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

This standard is issued under the fixed designation E 2303; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This document provides guidance in determining absorbed-dose distributions 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, other specific ISO and ISO/ASTM standards containing dose mapping requirements exist. For food irradiation, see ISO/ASTM 51204, Practice for Dosimetry in Gamma Irradiation Facilities for Food Processing and ISO/ASTM 51431, Practice for Dosimetry in Electron and Bremsstrahlung Irradiation Facilities for Food Processing. For the radiation sterilization of health care products, see ISO 11137: 1995, Sterilization of Health Care Products Requirements for Validation and Routine Control Radiation Sterilization. In those areas covered by ISO 11137, that standard takes precedence. ISO/ASTM Practice 51608, ISO/ASTM Practice 51649, and ISO/ASTM Practice 51702 also contain dose mapping requirements.

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

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

1.4 Dosimetry is only one component of a total quality program for an irradiation facility. Other controls besides dosimetry may be required for specific applications such as medical device sterilization and food preservation.

1.5 *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:*

E 170 Terminology Relating to Radiation Measurements and Dosimetry[2]

E 177 Practice for the Use of the Terms Precision and Accuracy Applied to Measurement of a Property of Material[3]

E 178 Practice for Dealing with Outlying Observations[3]

E 666 Practice for Calculating Absorbed Dose from Gamma or X Radiation[2]

E 668 Practice for the Application of Thermoluminescence-Dosimetry (TLD) Systems for Determining Absorbed Dose in Radiation-Hardness Testing of Electronic Devices[2]

E 1026 Practice for Using the Fricke Reference Standard Dosimetry System[2]

E 2232 Guide for Selection and Use of Mathematical Methods for Calculating Absorbed Dose in Radiation Processing Applications[2]

2.2 *ISO/ASTM Standards:*[4]

ISO/ASTM 51204 Practice for Dosimetry in Gamma Irradiation Facilities for Food Processing

ISO/ASTM 51205 Practice for Use of a Ceric-Cerous Sulfate Dosimetry System

ISO/ASTM 51261 Guide for Selection and Calibration of Dosimetry Systems for Radiation Processing

ISO/ASTM 51275 Practice for Use of a Radiochromic Film Dosimetry System

ISO/ASTM 51276 Practice for Use of a Polymethylmethacrylate Dosimetry System

ISO/ASTM 51310 Practice for Use of a Radiochromic Optical Waveguide Dosimetry System

ISO/ASTM 51400 Practice for Characterization and Performance of a High-Dose Radiation Dosimetry Calibration Laboratory

ISO/ASTM 51401 Practice for Use of a Dichromate Dosimetry System

ISO/ASTM 51431 Practice for Dosimetry in Electron and Bremsstrahlung Irradiation Facilities for Food Processing

ISO/ASTM 51538 Practice for Use of the Ethanol-Chlorobenzene Dosimetry System

ISO/ASTM 51540 Practice for Use of a Radiochromic Liquid Dosimetry System

ISO/ASTM 51607 Practice for Use of the Alanine-EPR Dosimetry System

[1] This guide is under the jurisdiction of ASTM Committee E10 on Nuclear Technology and Application and is the direct responsibility of Subcommittee E10.01 on Dosimetry for Radiation Processing.

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[2] *Annual Book of ASTM Standards*, Vol 12.02.

[3] *Annual Book of ASTM Standards*, Vol 14.02.

[4] Standards on Dosimetry for Radiation Processing ASTM International 2002. See *Annual Book of ASTM Standards*, Vol 12.02.

ISO/ASTM 51608 Practice for Dosimetry in an X-ray (Bremsstrahlung) Facility for Radiation Processing
ISO/ASTM 51631 Practice for Use of Calorimetric Dosimetry Systems for Electron Beam Dose Measurements and Dosimeter Calibrations
ISO/ASTM 51649 Practice for Dosimetry in an Electron beam Facility for Radiation Processing at Energies between 300 keV and 25 MeV
ISO/ASTM 51650 Practice for Use of Cellulose Acetate Dosimetry Systems
ISO/ASTM 51702 Practice for Dosimetry in a Gamma Irradiation Facility for Radiation Processing
ISO/ASTM 51707 Guide for Estimating Uncertainties in Dosimetry for Radiation Processing
ISO/ASTM 51818 Practice for Dosimetry in an Electron Beam Facility for Radiation Processing at Energies between 80 and 300 keV

2.3 *International Commission on Radiation Units and Measurements Reports:*[5]

ICRU Report 14 Radiation Dosimetry: X-Rays and Gamma Rays with Maximum Photon Energies Between 0.6 and 50 MeV
ICRU Report 17 Radiation Dosimetry: X-Rays Generated at Potentials of 5 to 150 kV
ICRU Report 34 The Dosimetry of Pulsed Radiation
ICRU Report 35 Radiation Dosimetry: Electron Beams with Energies Between 1 and 50 MeV
ICRU Report 37 Stopping Powers for Electrons and Positrons
ICRU Report 60 Fundamental Quantities and Units for Ionizing Radiation

2.4 *International Organization for Standardization:*[6]

ISO 11137 Sterilization of Health Care Products—Requirements for Validation and Routine Control—Radiation Sterilization

3. Terminology

3.1 *Definitions:*

3.1.1 *absorbed-dose mapping* —measurement of absorbed dose within a process load using dosimeters placed at specified locations to produce a one, two or three-dimensional distribution of absorbed dose, thus rendering a map of absorbed-dose values.

3.1.2 *calibration curve*—graphical representation of the dosimetry system's response function.

3.1.3 *container*—carrier, tote, cart, tray or other container in which product is loaded to traverse the irradiation field. In some instances, this may be the actual product package.

3.1.4 *dose map, dose mapping*—See *absorbed-dose mapping*.

3.1.5 *dose uniformity ratio*—ratio of the maximum to the minimum absorbed dose within a process load. The concept is also referred to as the max/min dose ratio.

3.1.6 *dose zone*—a volume 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).

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

3.1.8 *operational qualification (OQ)*—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)*—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 loading configuration irradiated as a single entity.

3.1.11 *reference position*—dose measurement position with an established relationship to the minimum and/or maximum dose zones.

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

3.1.12.1 *Discussion*—Simulated product may be used during operational qualification as a substitute for the actual product, material or substance to be irradiated. When used in routine production runs, it 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 E 170. Definitions in E 170 are compatible with ICRU 60; that document, therefore, may be used as an alternative reference.

4. Significance and Use

4.1 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.

4.2 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.

4.3 Radiation processing may require a minimum absorbed dose (to achieve a desired effect or to fulfill a legal requirement), and a maximum dose that can be tolerated (while the product, material or substance still meets functional specifications or to fulfill a legal requirement).

4.4 Dose mapping is used to characterize the radiation process and assess the reproducibility of absorbed-dose results, which may be used as part of operational qualification and performance qualification.

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

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

4.5 Dose mapping is used to 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.

4.6 Dose mapping is used to establish the relationship between the dose at a reference position and the dose within the minimum and maximum dose zones established for a process load.

4.7 Dose mapping is used to verify mathematical dose calculation methods. See Guide E 2232.

4.8 Dose mapping is used to determine the process shutdown and startup transit dose effect on the distribution of absorbed dose and the magnitude of the minimum and maximum doses.

4.9 Dose mapping is used to 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 density or product loading pattern may occur.

5. Prerequisites

5.1 *Installation Qualification, Dosimetry and Other Prerequisites to Dose Mapping*:

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

5.1.2 Select an appropriate dosimetry system(s) for the dose mapping experiments. See ISO/ASTM Guide 51261 for guidance.

NOTE 2—For requirements on the qualification of equipment and control systems, refer to ISO/ASTM Standard Practices 51204, 51431, 51608, 51649, 51702, and ISO 11137.

5.2 *Calibration of the Dosimetry System*:

5.2.1 Prior to use, the dosimetry system (consisting of a specific batch of dosimeters and specific measurement instruments) shall be calibrated in accordance with the user's documented procedure that specifies details of the calibration process and quality assurance requirements. This calibration process shall be repeated at regular intervals to ensure that the accuracy of the absorbed-dose measurement is maintained within required limits. Calibration methods are described in ISO/ASTM Guide 51261.

5.3 *Calibration Irradiation of Dosimeters*—Irradiation is a critical component of the calibration of the dosimetry system. Calibration irradiations shall be performed in one of three ways by irradiating the dosimeters at:

5.3.1 An accredited calibration laboratory that provides an absorbed dose (or an absorbed-dose rate) having measurement traceability to nationally or internationally recognized standards, or

5.3.2 An in-house calibration facility that provides an absorbed dose (or an absorbed-dose rate) having measurement traceability to nationally or internationally recognized standards, or

5.3.3 A production or research irradiation facility together with reference- or transfer-standard dosimeters that have measurement traceability to nationally or internationally recognized standards.

5.4 *Measurement Instrument Calibration and Performance Verification*—For the calibration of the instruments, and for the verification of instrument performance between calibrations, see ISO/ASTM Guide 51261 and/or instrument-specific operating manuals.

6. Dose Mapping

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

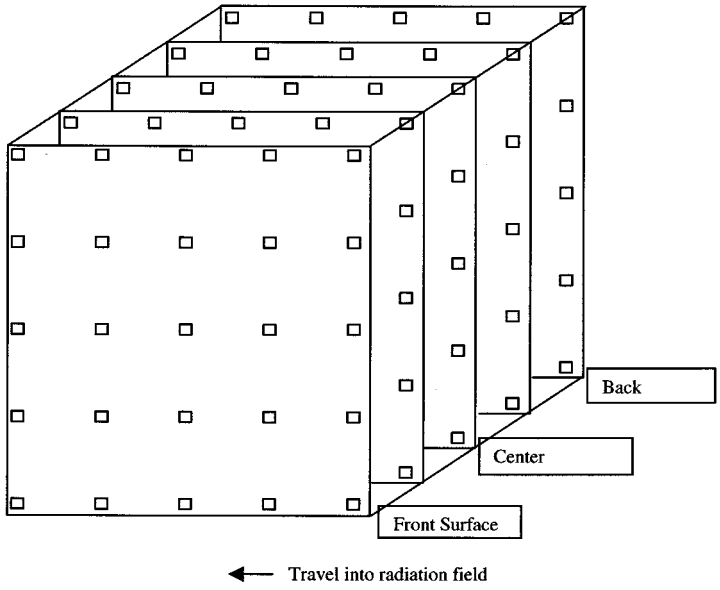
6.1.1 As specified in Practices ISO/ASTM 51204, ISO/ASTM 51431, ISO/ASTM 51608, ISO/ASTM 51649, ISO/ASTM 51702 and ISO 11137, perform irradiation facility dose mapping to characterize the irradiator with respect to the dose distribution and reproducibility of absorbed dose delivery. This should be performed in accordance with a formal validation program over 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 process load of homogeneous density material that fills the container to its design volume limits. Material densities should be within the density range for which the irradiator is to be used. In electron beam facilities, a single material density may be used provided the maximum and minimum process settings that affect dose are demonstrated (for example, conveyor speed, beam current, scan frequency and scan height or width). Determine absorbed dose distribution throughout the process load for each product path through the irradiation field.

Discussion—Electron beam irradiation facilities may satisfy the dose mapping requirements described in 6.1.2 using a two dimensional surface grid dose map with a separate penetration test performed in a homogenous density material. Appropriate methods should be used (see ISO/ASTM Practice 51649) to determine the electron beam energy. For process load fringe or edge effect studies in electron beam, several different densities of homogeneous material should be used. The maximum electron beam process area limits may be determined by demonstrating the uniformity of absorbed dose in both the direction of scan and direction of travel under the maximum and minimum process settings that affect dose (for example, conveyor speed, beam current, scan frequency and scan height or width). Different product paths through the radiation process field need not be a physical transport path but may be created by variation(s) made to irradiator process settings that affect the absorbed dose distribution (for example, single- and double-sided irradiations in electron beam facilities, changes made to electron beam energy, use of multiple source rack(s) or a source rack positioning change in gamma irradiators, etc.). The impact of process interruptions and process transit doses for each product path should also be demonstrated.

6.1.2.1 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 dosimeter placement array is given in Fig. 1.

6.1.2.2 Measure the dose at the same positions in three or more replicate process loads to determine the variability of the measured absorbed dose.



NOTE—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.

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

6.1.2.3 Following irradiation, retrieve and read the dosimeters, and evaluate the data in accordance with established procedures (see Section 7).

6.1.3 If changes that could affect the magnitude or location of the absorbed-dose extremes are made to the irradiator or mode of operation, repeat the absorbed-dose mapping to the extent necessary to establish the effects. The dose mapping may be repeated in its entirety or a reduced dosimeter placement grid can be justified. A single density of homogeneous material may be used to demonstrate equivalence to the original dose mapping.

6.1.4 The use of mathematical models in determining dosimeter locations for dose mapping or in predicting dose map results may be appropriate. See Guide E 2232 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 densities and distributions as the actual products.

NOTE 3—Different products with similar densities and distribution may be considered as a single processing category and the dose map data can be applied to all products in this group.

6.2.2 If a reference position is used for routine process monitoring, the relationship between these dose distributions and the reference position shall be established. Facilities that process only product loads exhibiting the same dose distribution characteristics as those used in the operational qualification (OQ) dose mapping(s) discussed in 6.1 can be considered to have met the product dose mapping requirements for performance qualification (PQ).

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 in 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 and/or maximum dose 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. The magnitude of dose gradients is also dependent on the type of radiation source; that is, gamma, x-ray, electron beam.

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 to be monitored in the map shall 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 and/or maximum dose 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 can involve cutting open the individual product inside the package to permit dosimeter positioning and retrieval.

6.2.4.3 The use of mathematical models in determining dosimeter locations for dose mapping or in predicting dose map results may be appropriate. See Guide E 2232 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 measurements. Each load should contain similar materials and dosimeter placements that are configured in the same way and should be processed under the same operating conditions.

6.2.6 Partially filled process loads may require additional dose mapping to evaluate the dose distribution results and effects on these and adjacent process loads. Alternatively, fill the container with simulated product.

6.2.7 Refer to Section 7 and Appendix X1 for discussions regarding uncertainties and the dose zone concept. Doses outside of the product dose specification are acceptable for dose mapping purposes. See Note 5 in 7.2.4 for additional discussion.

6.2.8 Repeat the dose mapping procedure if a change is made that may impact the previously characterized dose distribution.

7. Analysis of Dose Map Data

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

7.1.1 Analyze dose map data to confirm or establish the operational range of the irradiator pathway(s) and establish the dose delivery characteristics.

7.1.2 Determine the dose distribution including the minimum and maximum absorbed-dose locations in the process load. For some process loads, the minimum and maximum dose may not be limited to single locations. Estimates of the statistical uncertainty and of the mean value of the dose map data 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 Practice E 178 for guidance in the treatment of outlying observations.

7.1.3 Evaluate the reproducibility of the minimum and/or maximum absorbed-dose zone(s).

7.1.4 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.

NOTE 4—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 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 E 178 for guidance in the treatment of outlying observations.

7.2.3 Determine the reproducibility of dose at a reference position (if used) for the process load and establish a mathematical relationship of the dose at the reference position to the dose at the established minimum and/or maximum dose zones. 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 system designs, conveyor speed, beam current and beam scan parameters are linked and may be controlled as a combined parameter.

NOTE 5—Dose mapping may be carried out using a different dosimetry system from that used in routine processing provided both systems are calibrated and traceable to a national standard. In some circumstances, a dosimetry system may be used for dose mapping with an operating range that is not compatible with routine process doses if it can be demonstrated that the dose measurement results may be scaled up or down without sacrificing measurement quality or compromising relationships established in the dose map.

8. Measurement Uncertainty

8.1 To be meaningful, a measurement of absorbed dose shall be accompanied by an estimate of uncertainty.

8.2 Components of uncertainty shall be identified as belonging to one of two categories:

8.2.1 *Type A*—Those evaluated by statistical methods, or

8.2.2 *Type B*—Those evaluated by other means.

8.3 Other methods of categorizing uncertainty have been widely used and may be useful for reporting uncertainty. For example, the terms precision and bias or random and systematic (non-random) are used to describe different categories of uncertainty.

NOTE 6—The identification of Type A and Type B uncertainties is based on methodology for estimating uncertainties published in 1993 by the International Organization for Standardization (ISO) in the Guide to the Expression of Uncertainty in Measurement.[9] The purpose of using this type of characterization is to promote an understanding of how uncertainty statements are arrived at and to provide a basis for the international comparison of measurement results.

NOTE 7—ISO/ASTM Guide 51707 defines possible sources of uncertainty in dosimetry performed in radiation processing facilities, and offers

[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] "Guide to the Expression of Uncertainty in Measurement," International Organization for Standardization, 1993, ISBN 92-6710188-9.

procedures for estimating the magnitude of the resulting uncertainties in the measurement of absorbed dose using a dosimetry system. The document defines and discusses basic concepts of measurement, including estimation of the measured value of a quantity, "true" value, error and uncertainty. Components of uncertainty are discussed and methods are provided for estimating their values. Methods are also provided for calculating the combined standard uncertainty and estimating expanded (overall) uncertainty.

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 or response function used to convert measurements to absorbed-dose values in water or the product. (Refer to ISO/ASTM Guide 51261.)

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 Guide 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 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.

9.8 Document the dose map data analysis.

9.9 Ensure that each dose mapping set is uniquely identified. Assure that the processing documentation bears identification that distinguishes it from all other processes or dose maps. Certify, in accordance with an established quality assurance program, the absorbed doses and the process parameters. Certification shall be performed by authorized personnel as documented in the quality assurance program. Audit all documentation to ensure that records are accurate and complete. If deficiencies are found assure 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 rays; irradiator characterization; maximum dose; minimum dose; operational qualification; performance qualification; radiation processing; reference monitoring; sterilization; uncertainty; X-rays

APPENDIXES

(Nonmandatory Information)

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

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 Fig. 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

Electron Beam Dose Map - Summary Dose Measurements & Analysis

Zone	Left	Bottom	Front	Dose in kGy water Run 1	Run 2	Run 3	Mean	STDEV	CV	(X1.3.4) Sum of Squared Differences	(X1.4.3) Min & Max Equivalence Zones
1	12.50	20.50	15.00	20.8	21.7	22.0	21.5	0.6	2.9	0.78	
2	12.50	20.50	12.50	22.7	22.9	22.1	22.6	0.4	1.8	0.35	
3	12.50	20.50	10.00	24.9	25.0	24.4	24.8	0.3	1.3	0.21	
4	12.50	20.50	7.50	28.8	28.1	29.2	28.7	0.6	1.9	0.62	
5	12.50	20.50	5.00	26.0	25.1	25.4	25.5	0.5	1.8	0.42	
6	12.50	20.50	2.50	21.2	22.1	23.9	22.4	1.4	6.1	3.78	
7	12.50	20.50	0.00	21.2	21.0	22.5	21.6	0.8	3.8	1.33	
8	25.00	20.50	15.00	20.4	19.6	19.6	19.9	0.5	2.3	0.43	MinZone
9	25.00	20.50	12.50	21.5	21.5	22.6	21.9	0.6	2.9	0.81	
10	25.00	20.50	10.00	23.3	23.8	24.4	23.8	0.6	2.3	0.61	
11	25.00	20.50	7.50	23.9	24.7	24.6	24.4	0.4	1.8	0.38	
12	25.00	20.50	5.00	23.0	23.4	23.1	23.2	0.2	0.9	0.09	
13	25.00	20.50	2.50	21.3	22.1	22.0	21.8	0.4	2.0	0.38	
14	25.00	20.50	0.00	19.4	21.2	21.0	20.5	1.0	4.8	1.95	MinZone
15	12.50	10.25	15.00	22.0	22.5	22.8	22.4	0.4	1.8	0.33	
16	12.50	10.25	12.50	22.7	22.9	23.1	22.9	0.2	0.9	0.08	
17	12.50	10.25	10.00	24.9	25.0	24.4	24.8	0.3	1.3	0.21	
18	12.50	10.25	7.50	29.8	30.6	30.2	30.2	0.4	1.3	0.32	MaxZone
19	12.50	10.25	5.00	26.0	25.1	25.4	25.5	0.5	1.8	0.42	
20	12.50	10.25	2.50	22.6	22.1	23.4	22.7	0.7	2.9	0.86	
21	12.50	10.25	0.00	21.2	21.0	22.5	21.6	0.8	3.8	1.33	
22	25.00	10.25	15.00	21.8	21.0	21.4	21.4	0.4	1.9	0.32	
23	25.00	10.25	12.50	22.5	22.7	22.0	22.4	0.4	1.6	0.26	
24	25.00	10.25	10.00	23.3	23.8	24.4	23.8	0.6	2.3	0.61	
25	25.00	10.25	7.50	25.0	24.7	24.6	24.8	0.2	0.8	0.09	
26	25.00	10.25	5.00	23.0	23.4	23.1	23.2	0.2	0.9	0.09	
27	25.00	10.25	2.50	23.0	22.1	22.8	22.6	0.5	2.1	0.45	
28	25.00	10.25	0.00	21.7	21.5	22.0	21.7	0.3	1.2	0.13	
29	12.50	0.00	15.00	21.6	21.2	22.2	21.7	0.5	2.3	0.51	
30	12.50	0.00	12.50	22.6	22.9	23.1	22.9	0.3	1.2	0.15	
31	12.50	0.00	10.00	24.8	25.0	23.8	24.5	0.6	2.6	0.81	
32	12.50	0.00	7.50	27.6	29.0	30.5	29.0	1.5	5.0	4.21	
33	12.50	0.00	5.00	25.5	25.1	25.4	25.3	0.2	0.8	0.09	
34	12.50	0.00	2.50	22.7	22.1	22.9	22.6	0.4	1.8	0.35	
35	12.50	0.00	0.00	21.6	22.2	22.0	21.9	0.3	1.5	0.21	
36	25.00	0.00	15.00	20.3	22.0	21.4	21.0	0.8	4.0	1.43	
37	25.00	0.00	12.50	22.7	22.7	22.0	22.5	0.4	1.8	0.33	
38	25.00	0.00	10.00	23.8	23.8	24.4	24.0	0.3	1.4	0.23	
39	25.00	0.00	7.50	25.0	24.7	24.6	24.8	0.2	0.8	0.09	
40	25.00	0.00	5.00	23.2	23.4	23.1	23.2	0.2	0.7	0.05	
41	25.00	0.00	2.50	21.8	22.1	22.8	22.2	0.5	2.3	0.53	
42	25.00	0.00	0.00	19.7	21.5	21.6	20.9	1.1	5.1	2.29	

Zone	Left	Bottom	Front	Load 1	Load 2	Load 3	Mean	STDEV	CV
Ref.	12.50	9.00	0.00	22.7	n/a	n/a			
Ref.	12.50	9.00	0.00	n/a	22.2	n/a	22.5	0.3	1.2
Ref.	12.50	9.00	0.00	n/a	n/a	22.6			

kGy
0.34 Pooled variance (X1.3.4)
0.80 Minimum Detectable Difference (X1.4.3)
19.9 Minimum Dose
30.2 Maximum Dose

Dose Ratio Estimator (X2.1.3)
Reference to Minimum 1.13
Reference Maximum 0.75

Ratio Estimator Bias Contribution to Uncertainty
Bias of sample ratio 9.847E-04
Variance of sample ratio 1.985E-03
CV Min Ratio 3.93

Photon (gamma or x-ray) Dose Map - Summary Dose Measurements & Analysis

Zone	Left	Bottom	Front	Dose in kGy water Run 1	Run 2	Run 3	Mean	STDEV	CV	(X1.3.4) Sum of Squared Differences	(X1.4.3) Min & Max Equivalence Zones
1	12.50	36.00	30.00	27.4	29.1	29.2	28.6	1.0	3.5	2.05	
2	12.50	36.00	25.00	26.0	25.1	28.0	26.4	1.5	5.6	4.41	
3	12.50	36.00	20.00	24.9	25.0	26.0	25.3	0.6	2.4	0.74	
4	12.50	36.00	15.00	24.4	23.7	24.1	24.1	0.4	1.5	0.25	MinZone
5	12.50	36.00	10.00	24.5	25.1	25.4	25.0	0.5	1.8	0.42	
6	12.50	36.00	5.00	26.0	25.1	25.4	25.5	0.5	1.8	0.42	
7	12.50	36.00	0.00	29.2	28.0	28.4	28.5	0.6	2.1	0.75	
8	25.00	36.00	30.00	29.0	28.1	28.9	28.7	0.5	1.7	0.49	
9	25.00	36.00	25.00	26.9	25.1	26.2	26.1	0.9	3.5	1.65	
10	25.00	36.00	20.00	24.9	25.0	26.0	25.3	0.6	2.4	0.74	
11	25.00	36.00	15.00	24.0	23.7	25.1	24.3	0.7	3.0	1.09	MinZone
12	25.00	36.00	10.00	25.2	24.4	25.4	25.0	0.5	2.1	0.56	
13	25.00	36.00	5.00	26.3	26.0	25.4	25.9	0.5	1.8	0.42	
14	25.00	36.00	0.00	28.7	28.5	29.0	28.7	0.3	0.9	0.13	
15	12.50	18.00	30.00	31.4	30.6	31.0	31.0	0.4	1.3	0.32	MaxZone
16	12.50	18.00	25.00	29.7	29.4	28.6	29.2	0.6	1.9	0.65	
17	12.50	18.00	20.00	28.0	27.2	27.0	27.4	0.5	1.9	0.56	
18	12.50	18.00	15.00	25.7	24.9	25.0	25.2	0.4	1.7	0.38	
19	12.50	18.00	10.00	26.5	27.7	28.6	27.6	1.1	3.8	2.22	
20	12.50	18.00	5.00	30.0	29.1	29.1	29.4	0.5	1.8	0.54	
21	12.50	18.00	0.00	31.0	30.1	31.3	30.8	0.6	2.0	0.78	MaxZone
22	25.00	18.00	30.00	31.2	30.6	30.9	30.9	0.3	1.0	0.18	MaxZone
23	25.00	18.00	25.00	28.2	29.1	27.7	28.3	0.7	2.5	1.01	
24	25.00	18.00	20.00	28.0	27.2	27.0	27.4	0.5	1.9	0.56	
25	25.00	18.00	15.00	24.3	24.9	24.8	24.7	0.3	1.3	0.21	MinZone
26	25.00	18.00	10.00	26.5	28.0	28.6	27.7	1.1	3.9	2.34	
27	25.00	18.00	5.00	30.5	29.0	29.1	29.5	0.8	2.8	1.41	
28	25.00	18.00	0.00	31.0	30.6	29.9	30.5	0.6	1.8	0.62	MaxZone
29	12.50	0.00	30.00	30.4	29.6	29.3	29.8	0.6	1.9	0.65	
30	12.50	0.00	25.00	29.1	28.0	29.1	28.7	0.6	2.2	0.81	
31	12.50	0.00	20.00	27.0	27.1	27.7	27.3	0.4	1.4	0.29	
32	12.50	0.00	15.00	23.8	23.7	24.4	24.0	0.4	1.6	0.29	MinZone
33	12.50	0.00	10.00	26.0	25.1	25.4	25.5	0.5	1.8	0.42	
34	12.50	0.00	5.00	27.3	26.6	29.1	27.7	1.3	4.7	3.33	
35	12.50	0.00	0.00	29.2	29.3	29.8	29.4	0.3	1.1	0.21	
36	25.00	0.00	30.00	29.0	29.2	28.9	29.0	0.2	0.5	0.05	
37	25.00	0.00	25.00	26.9	25.1	26.2	26.1	0.9	3.5	1.65	
38	25.00	0.00	20.00	24.9	25.0	26.0	25.3	0.6	2.4	0.74	
39	25.00	0.00	15.00	24.0	23.7	25.1	24.3	0.7	3.0	1.09	MinZone
40	25.00	0.00	10.00	25.2	24.4	25.4	25.0	0.5	2.1	0.56	
41	25.00	0.00	5.00	26.3	26.0	25.4	25.9	0.5	1.8	0.42	
42	25.00	0.00	0.00	28.7	29.6	29.5	29.3	0.5	1.7	0.49	

Zone	Left	Bottom	Front	Load 1	Load 2	Load 3	Mean	STDEV	CV
Ref.	12.50	16.00	0.00	31.2	n/a	n/a			
Ref.	12.50	16.00	0.00	n/a	30.5	n/a	30.7	0.4	1.2
Ref.	12.50	16.00	0.00	n/a	n/a	30.5			

kGy
0.44 Pooled variance (X1.3.4)
0.90 Minimum Detectable Difference (X1.4.3)
24.0 Minimum Dose
31.0 Maximum Dose

Dose Ratio Estimator (X2.1.3)
Reference to Minimum 1.28
Reference Maximum 0.99

Ratio Estimator Bias Contribution to Uncertainty
Bias of sample ratio 9.782E-04
Variance of sample ratio 2.017E-03
CV Min Ratio 3.50

NOTE—Provided are representative absorbed-dose results from photon and electron beam dose maps of a run of three replicate process loads of homogeneous material (Fig. X1.1 not related to Fig. 1). The three dimensional coordinates indicate the dosimeter placement with the bottom left front location being 0,0,0. The same dosimeter positions were monitored on each process load and a mean dose calculated for each dose position along with the calculation of the standard deviation. The formula in X1.3.4 was also applied to calculate the sum of the squared differences that can be used to measure the variance between the replicate process loads. Eq X1.4 was used to identify statistically similar positions. These positions were aggregated into maximum and minimum dose zones. The dose ratios of the reference zone with the extreme (high and low) dose zones and their associated bias were calculated using the formulas in X2.1.3 and X2.1.5. The CV of the ratio estimator contribution to uncertainty for the minimum zone was also calculated to facilitate a comparison of measuring at the minimum versus measurement at a reference.

FIG. X1.1 Summary Dose Measurements and Analysis

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 *i*th 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* 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 of the dose measurements about the mean is estimated as:

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

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 is given by:

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

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 mean dose statistically equivalent to either the maximum or minimum dose may be used for process monitoring.

X1.4.3 The difference between the dose means from any two zones must 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.

NOTE X1.2— $S_{overall}^2$ 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 categories 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 categories.

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 X1.3—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 positions.

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. 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.

X1.5.4 Zones with mean values that differ by less than the selected critical relative differences are statistically equivalent.

X2. ESTIMATING A DOSE EXTREME FROM A REFERENCE ZONE

X2.1 A dose map may be used to estimate the relationship between the absorbed dose in either the maximum or minimum dose zone and the absorbed dose in a reference zone. The reference zone is sometimes more accessible or easier to measure during routine processing than the actual minimum or maximum dose positions. Using a reference position adds additional uncertainty to the dose estimate. This section presents one method for estimating the magnitude of the uncertainty.

X2.1.1 It can be assumed that the relationship between the dose in the reference zone and the dose extremes that were established during dose mapping remains essentially the same during routine processing. Any change in process conditions that may change this relationship would require a new dose map.

X2.1.2 The typical ratio estimator is biased and the uncertainty associated with using a reference zone should be combined with the uncertainty associated with product dose extremes when setting irradiator parameters appropriate to deliver a dose that insures the product specifications are met, (sometimes referred to as a target dose).

X2.1.3 During routine processing the dose received at the maximum or minimum dose zone can be estimated using a ratio estimator:

$$D_{ref} = R_{\min} D_{\min} \quad \text{(X2.1)}$$

$$\text{or } D_{ref} = R_{\max} D_{\max}$$

The ratio estimator is calculated as:

$$R_{\min} = \frac{\bar{D}_{ref}}{\bar{D}_{\min}} \text{ for the minimum dose zone and}$$

$$R_{\max} = \frac{\bar{D}_{ref}}{\bar{D}_{\max}} \text{ for the maximum dose zone}$$

X2.1.4 $R_{\min}$ will be used in the rest of this section, as this is the value of typical interest. $R_{\max}$ may be used by substituting "max" for "min" in the following subsections.

X2.1.5 The ratio estimator $R_{\min}$ has uncertainty, the magnitude of which should be determined. Example calculation: If $\bar{D}$ is the mean value of D and E ($R_{\min}$) is the expected value of $R_{\min}$ then E ($R_{\min}$) is approximately:

$$E(R_{\min}) = \frac{\bar{D}_{ref}}{\bar{D}_{\min}} + \frac{\bar{D}_{ref}}{\bar{D}^3_{\min}} Var(D_{\min}) \quad \text{(X2.2)}$$

Note that var($D_{\min}$) is the population variance and is estimated by $S^2_{overall}$. The second term on the right hand side is the uncertainty in $R_{\min}$. This formula is based on a Taylor series expansion of the expected value of a ratio, assuming that the covariance of $D_{\min}$ and D_{ref} is zero. An example of a bias calculation is shown in Fig. X1.1.

X2.1.6 The variance of the ratio estimator is approximately:

$$Var(R_{min}) = \frac{\bar{D}^2_{ref}}{\bar{D}^2_{\min}} \left(\frac{Var(D_{\min})}{\bar{D}^2_{\min}} + \frac{Var(D_{ref})}{\bar{D}^2_{ref}} \right) \quad \text{(X2.3)}$$

where the covariance between $D_{\min}$ and D_{ref} is assumed to be zero and the variance is approximated by the first two terms of a Taylor series expansion. An example of an uncertainty calculation is shown in Fig. X1.1. The uncertainty of the ratio estimator R is included in the total uncertainty used to set the operational parameters used to obtain the target dose.