



Designation: F3604 – 23

Standard Practice for Validating the Additive Manufacturing (AM) Production Process for Medical Devices Produced Using Laser Powder Bed Fusion¹

This standard is issued under the fixed designation F3604; 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.

INTRODUCTION

This practice provides recommendations to perform process validation in which medical devices are manufactured using powder bed fusion by laser beam (PBF-LB/M). Areas of interest for process validation are machine qualifications, software used in the manufacturing process, the importance of design specification and verification on process validation, and raw materials.

1. Scope

1.1 This practice provides an overview of how to perform process validation for medical devices manufactured using PBF/LB/M. The topics that will be covered include machine qualifications, software used in the manufacturing process, the importance of design specification and verification on process validation, and raw materials.

1.2 This practice also provides recommendations for process characterization, risk management, additive manufacturing (AM) facility qualification, and process control as a prerequisite for qualification activity, including installation qualification/operational qualification/performance qualification (IQ/OQ/PQ).

1.3 The practice is primarily focused on non-device-specific AM system(s) validation. Additional information may be needed in reference to the performance of the actual device.

1.4 *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, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

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

¹ This practice is under the jurisdiction of ASTM Committee F42 on Additive Manufacturing Technologies and is the direct responsibility of Subcommittee F42.07 on Applications.

Current edition approved Oct. 15, 2023. Published February 2024. DOI: 10.1520/F3604-23.

2. Referenced Documents

2.1 ASTM Standards:²

F2971 Practice for Reporting Data for Test Specimens Prepared by Additive Manufacturing

F3049 Guide for Characterizing Properties of Metal Powders Used for Additive Manufacturing Processes

F3456 Guide for Powder Reuse Schema in Powder Bed Fusion Processes for Medical Applications for Additive Manufacturing Feedstock Materials

2.2 ISO Standards:³

ISO 9712 Non-destructive Testing—Qualification and Certification of NDT Personnel

ISO 13485 Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes

ISO 14971 Medical Devices—Application of Risk Management to Medical Devices

2.3 ISO/ASTM Standards:²

52900 Additive Manufacturing—General Principles—Terminology

52902 Additive manufacturing—Test artifacts—Geometric capability assessment of additive manufacturing systems

52907 Additive manufacturing—Feedstock materials—Methods to characterize metallic powders

52910 Standard Guidelines for Design for AM

52911-1 Additive manufacturing—Design—Part 1: Laser-based powder bed fusion of metals

² For referenced ASTM or 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 Organization for Standardization (ISO), ISO Central Secretariat, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, <http://www.iso.org>.

- 52911-2 Additive manufacturing—Design—Part 2: Laser-based powder bed fusion of polymers
- 52913-1 Additive manufacturing—Feedstock materials—Part 1 Parameters for characterization of powder flow properties
- 52915 Specification for additive manufacturing file format (AMF) Version 1.2
- 52920 Standard specification for quality assurance processes at AM centers
- 52930 Additive manufacturing—Qualification principles—Installation, operation, and performance (IQ/OQ/PQ) of PBF-LB equipment
- 52931 Standard guideline for use of metallic materials
- 52933 Standard specification on indoor air quality management
- 52950 Additive manufacturing—General principles—Overview of data processing
- 2.4 *ISO/DIS Standard:*
ISO/DIS 14644-9 Cleanrooms and associated controlled environments—Part 9: classification of surface particles cleanliness³
- 2.5 *Federal Standards:*⁴
21 CFR Part 11 Electronic Records, Electronic Signatures
21 CFR Part 820 Quality System Regulation

3. Terminology

3.1 *Definitions*—Standard additive manufacturing (AM) terminology is defined in ISO/ASTM 52900. For the purposes of this guide, the definitions in 3.2 apply. The International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) maintain terminological databases for use in standardization at the following addresses: ISO online browsing platform available at <https://www.iso.org/obp> and IEC Electropedia available at <http://www.electropedia.org/>.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *build interruption, n*—unplanned delay during the AM cycle that halts the general progression of the process.

3.2.2 *build pause, n*—longer than typical dwell time spacing between layers and may be planned as part of the print job or the automatic machine control function, for example, to allow powder transfer.

3.2.3 *calibration, n*—configuration and verification of all critical sensors, accessories, and instruments against control standards defined by original equipment manufacturer (OEM) guidance.

3.2.4 *critical to quality, CTQ, n*—attribute or feature that is critical to the overall quality of the device or process.

3.2.5 *factory acceptance test, n*—system acceptance test performed at OEM facility.

3.2.6 *installation qualification, n*—establishing by objective evidence that all key aspects of the installation process associated with both the printing equipment and ancillary

equipment adhere to the manufacturer's approved specification and the recommendations of the supplier of the equipment are suitably considered.

3.2.6.1 *Discussion*—Consideration should be given to ISO/ASTM 52930.

3.2.7 *machine fleet variation, n*—variations within multiple machines of the same model.

3.2.8 *process operational qualification, n*—establishing by objective evidence that process control limits have been sufficiently challenged and result in outputs that meet all predetermined requirements.

3.2.9 *process performance qualification, n*—establishing by objective evidence that the process, under anticipated conditions, consistently produces a product that meets all predetermined requirements.

3.2.10 *process re-validation, n*—establishing by objective evidence that the process under anticipated conditions consistently produces a product that meets all predetermined requirements once specific changes that could sufficiently change a product's performance have occurred.

3.2.11 *process validation, n*—establishing by objective evidence that a process can produce a result or product meeting its predetermined requirements, for example, part cleaning.

3.2.11.1 *Discussion*—Consideration should be given to the difference between machine types, fleet of one or more machines versus a single machine for process validation.

3.2.12 *process validation protocol, n*—document stating how validation will be conducted, including test parameters, product characteristics, manufacturing equipment, feedstock, and decision points on what constitutes acceptable test results.

3.2.13 *product verification, n*—confirmation by examination and provision of objective evidence that the specified product requirements have been fulfilled, for example, part dimensions.

3.2.13.1 *Discussion*—Verification should include product performance testing for worse-case process and material configuration(s).

3.2.14 *production process, n*—encompasses the end-to-end AM process and associated post processing to manufacture a finished medical device.

3.2.15 *raw material, n*—as-received powder material and blend used to produce the final mechanical and physical properties of the device.

3.2.16 *risk, n*—combination of the probability of occurrence of harm and the severity of that harm.

3.2.16.1 *Discussion*—This definition is derived from ISO 13485:2016 and differs from the definition of “risk” in ISO 9000:2015.

3.2.17 *risk analysis, n*—a listing of all the hazards associated with process and the level of severity, occurrence and detection for each risk and associated failure mode.

3.2.18 *risk assessment, n*—overall process of risk analysis and risk evaluation.

3.2.19 *risk management, n*—systematic application of management policies, procedures and practices aimed at analyzing, evaluating, controlling, and monitoring risk.

⁴ Available from U.S. Government Publishing Office (GPO), 732 N. Capitol St., NW, Washington, DC 20401, <http://www.gpo.gov>.

3.2.19.1 *Discussion*—This definition is derived from ISO 13485:2016.

3.2.20 *site acceptance test, n*—series of documented procedures and tests agreed between the equipment supplier and equipment purchaser with results meeting predetermined requirements.

3.2.20.1 *Discussion*—The site acceptance test is performed after installation of the machine at the final production location. This should include facility and environmental conditions assessment, material characterization, environment health and safety assessment, equipment computer systems qualification, training of production personnel, and operations.

3.2.21 *software workflow, n*—manufacturing software used during the manufacturing process.

3.2.22 *special process, n*—a process whereby the resulting output cannot be verified by subsequent monitoring or measurement.

3.3 Abbreviations:

3.3.1 *LIMS, n*—Laboratory Information Management System

3.3.2 *MES, n*—Manufacturing Execution System

4. Significance and Use

4.1 Overview:

4.1.1 Assurance of product quality is derived from careful attention to many factors but is not limited to raw material acceptance, software workflow definition, product and process design and control, printing and post processing, equipment and systems installation, maintenance, and in-process and end-product testing.

4.1.2 By managing these factors, a manufacturer can establish confidence that all finished manufactured units from successive lots will be acceptable and meet lot release criteria.

4.1.3 The basic principles of quality assurance (QA) have as their goal the production of articles that are fit for their intended use. These principles may be stated as:

4.1.3.1 Quality, safety, and effectiveness shall be designed and built into the product as well as the production process.

4.1.3.2 AM product characteristics all cannot currently be verified after the process without destructive testing and therefore requires validation. Suitable consideration should be designed into the product and controls should be applied to the process during process validation.

4.1.3.3 Critical steps of the production process impacting quality shall be controlled to maximize the probability that the finished product meets all quality and design specifications.

4.1.4 Process validation is a key element in ensuring that these QA goals are met. Routine end-product testing alone is often not sufficient to assure product quality. Some end-product tests have limited sensitivity. In some cases, destructive testing would be required to show that the manufacturing process is adequate, and in other situations, end-product testing does not reveal all variations that may occur in the product that may have an impact on device performance. However, successfully validating a process may reduce the dependence on intensive in-process and finished product testing. Note that, in most

cases, end-product testing plays a major role in supporting QA goals, that is, validation and end-product testing are not mutually exclusive.

4.1.5 Key process variables should be monitored and documented using statistical process control where applicable. Analysis of the data collected from monitoring should establish the potential variability of process parameters for individual production runs to ensure that a process is within acceptable control limits and the equipment can consistently produce the product within specification.

4.2 Preliminary Considerations:

4.2.1 A manufacturer should evaluate all factors that affect product quality through appropriate documented process characterization.

4.2.2 Risk management and an analysis file shall be created in line with ISO 14971. These factors may vary considerably among different products, manufacturing technologies, and facilities. No single approach to process validation will be appropriate and complete in all cases; however, the following quality steps should be undertaken.

4.2.3 All pertinent aspects of the production processes that have an impact on device design (product's end use) should be considered during process validation. These aspects include, but are not necessarily limited to, performance, reliability, and stability. Performance limits and variation should be established for each characteristic acceptance criteria and expressed in readily measurable terms. Once a product specification is defined it is important that any changes to it be made in accordance with documented change control procedures and the device history file.

5. Elements of Process Validation

5.1 General:

5.1.1 Process validation shall be considered when a new product is introduced or there is a critical change in the production process that may affect any or all the product's dimensional, material characteristics, and device functionality.

5.1.2 The following are considered as pre-requisites to process validation:

5.1.2.1 Process mapping

5.1.2.2 Risk assessment

5.1.2.3 Control Plans

5.1.3 The following are considered as key elements of process validation:

5.1.3.1 Process master validation planning (MVP)

5.1.3.2 Process characterization

5.1.3.3 Software workflow validation

5.1.3.4 Equipment Validation

(1) Installation qualification (IQ)

5.1.3.5 Process Validation

(1) Operational qualification (OQ)

(2) Performance qualification (PQ)

5.1.4 It is essential that the validation documentation is properly maintained and fully traceable in accordance with ISO 13485 and 21 CFR Part 11. For ongoing production, it is important to adequately record or monitor or both facility and process variables defined during the risk assessment and validation as well as any critical changes to the process.

example of the full AM workflow (see Fig. 1) and impact on final device quality should be considered when assessing individual process steps.

5.2 Process Validation Pre-Requisites:

5.2.1 *Overview*—The personnel involved in the steps below should be a good cross functional team of personnel involved in the AM process to ensure all perspectives are included.

5.2.2 Process Mapping:

5.2.2.1 Full end to end AM process mapping is required to define process steps to be covered for risk assessment.

5.2.2.2 The output from the process mapping will define which process steps can be verified and which process steps need to be validated.

(1) See Terminology section for verification / validation.

5.2.2.3 Process steps that cannot be fully verified will need to be validated. To help determine when a process “cannot be fully verified,” the following guidelines may be considered:

(1) Routine end-product tests have insufficient sensitivity to verify the validated performance of the finished devices.

(2) Clinical or destructive testing would be required to show that the manufacturing process has produced the desired result or product.

(3) Routine end-product tests do not reveal all variations in device performance that may occur in the finished devices.

(4) Process capability is unknown and device features challenge the process repeatability.

5.2.2.4 Software workflow is critical to the AM device file preparation (for example, lattice generation, supports, slice hatch), production, MES, data collection, and final performance. Multiple file conversions and translation steps from digital to printable forms can impact product quality, data integrity, and traceability. Manual intervention is a major part

of the end-to-end software workflow, and therefore, it is critical that system controls are established at each stage of the product life cycle and the workflow impact on the final product quality is established.

5.2.3 Risk Management and Analysis:

5.2.3.1 A risk management and analysis file shall be created in accordance with ISO 14971. Process and design failure mode and effects analysis (FMEA), or other risk analysis tools, should link characteristics of the production process that influence medical device performance (dimensional/material characteristics and functionality).

5.2.3.2 Risk assessments are living documents and should be updated after process validation. Risk assessments should also be reviewed on a periodic basis.

5.2.3.3 The risk assessment may be based on hypothesized risk or historical data, or both. Historical data should be used wherever possible.

5.2.4 Control Plans:

5.2.4.1 Control plans are an output from risk assessment. The risk assessment identifies high risk process steps related to high severity, high occurrence, low detection, or the resulting severity X occurrence X detection score. The control plan is meant to control the process and ensure the process produces quality parts that meet the customer requirements.

5.2.4.2 When assessing software workflow controls, it is important to consider the following:

(1) Relevant risks and controls for each individual step and their impact on final device quality.

(2) Digital error stack throughout the end-to-end workflow.

(3) Verification steps required when validation is not possible.

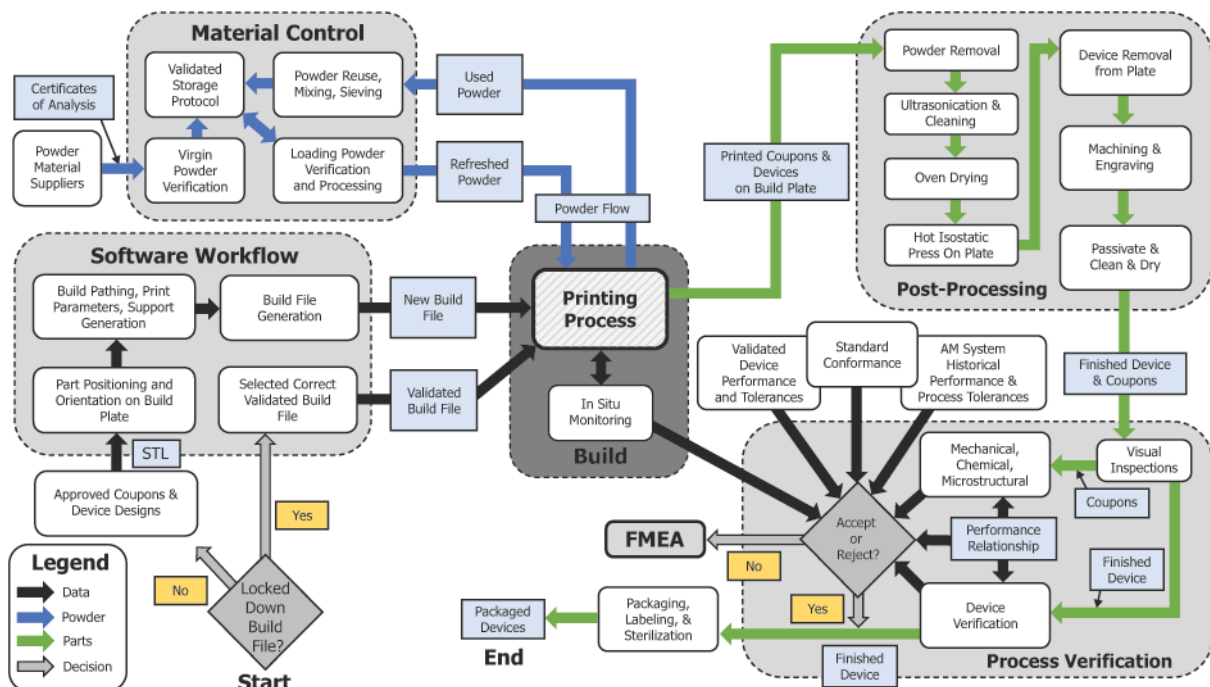


FIG. 1 Example of an Additive Manufacturing Workflow

(4) Routine end-product tests do not reveal all variations in device performance that may occur in the finished devices and, therefore, may require a worse case combination of digital stack-up error to demonstrate true design window and end-product performance.

(5) Highlight and establish controls on manual operations when human error can impact device performance.

5.2.4.3 Control plans should also be periodically reviewed and updated. This may include but not limited to the following:

(1) Implementation of corrective actions against the customer complaints, when applicable.

(2) When there is any change that occurs affecting products, production process, measurements, supply chain, and failure mode effect analysis (FMEA).

(3) At a defined frequency set as per customer requirement or based on risk analysis.

5.3 Validation Planning:

5.3.1 Validation planning should result in a documented master validation plan (MVP). This should include the following elements:

5.3.1.1 A process flowchart containing all validated and verified steps.

5.3.1.2 Equipment Validation Strategy: A list of all equipment that needs validation. Equipment validation is done per section 5.4.

5.3.1.3 Software Workflow Validation: Required when computers or automated data-processing systems are used as part of the production or quality system in line with regulatory guidance (for example, 21 CFR 820.70(i)).

5.3.1.4 Process Validation Strategy:

(1) This includes identification of processes that can be verified and processes that will need to be validated.

(a) Processes that can be verified do not need special validation as the output of the process step can be verified.

(b) Process validation is required when the results of a process cannot be fully verified by subsequent inspection and testing [for example, 21 CFR 820.75(a)]. In most instances, this includes the test methods used to assure a product complies with key specifications (that is, dimensional and material characteristics and functionality).

(2) Special processes should be identified, and appropriate level of consideration given. This includes software workflow validation.

5.3.1.5 Adequate controls within the quality management system (QMS) should be in place for all sub-tier suppliers.

5.3.1.6 Nonconformance procedures should be established for the production process.

5.3.1.7 All validation protocols, product criteria, and process acceptance criteria should be agreed upon and finalized during the planning stage.

5.4 Equipment Validation:

5.4.1 General:

5.4.1.1 A list of all equipment (manufacturing and test equipment) shall be made and be part of the MVP. This list will form the basis on which equipment installation qualifications will be needed.

5.4.1.2 Any equipment that does not need validation shall be documented and justified as to why validation is not needed, for example hand tools used in manufacturing or test, callipers, etc.

5.4.2 Installation Qualification (IQ):

5.4.2.1 Pre-Requisites:

(1) The following items must be completed before execution of an IQ protocol:

(a) The equipment is located in its final location.

(b) The IQ protocol and supporting documentation must be approved before starting execution of the IQ protocol.

(c) All personnel executing the IQ protocol shall be trained to the validation plan and IQ protocol prior to execution.

5.4.2.2 General:

(1) Installation qualification studies establish confidence that the process equipment and ancillary systems are capable of consistently operating within established limits and tolerances. After process equipment is designed or selected, it should be evaluated and tested to verify that it can operate satisfactorily within the operating limits required by the process in a factory acceptance test. This phase of validation includes examination of equipment design; determination of calibration, environmental conditions, maintenance, and adjustment requirements; and identifying critical equipment features and configuration management of software workflow that could affect the process and product. Information obtained from these studies should be used to establish written procedures covering equipment calibration, maintenance, monitoring, and control.

(2) In assessing the suitability of a given piece of equipment, it is usually insufficient to rely solely upon the representations of the equipment supplier or experience in producing similar product. Sound theoretical and practical engineering principles and considerations are the first step in the assessment with respect to the product functionality, material and dimensional characteristics, and functionality. It is important that equipment qualification represent production conditions, including those that are "worst-case" situations. These conditions shall be defined by the user of the equipment.

(3) Tests and challenges should be repeated with statistical significance to assure reliable and meaningful results. All acceptance criteria shall be met during the test or challenge. If any test or challenge shows that the equipment does not perform within its specifications, an evaluation should be performed to identify the root cause of the failure. Corrections should be made, and additional test runs performed as needed to verify that the equipment performs within specifications in the production setting. The observed variability of the equipment between and within runs can be used as a basis for determining the overall process window for the subsequent operational and performance qualification studies of the process.

5.4.2.3 Equipment Design Validation and Installation:

(1) *Systems Acceptance Testing*—System acceptance testing should be completed and documented during the installation in the production setting. Systems acceptance testing may include: