that may be used to analyze dose map data.

1.4 Dose mapping for bulk flow processing and fluid streams is not discussed.

1.5 Dosimetry is an element of a total quality management system for an irradiation facility. Other controls besides dosimetry may be required for specific applications such as medical device sterilization and food preservation.

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 and health practices and determine the applicability of regulatory requirements prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

E170 Terminology Relating to Radiation Measurements and Dosimetry

E178 Practice for Dealing With Outlying Observations

E2232 Guide for Selection and Use of Mathematical Methods for Calculating Absorbed Dose in Radiation Processing Applications

2.2 *ISO/ASTM Standards:*[2]

51261 Guide for Selection and Calibration of Dosimetry Systems for Radiation Processing

51431 Practice for Dosimetry in Electron Beam and X-Ray (Bremsstrahlung) Irradiation Facilities for Food Processing

51608 Practice for Dosimetry in an X-ray (Bremsstrahlung) Facility for Radiation Processing

51649 Practice for Dosimetry in an Electron Beam Facility for Radiation Processing at Energies between 300 keV and 25 MeV

51702 Practice for Dosimetry in a Gamma Irradiation Facility for Radiation Processing

51707 Guide for Estimating Uncertainties in Dosimetry for Radiation Processing

51818 Practice for Dosimetry in an Electron Beam Facility for Radiation Processing at Energies between 80 and 300 keV

52628 Practice for Dosimetry in Radiation Processing

2.3 *International Commission on Radiation Units and Measurements Reports:*[3]

ICRU Report 85a Fundamental Quantities and Units for Ionizing Radiation

2.4 *International Organization for Standardization:*[4]

ISO 11137-1 Sterilization of health care products – Radiation – Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices

2.5 *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[5]

[1] This guide is under the jurisdiction of ASTM Committee E61 on Radiation Processing and is the direct responsibility of Subcommittee E61.03 on Dosimetry Application and is also under the jurisdiction of ISO/TC 85/WG 3.

Current edition approved Feb. 9, 2015. Published June 2015. Originally published as ASTM E2303–03. Last previous ASTM edition E2303–11$^{\varepsilon 1}$. The present International Standard ISO/ASTM 52303–2015(E) replaces ASTM E2303–11$^{\varepsilon 1}$.

[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.

[3] Available from International Commission on Radiation Units and Measurements, 7910 Woodmont Ave., Suite 800, Bethesda, MD 20814.

[4] Available from International Organization for Standardization (ISO), 1 rue de Varembé, Case postale 56, CH-1211, Geneva 20, Switzerland.

[5] Document produced by Working Group 1 of the Joint Committee for Guides in Metrology (JCGM/WG 1). Available free of charge at the BIPM website (http://www.bipm.org).

JCGM 200:2012, VIM International vocabulary of metrology – Basis and general concepts and associated terms[6]

3. Terminology

3.1 *Definitions:*

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

3.1.1.1 *Discussion*—For a process load, such a dose map is obtained using dosimeters placed at specified locations within the process load.

3.1.2 *calibration curve (VIM:2008)*—expression of the relation between indication and corresponding measured quantity value.

3.1.2.1 *Discussion*—In radiation processing standards, the term "dosimeter response" is generally used for "indication."

3.1.3 *dose map, dose mapping*—see *absorbed-dose mapping*.

3.1.4 *dose uniformity ratio*—ratio of the maximum to the minimum absorbed dose within the irradiated product.

3.1.4.1 *Discussion*—The concept is also referred to as the max/min dose ratio. Product generally refers to the "process load."

3.1.5 *dose zone*—a region or discrete point(s) within a process load that receives the same absorbed dose within the statistical uncertainty of the irradiation process and absorbed-dose measurement(s).

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

3.1.7 *irradiation container*—holder in which process load is transported through the irradiator.

3.1.7.1 *Discussion*—"Irradiation container" is often referred to simply as "container" and can be a carrier, cart, tray, product carton, pallet, product package or other holder.

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

3.1.9 *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 meeting its specification.

3.1.10 *process load*—a volume of material with a specified product loading configuration irradiated as a single entity.

3.1.11 *processing category*—group of different product that can be processed together.

3.1.11.1 *Discussion*—Processing categories can be based on, for instance, composition, density or dose requirements.

3.1.12 *reference material*—homogeneous material of known radiation absorption and scattering properties used to establish characteristics of the irradiation process, such as scan uniformity, depth-dose distribution, throughput rate, and reproducibility of dose delivery.

3.1.13 *routine monitoring position*—position where absorbed dose is monitored during routine processing to ensure that the product is receiving the absorbed dose specified for the process.

3.1.13.1 *Discussion*—This position may be a location of minimum or maximum dose in the process load or it may be an alternate convenient location in, on or near the process load where the relationship of the dose at this position with the minimum and maximum dose has been established.

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

3.1.14.1 *Discussion*—Simulated product is used during irradiator characterization as a substitute for the actual product, material or substance to be irradiated. When used in routine production runs in order to compensate for the absence of product, simulated product is sometimes referred to as compensating dummy. When used for absorbed-dose mapping, simulated product is sometimes referred to as phantom material.

3.2 Definitions of other terms used in this standard that pertain to radiation measurement and dosimetry may be found in Terminology E170. Definitions in E170 are compatible with ICRU Report 60; that document, therefore, may be used as an alternative reference.

4. Significance and use

4.1 This guide is one of a set of guides and practices that provide recommendations for properly implementing dosimetry in radiation processing. In order to understand and effectively use this and other dosimetry standards, consider first "Practice for Dosimetry in Radiation Processing," ASTM/ISO 52628, which describes the basic requirements that apply when making absorbed dose measurements in accordance with the ASTM E10.01 series of dosimetry standards. In addition, ASTM/ISO 52628 provides guidance on the selection of dosimetry systems and directs the user to other standards that provide information on individual dosimetry systems, calibration methods, uncertainty estimation and radiation processing applications.

4.2 Radiation processing is carried out under fixed path conditions where (*a*) a process load is automatically moved through the radiation field by mechanical means or (*b*) a process load is irradiated statically by manually placing product at predetermined positions before the process is started. In both cases the process is controlled in such a manner that the process load position(s) and orientation(s) are reproducible within specified limits.

NOTE 2—Static irradiation encompasses irradiation of the process load using either manual rotation, no rotation or automated rotation.

4.3 Some radiation processing facilities that utilize a fixed conveyor path for routine processing may also characterize a region within the radiation field for static radiation processing, sometimes referred to as "Off Carrier" processing.

[6] Document produced by Working Group 2 of the Joint Committee for Guides in Metrology (JCGM/WG 2). Available free of charge at the BIPM website (http://www.bipm.org).

4.4 Many radiation processing applications require a minimum absorbed dose (to achieve a desired effect or to fulfill a legal requirement), and a maximum absorbed dose (to ensure that the product, material or substance still meets functional specifications or to fulfill a legal requirement).

4.5 Information from the dose mapping is used to:

4.5.1 Characterize the radiation process and assess the reproducibility of absorbed-dose values, which may be used as part of operational qualification and performance qualification.

4.5.2 Determine the spatial distribution of absorbed doses and the zone(s) of maximum and minimum absorbed doses throughout a process load, which may consist of an actual or simulated product.

4.5.3 Establish the relationship between the dose at a routine monitoring position and the dose within the minimum and maximum dose zones established for a process load.

4.5.4 Verify mathematical dose calculation methods. See ASTM Guide E2232.

4.5.5 Determine the effect of process interruptions on the distribution of absorbed dose and the magnitude of the minimum and maximum doses.

4.5.6 Assess the impact on the distribution of absorbed dose and the magnitude of the minimum and maximum doses resulting from the transition from one process load to another where changes, for example, in product density or product loading pattern may occur.

5. Prerequisites

5.1 *Prerequisites to Dose Mapping: Installation Qualification and Dosimetry System Calibration:*

5.1.1 Prior to performing dose mapping for irradiator operational qualification (OQ) and performance qualification (PQ), confirm that installation qualification (IQ) is complete.

5.1.1.1 For electron beam and X-ray irradiation facilities, IQ includes dosimetric testing to confirm the characteristics of the beam (electron energy, average beam current, and if applicable, scan width and scan uniformity). Refer to ISO/ASTM 51431, 51608, 51818, 51649 and ISO 11137-1.

5.1.1.2 For gamma irradiation facilities, dosimetric testing is not required during IQ; however, the activity of the source and location of the individual components of the source should be confirmed and documented. Refer to ISO/ASTM 51702 and ISO 11137-1.

5.1.2 Select an appropriate dosimetry system(s) for the dose mapping exercises. See 6.2.4.1 and ISO/ASTM 52628 for guidance.

5.2 *Calibration of the Dosimetry System:*

5.2.1 Prior to use, the dosimetry system, consisting of dosimeters measurement instruments and their associated reference standards, and procedures for the system's use, should be calibrated in accordance with the user's documented procedure that specifies details of the calibration process and quality assurance requirements. Calibration methods are described in ISO/ASTM 51261.

NOTE 3—A dosimetry system calibration obtained using irradiation conditions different from the conditions of use may be used for relative dose measurement applications. For example, an irradiation facility may perform a lab-based calibration with subsequent verification using reference standard dosimeters under the conditions of use. While dose mapping at the irradiation facility may be performed using dose values from the lab-based calibration (prior to completing the verification exercise) to assess the dose distribution and locations of minimum and maximum absorbed dose, these dose measurements would be considered preliminary (i.e. relative) pending the outcome of the verification exercise.

5.2.2 For the calibration of the instruments, and for the verification of instrument performance between calibrations, see ISO/ASTM 51261 or instrument-specific operating manuals, or both.

6. Dose mapping

6.1 *Dose Mapping for Operational Qualification of the Irradiation Facility:*

6.1.1 As specified in ISO/ASTM Practices 51431, 51608, 51649, 51702, and ISO 11137-1, perform irradiation facility dose mapping to characterize the irradiator with respect to the dose distribution and reproducibility of absorbed dose delivery. This should be performed in accordance with a formal validation program, and should cover the operational range that will be used in the irradiation of products.

6.1.2 Perform irradiation facility dose mapping by placing dosimeters in a number of process loads of reference material that fills the container to its design volume limits. The number of process loads to be dose mapped should be large enough (3 or more) to determine the variability of dose. For those irradiation facilities that vary operating parameters which impact dose distribution, dose mapping should be carried out over a range of selected operating parameters which cover the operational limits to be used in the irradiation of products.

6.1.2.1 *Specific to Photon-based Facilities (gamma or X-ray)*—Material densities should be within the density range for which the irradiator is to be used. When processing multiple densities, dose mapping should be done for at least two densities close to the minimum and maximum density to be processed to assess the impact density has on the magnitude and distribution of the absorbed dose. A user may consider dose mapping for additional intermediate densities to gain additional performance information.

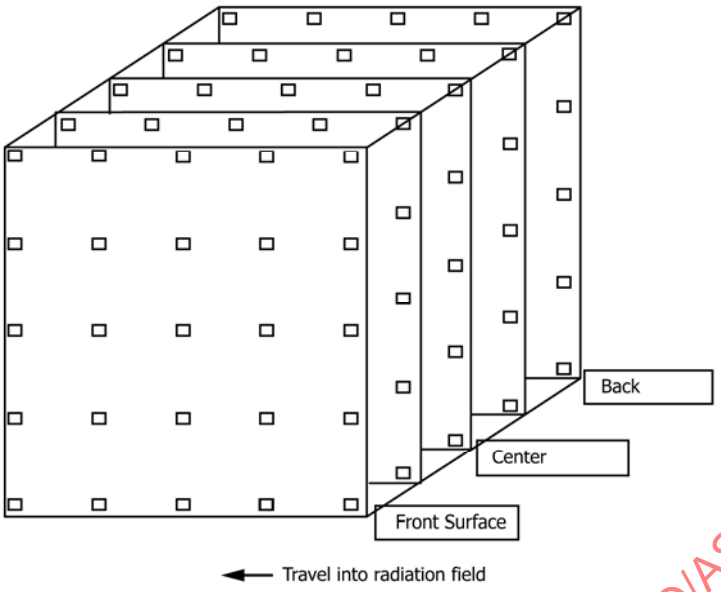
6.1.2.2 *Specific to Electron Beam Facilities*—For irradiation facility dose mapping, use one or more reference materials having densities within the density range for which the irradiator is to be used.

6.1.2.3 Determine absorbed-dose distribution throughout the process load for each product path through the irradiation field and each set of process parameters.

NOTE 4—Additional ways to influence the absorbed-dose distribution within a given process load include: performing single- versus double-sided irradiation in electron beam and X-ray facilities, or using multiple source rack(s) or source rack positioning changes in gamma irradiators.

6.1.2.4 For each process load, place a sufficient number of dosimeters in an array to determine the absorbed-dose distribution. Dosimeter strips or sheets may be used to increase the spatial resolution of the dose map. An example of dosimeter placement array is given in Fig. 1.

6.1.2.5 Measure the dose at the same positions in three or more replicate process loads to determine the variability of the measured absorbed dose and absorbed-dose distribution for each product path and set of process parameters.



NOTE 1—In this drawing the small squares represent dosimeter positions. The "Front" is defined as the initial and in some cases only surface to directly face the radiation source during processing. The number of dosimeters and the number of planes (surfaces) to be mapped will depend on several factors, including but not limited to, the radiation type (electrons versus photons), single- versus double-sided irradiation, and resolution of absorbed dose required.

FIG. 1 An Example of a Dosimeter Placement Array in a Three-Dimensional Grid Pattern for an Operational Qualification Dose Mapping

(1) For process loads transported through the irradiation field, a sufficient number of similar process loads should precede and follow those being dose mapped to minimize variations on the absorbed-dose distribution in the dose-mapped process loads.

(2) Depending on the irradiator design, additional dose map studies may be needed to determine effects on dose and dose distribution associated with changes during processing in process loading configurations and their density (sometimes referred to as "phase-in and phase-out" effects). The effect of density changes on dose and dose distribution can be evaluated by irradiating two different density process loads sequentially and dose mapping the last process load of the one density and the first process load of the second density and comparing these results against the results obtained from the uniform density dose map described in 6.1.2.5, (1).

(3) If OQ measurements show that effects of "phase-in/phase-out" may exist, then the effect on actual product may also have to be assessed during PQ (see 6.2.5.1).

6.1.2.6 Following irradiation, retrieve and measure the response of each dosimeter, and evaluate the data in accordance with established procedures (see Section 7).

6.1.3 If changes are made to the irradiation system that could affect the absorbed-dose or absorbed-dose distribution, it may be necessary to repeat the dose mapping.

NOTE 5—ISO 11137-1 provides additional guidance regarding changes to the irradiation system and recommended post-change qualification activities.

6.1.4 The use of mathematical models in determining dosimeter locations for dose mapping or in predicting dose map results may be useful. See Guide E2232 for guidance.

6.2 *Dose Mapping for Performance Qualification of Process Loads*

6.2.1 Perform dose mapping for specific products and load configurations to determine the dose distribution expected during the routine processing of process loads. Products, materials or substances should be actual product or may be simulated product of materials with similar density, distributions and packaging configuration as the actual products.

6.2.2 If a routine monitoring position is used for process monitoring, the relationships between minimum dose, maximum dose and the dose at the routine monitoring position should be established.

6.2.3 Specify a loading pattern that describes the products, materials or substances contained within the process load, including dimensions, mass or density, and if applicable, the orientation of the product within the process load as well as the orientation of the process load itself with respect to the radiation field.

6.2.4 Specify or determine the location of the dosimeters used for the dose map, taking into consideration voids, density variations or any material interfaces that may cause significant localized dose gradients that could affect the location of minimum or maximum dose, or both, within the process load.

6.2.4.1 Use dosimeters capable of measuring any localized dose gradients and of a size that does not significantly influence the radiation field or the interpretation of absorbed-dose measurements.

6.2.4.2 Process loads containing voids, density variations or materials interfaces that could cause localized dose gradients require that the dosimeters be placed directly on the material surfaces. Selection of the dosimeter positions for dose mapping should include areas of suspected high dose gradients based on a physical assessment of the materials and their composition that make up the process load being dose mapped. These positions may be concentrated in the expected zones of

minimum or maximum dose, or both, known from the irradiator operational qualification (OQ) dose map. Heterogeneous products such as metal implants or certain foods may require placement of appropriately sized dosimeters positioned at internal locations within the individual products. This may involve cutting open the individual product inside the package to permit dosimeter positioning and retrieval, or removal of dosimeters from their protective packaging to facilitate dosimeter placement. The latter requires assurances that the dosimeters can be characterized and perform acceptably when used without protective packaging.

NOTE 6—When dosimeters are calibrated in their protective packaging but used outside the packaging for a specific application, this usage may alter the calibrated state of the dosimeters. The impact on absorbed-dose measurement for this usage should be assessed.

6.2.4.3 The use of mathematical models in determining dosimeter locations for dose mapping or in predicting dose map results may be useful. See Guide E2232 for guidance.

6.2.5 Measure the dose at the same position(s) in the maximum and minimum dose zones in three or more process loads to determine the variability of the absorbed-dose delivery and measurements. Each process load should contain similar materials and dosimeter placements that are configured in the same way and should be processed under the same operating conditions.

6.2.5.1 A sufficient number of process loads should precede and follow the dose mapped process loads to minimize phase-in/out effects (see 6.1.2.5, Item 1).

6.2.6 Doses outside of the product dose specification are acceptable for dose mapping purposes. See Note 9 in 7.2.4 for additional discussion.

6.2.7 Repeat the dose mapping procedure if a change is made to the product or the irradiation facility that may impact the previously characterized dose distribution.

6.2.8 If measurements done according to 6.1.3 lead to the conclusion that dose or dose distribution has changed, then repeat of product dose map is needed.

6.2.9 Practical considerations for Product Dose Mapping (see 6.2.1).

6.2.9.1 Facilities typically irradiate a variety of products and dose mapping of all products may be impractical. If products have similar loading configurations and are known to have densities and radiation absorption characteristic equivalent to a product (actual or simulated) that has already been dose mapped, then it is not necessary to perform dose mapping for them, and a processing category can be established consisting of product that can be irradiated together.

6.2.9.2 Criteria for including product in processing categories shall be documented, and should include:

(1) dimension of the process load
(2) weight of the process load
(3) density of the process load
(4) composition of the product
(5) orientation of the product items with the process load
(6) number of product items within the process load
(7) the required minimum dose
(8) the maximum acceptable dose

6.2.9.3 If facilities irradiate only process loads that can be demonstrated to have the same dose distribution characteristics as those used in the operational qualification (OQ) dose mapping(s) discussed in 6.1, then it is not necessary to conduct performance qualification (PQ) dose mapping.

6.3 *Other Dose Mapping Studies*—The dynamics of routine processing may require additional studies relevant to each processing path be performed during operational or performance qualification, or both, to further characterize irradiator performance and its impact on the magnitude and distribution of absorbed dose. The number of studies required will generally depend on the specific irradiation system; however, selected studies common to many irradiation systems, including process interruption, partially-filled irradiation containers, and center-loading of product in irradiation containers, are described in the following sections.

6.3.1 *Process Interruption*—The result of intentional or unintentional stoppage of the irradiation process. The process interruption and subsequent restart of the irradiation process can impact the absorbed dose delivered to the product. For many gamma irradiators, this typically means irradiation containers remain stationary while the source transitions between the fully raised and storage positions, which contributes additional dose to product. For many electron beam and X-ray irradiators, a system shutdown may impact the irradiation source or the product conveyor system, or both, and the impact on the absorbed-dose distribution will depend on whether one or both systems shut down. In order to assess the effect of process interruption on the absorbed dose delivered to the product, a dose map should be performed.

6.3.1.1 For gamma irradiators where product is conveyed in containers through a defined irradiation path, the dose map would generally require:

(1) placement of dosimeters in process loads closest to the source (during interruption), where dose is expected to be most influenced by source transitions,

(2) raising and lowering the source (while containers remain stationary) a sufficient number of times to ensure the dose measured by the dosimeters is within its calibrated range, and

(3) reporting the dose per source transition.

This information can then be used in situations where process interruptions occur to assess the impact, if any, on the reported dose values. The dose map results may be complemented by calculations performed using mathematical models (see ASTM Guide E2232).

6.3.1.2 For electron beam or X-ray irradiators where product is conveyed past the beam, the system is typically designed such that a conveyor stoppage would result in the beam shutting off, and conversely, the beam shutting off would result in the conveyor stopping. This feature is intended to minimize the impact on the dose distribution as the result of either a shutdown of the beam or conveyor system. In order to assess the impact of one or more interruptions, the dose map would typically require placement of dosimeters on the product surface, and possibly at selected depths.

NOTE 7—The dosimeter placement pattern has to be appropriate to capture the dose gradients to assess the impact of process interruptions.

For example, use of film strips or closely spaced dosimeters may be necessary.

6.3.2 *Partially-Filled Irradiation Containers*—During routine production, irradiation containers may not always be filled to their design limits or to what is defined to be a fully-loaded container configuration for a given product. This can impact the magnitude and distribution of dose within the partially-filled container as well as within adjacent containers. Furthermore, the dose profile of the partially-filled container may vary according to the degree (level) to which the container is filled. Therefore, if partially-filled irradiation containers are part of normal operations, absorbed-dose mapping should be performed to assess the impact to the dose distribution, if any, to partially-filled containers and any adjacent containers that may be influenced by the partially-filled containers. Alternately, partially filled carriers should be filled with simulated product to achieve a full container loading.

6.3.3 *Center-loading of Product*—Represents a unique way of loading product within the irradiation container to improve (reduce) the dose uniformity ratio relative to that which would be achieved if the container were fully loaded with that product. Center-loading is done when the fully-loaded configuration would result in the dose to product exceeding its specification. If center-loading is to be performed, each unique center-loading configuration should be dose mapped.

7. Analysis of dose map data

7.1 *Analysis of Operational Qualification (OQ) Dose Map Data:*[7,8]

7.1.1 Analyze the dose distribution data for each irradiator pathway and mode of operation (see Note 4 in 6.1.2.3).

7.1.1.1 Determine the dose distribution in the process load. Estimates of the statistical variability and the mean value of the dose for a given location (or zone) may be used to determine equivalent dose zones. See Appendix X1 for a discussion of the use of statistical methods to determine equivalent dose zones and ASTM Practice E178 for guidance in the treatment of outlying observations.

7.1.1.2 Evaluate the reproducibility of the absorbed-dose zone(s).

7.1.1.3 The absorbed-dose results from dose maps may be plotted in a variety of 2- and 3-dimensional views as an aid to evaluating results and gaining and understanding of dose delivery.

NOTE 8—Knowledge of the location of maximum and minimum dose zones and their dose values may be useful in estimating the process parameters to be used during routine processing of homogeneous process loads of different densities. This information is retained as baseline data. Any estimates of timer settings or conveyor speeds derived from this data should be verified during performance qualification.

7.2 *Analysis of Performance Qualification (PQ) Dose Map Data:*

7.2.1 Identify the maximum and minimum absorbed dose in one or more dose zones (may be a single dosimeter location) within a process load. The dose at each location or dose zone is estimated by the mean value of dose received by three or more replicate process loads. The absorbed-dose results from dose maps may be plotted in a variety of 2- and 3-dimensional views as an aid to evaluating results and gaining an understanding of dose delivery.

7.2.2 Estimates of the statistical uncertainty and of the mean values of the dose map data may be used to identify equivalent dose zones. See Appendix X1 for discussion and Practice E178 for guidance in the treatment of outlying observations.

7.2.3 Determine the reproducibility of dose at a routine monitoring position, if used, for the process load and establish a quantitative relationship of the dose at this position to the dose at the established minimum or maximum dose zones, or both. See Appendix X2 for a discussion.

7.2.4 Establish all of the process parameters necessary to achieve the absorbed doses within the set requirements, for example, irradiator timer settings or conveyor speed, electron beam energy, beam current, beam scan width, process load characteristics, process geometry, multiple exposure, multiple passes, partial loads, etc. In some electron beam irradiator designs, conveyor speed, beam current and beam scan parameters are linked and may be controlled as a combined parameter.

NOTE 9—A dosimetry system may be used for dose mapping with an operating range that is not compatible with routine process doses, so that the doses measured during dose map will be significantly different from the doses needed for processing. In order for this method to be valid, it must have been demonstrated that there is proportionality between key parameters of the irradiation facility and dose to the product.

NOTE 10—Where a different dosimetry system is used for mapping versus routine processing, differences in absorbed-dose measurements between the different dosimetry systems may result in realization of greater variation in process monitoring, which may have significance when considering the dosimeter location for routine process monitoring.

8. Measurement uncertainty

8.1 All dose measurements need to be accompanied by an estimate of uncertainty. Appropriate procedures are recommended in ISO/ASTM 51707 and ISO/ASTM 51261 (see also GUM).

8.1.1 All components of uncertainty should be included in the estimate, including those arising from calibration, dosimeter variability, instrument reproducibility, and the effect of influence quantities. A full quantitative analysis of components of uncertainty is referred to as an uncertainty budget, and is then often presented in the form of a table. Typically, the uncertainty budget will identify all significant components of uncertainty, together with their methods of estimation, statistical distributions and magnitudes.

9. Documentation accumulation

9.1 Document the dosimetry system used for each radiation process dose map. Identify the dosimeter manufacturer, type, batch number, instrumentation, and the calibration curve used to convert dosimeter response measurements to absorbed-dose values in water or the product (refer to ISO/ASTM 51261).

[7] McLaughlin, W. L., Boyd, A. W., Chadwick, K. C., McDonald, J. C., Miller, A., *Dosimetry for Radiation Processing*, Taylor and Francis, Ltd., London, 1989.

[8] Saylor, M. C., Baryschpolec, S. W., Hurwitz, L. M., and McLaughlin, W. L., "Radiation Process Data Collection, Analysis, and Interpretation," *Sterilization of Medical Products*, Vol VI, R.F. Morrisey, Ed., Polyscience Publications, Morin Heights, Quebec, Canada, 1997, pp. 240-260.

9.2 Document the procedural methods, protocols, equipment and instrumentation used to measure the dosimeter response, and the calibration and maintenance of the equipment and instrumentation (refer to ISO/ASTM 51261).

9.3 Document the irradiation environmental conditions that may have an effect on the performance of the specific dosimetry system; for example, temperature, relative humidity, and surrounding atmosphere (if other than air).

9.4 Document or reference a description of the radiation source characteristics used in dose mapping, for example, the type, configuration, and nominal gamma source activity or electron beam parameters.

9.5 Document or reference the manufacturer, product type, physical parameters (such as, but not limited to, density, mass, volume, internal orientation), dose specifications, and lot or batch number (if any) for the product, material or substance being mapped.

9.6 Document or reference the product, material or substance loading diagrams, dosimeter positions, starting date and time of irradiation, completion date and time of irradiation, product path, radiation field, identification of the personnel involved, and any special irradiation or handling conditions that could affect the absorbed dose to the product.

9.7 Document the absorbed dose for each dosimeter position and the uncertainties in the dose values.

9.8 Document the dose map data analysis.

9.9 Ensure that each dose mapping set is uniquely identified. Ensure that the processing documentation bears identification that distinguishes it from all other processes or dose maps. Document, in accordance with an established quality assurance program, the absorbed doses and the process parameters. Review and approval of process documentation should be performed by authorized personnel as specified in the quality assurance program. If deficiencies are found, ensure that corrective action has been taken.

9.10 Retain documentation for a period of time specified by relevant authorities and have them available for inspection as needed.

10. Keywords

10.1 absorbed dose; bremsstrahlung; dose distribution; dose mapping; dose zone; dosimetry; electron beam; gamma radiation; irradiator characterization; maximum dose; minimum dose; operational qualification; performance qualification; radiation processing; routine process monitoring; sterilization; uncertainty; X-radiation

APPENDIXES

Informative

X1. Determining Zones of Equivalent Dose and Establishing Zones of Maximum and Minimum Dose Extremes

X1.1 *Defining Statistically Equivalent Dose Zones*:

X1.1.1 Appendix X1 describes the definition of dose zones based on the mathematical relationship defined by the statistical uncertainty of the measurement.

X1.2 *Estimating Statistical Uncertainty within Zones*:

X1.2.1 Values of dose within a dose zone when measured across replicate process loads will differ. Variations of the measured dose within a dose zone may be due to uncertainties in processing, variation of process loads and product, positioning of dosimeters and uncertainty of the dosimetry system. The Type A or statistical uncertainty of a dose map is estimated from the standard deviation of the replicate dose values in each zone.

X1.2.2 There are two methods available to estimate the dose map uncertainty. One method uses estimates of the mean and standard deviation to estimate a statistical coverage for uncertainty based on parametric statistics (see X1.3 and X1.4, and examples in Table X1.1). Another method uses non-parametric statistics and estimates the statistical coverage based on ranking the uncertainty of each set of measurements (see X1.5).

X1.3 *Statistical Uncertainty within Zones Using Mean and Standard Deviation*:

X1.3.1 The parametric method may be used with small to large numbers of measurements within a dose zone. It assumes that the magnitude of the uncertainty is estimated by the standard deviation, and that the magnitude of the uncertainty is independent of the mean dose. For purposes of identifying doses statistically equivalent to the maximum or minimum dose, the parametric method assumes that the measured doses in each zone are normally distributed.

X1.3.2 If the $D_{i,z}$ is dose measured by the ith dosimeter in zone z and there are n_z independent measurements made of zone z then the mean absorbed dose expected in each zone z, $\bar{D}_z$, is estimated by:

$$\bar{D}_z = \frac{\sum_{i}^{n_z} D_{i,z}}{n_z} \quad \text{(X1.1)}$$

X1.3.3 Within each zone the variance, S_z^2, of the dose measurements about the mean is estimated as:

$$S_z^2 = \frac{\sum_{i=1}^{n_z} \left(D_{i,z} - \bar{D}_z\right)^2}{n_z - 1} \quad \text{(X1.2)}$$

X1.3.4 If the variability of dose about the mean for each zone can be assumed to be similar, even though the mean dose in each zone may differ, then an estimate of the common ("pooled") standard deviation, S_{pooled}, is given by:

$$S_{overall} = \sqrt{\frac{\sum_{z}^{Z_{total}} \sum_{i}^{n_z} \left(D_{i,z} - \bar{D}_z\right)^2}{N - Z_{total}}} = \sqrt{\frac{\sum_{z}^{Z_{total}} (n_z - 1) S_z^2}{N - Z_{total}}} \quad \text{(X1.3)}$$

where:

$\bar{D}_z$ = the zone mean defined in X1.3.2,
Z_{total} = the total number of zones, and
N = the total number of measurements

$$N = \sum_{z}^{Z_{total}} n_z$$

NOTE X1.1—If the assumption of homogeneity of variance over all zones is not justified, the pooled standard deviation may be calculated for any two comparable zones for which the mean values are being compared.

X1.4 *Identifying Equivalent Zones Using Parametric Statistics*:

X1.4.1 Statistically equivalent zones have mean dose estimates that do not differ significantly. Zones that are statistically equivalent may be measured interchangeably during routine processing according to ease of access or other criteria.

X1.4.2 Zones with a known statistical relationship to the minimum and maximum doses should be used for process monitoring.

X1.4.3 The difference between the dose means from any two zones should be greater than the minimum detectable difference or least significant difference to be statistically significant. The minimum detectable difference is calculated as:

$$\delta = k \sqrt{\frac{2S_{overall}^2}{\bar{n}_z}} \quad \text{(X1.4)}$$

where:

$\bar{n}_z$ = the average number of independent measurements made in each zone (note: the number of measurements should be the same in each zone), and
k = a coverage factor.

$S_{overall}^2$ may be calculated from all categories or the two categories being compared.

X1.4.4 The coverage factor k for statistically based uncertainty estimates (the standard deviation) is typically based on the t distribution:

$$k = t_{\alpha,\, N - Z_{total}} \quad \text{(X1.5)}$$

where:

α = one minus the desired confidence of not declaring that two zones are different when they are actually the same,
Z_{total} = the number of zones used to calculate $S_{overall}^2$, and
N = the total number of measurements made in those zones.

For example, for measurements made in 20 zones each replicated 3 times ($N = 3 \cdot 20 = 60$) and a 95 % confidence of zones being statistically equivalent is desired, then $k = t_{0.05,\, 60-20} = t_{0.05,\, 40} = 1.684$.

NOTE X1.2—A "one sided" t-value is used because the comparison is being made to a maximum or minimum value. This value differs from the common use of $k = 2$ due to the use of one sided statistics and the recognition of small sample sizes.

X1.4.5 A dose in a given zone, $\bar{D}_z$, is statistically equivalent to the minimum $\bar{D}_{min}$, if $\bar{D}_z$ is less than or equal to the value $\bar{D}_{min} + \delta$.

X1.4.6 A dose in a given zone, $\bar{D}_z$, is statistically equivalent to the maximum $\bar{D}_{max}$, if $\bar{D}_z$ is greater than or equal to the value $\bar{D}_{max} - \delta$.

X1.5 *Identifying Equivalent Zones with Non-Parametric Statistics*:

X1.5.1 Zones of similar dose may be identified using non-parametric statistics. Non-parametric statistics rank differences among replicate measurements from largest to smallest. This makes the fewest assumptions about the statistical distribution of uncertainties; however it requires more measurements to provide reliable estimates. Identifying zones of similar dose using non-parametric statistics is appropriate when a dose map measures 100 or more measurement locations.

X1.5.2 Let the relative difference among dosimeters in a zone be calculated as:

$$\delta_{rel,\, z} = \frac{Max(D_z) - Min(D_z)}{Mean(D_z)} \quad \text{(X1.6)}$$

where z is indexed over all zones.

X1.5.3 Arrange the $\delta_{rel,z}$ from smallest to largest. If there are Z_{total} zones then the $0.95 \cdot Z_{total}$ entry is an estimate of the 95th percentile of relative differences among dosimeters within a zone. For example, if exactly 100 zones were identified and measured in replicate, then there would be 100 relative differences, one for each zone. When these values are sorted from smallest to largest, the 5th largest value (number 95 on the list) is an estimate of the 95th percentile of the relative differences. This critical difference is used to compare zones for statistical similarity.

X1.5.4 When there are a different number of zones, it is necessary to interpolate between values in the list. For example if 150 zones were measured the 95th percentile would be estimated by the value in position 142.5. Since there is no half position, the value would be estimated by a value halfway between the value at position 142 and the value at position 143.

X1.5.5 Zones with mean values that differ by less than the selected critical relative differences are statistically equivalent.

NOTE X1.3—In Table X1.1, section numbers associated with the computation of values for key variables are shown in parentheses.

NOTE X1.4—Different computer software may handle computations differently. For example, the spreadsheet used in Table X1.1 does internal