Bioprocessing Equipment

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ASME Standards and Certification
CHAPTER 1
INTRODUCTION, SCOPE,
AND GENERAL REQUIREMENTS

PART GR
GENERAL REQUIREMENTS

GR-1 INTRODUCTION

The ASME Bioprocessing Equipment (BPE) Standard was developed to aid in the design and construction of new fluid processing equipment used in the manufacture of biopharmaceuticals, where a defined level of purity and bioburden control is required.

The Standard typically applies to:
(a) components that are in contact with the product, raw materials, or product intermediates during manufacturing, development, or scale-up
(b) systems that are a critical part of product manufacture (e.g., water for injection (WFI), clean steam, filtration, and intermediate product storage).

The General Requirements Part states the scope of the ASME BPE Standard and provides references and definitions that apply throughout the Standard.

When operating under pressure conditions, systems shall be constructed in accordance with the ASME Boiler and Pressure Vessel Code (BPVC), Section VIII, and/or ASME B31.3 Process Piping Code or applicable local, national, or international codes or standards. The owner/user may stipulate additional or alternative specifications and requirements.

This Standard shall govern the design and construction of piping systems for hygienic service. For process piping systems designed and constructed in accordance with ASME B31.3, it is the owner’s responsibility to select a fluid service category for each fluid service. Should any fluid service meet the definition of high-purity fluid service (ASME B31.3, Chapter X) it is recommended that such fluid service be selected and the requirements of this Standard and ASME B31.3, Chapter X be met.

When an application is covered by laws or regulations issued by an enforcement authority (e.g., municipal, provincial, state, or federal), the final construction requirements shall conform to those laws.

Items or requirements that are not specifically addressed in this Standard are not prohibited. Engineering judgments must be consistent with the fundamental principles of this Standard. Such judgments shall not be used to override mandatory regulations or specific prohibitions of this Standard.

New editions of the ASME BPE Standard may be used beginning with the date of issuance and become effective 6 months after the date of issuance.
GR-2 SCOPE OF THE ASME BPE STANDARD

The ASME BPE Standard provides requirements for systems and components that are subject to cleaning and sanitization and/or sterilization including systems that are cleaned in place (CIP’d) and/or steamed in place (SIP’d) and/or other suitable processes used in the manufacturing of biopharmaceuticals. This Standard also provides requirements for single-use systems and components used in the above listed applications. This Standard may be used, in whole or in part, for other applications where bioburden risk is a concern.

This Standard applies to:
(a) new system (and component) design
(b) definition of system boundaries
(c) specific metallic, polymeric, and elastomeric (e.g., seals and gaskets) materials of construction
(d) component dimensions and tolerances
(e) surface finishes
(f) materials joining
(g) examinations, inspections, and testing
(h) certification

This Standard is intended to apply to new fabrication and construction. If the provisions of this Standard are optionally applied by an owner/user to existing, in-service equipment, other considerations may be necessary. For installations between new construction and an existing, in-service system, such as a retrofit, modification, or repair, the boundaries and requirements must be agreed to among the owner/user, engineer, installation contractor, and inspection contractor.
The owner/user determines which requirements of the Standard are applicable to individual components, equipment, or systems based on intended service. However, for a component, equipment, or system to be BPE-conforming, adherence to all applicable requirements of this Standard is mandatory.

**GR-3 MANUFACTURER’S QUALITY ASSURANCE PROGRAM**

The manufacturer shall implement a quality assurance program describing the systems, methods, and procedures used to control materials, drawings, specifications, fabrication, assembly techniques, and examination/inspection used in the manufacturing of bioprocessing equipment.

Nonmandatory Appendix Z, Quality Management System, provides guidance on quality assurance programs. This is only required for organizations that are ASME BPE Certificate Holders or applicants (see Part CR). However, it may be used by any organization that implements this Standard.

**GR-4 EXAMINATION, INSPECTION, AND TESTING**

The examination, inspection, and testing requirements are specified in each Part of this Standard. If an inspection or examination plan is required, it shall be developed and agreed to by the owner/user, contractor, inspection contractor, and/or engineer ensuring that the systems and components meet this Standard.

As it relates to pressure vessels, vessels not rated for pressure service, process piping and tubing, and process contact equipment, this Standard uses the terms examination, inspection, and testing other forms of these terms in a manner consistent with the uses in ASME BPVC, Section VIII, and ASME B31.3. References for examination, inspection, and testing for this Standard are listed in Nonmandatory Appendix CC. These requirements are in addition to the requirements of ASME BPVC, Section VIII, and ASME B31.3. This Standard also uses the common language meaning of these terms. Be aware of the differences between the usage as defined in GR-8 versus common usage.

**GR-4.1 Inspector/Examiner**

Inspector and examiner in this Standard shall be defined for the following:

(a) **Pressure Vessels.** Authorized Inspector, as defined in ASME BPVC, Section VIII.

(b) **Piping, Tubing, and Non-Code Vessels.** Owner’s Inspector, as defined in ASME B31.3, paras. 340.4(a) and 340.4(b). Quality Inspector’s Delegate, as defined in GR-8, meets the additional requirements listed in GR-4.2.

(c) **Piping and Tubing.** Examiner, defined as a person who performs quality control examinations for a manufacturer as an employee of the manufacturer as defined in ASME B31.3, para. 341.1.

When local regulations require that pressure equipment be designed and constructed in accordance with standards other than ASME codes/standards, the inspector in this Standard is defined as one who is acceptable to the relevant regulatory authority.

**GR-4.2 Quality Inspector’s Delegate**

Quality Inspector’s Delegate qualifications shall be in accordance with the requirements listed herein. The employer of the Quality Inspector’s Delegate shall have documented training and qualification programs to ensure the qualifications and capabilities of personnel are met.

The capabilities requirements are listed in Table GR-4.2-1. It is required that a capability listed for a lower level of qualification is also required for subsequent higher levels of qualification.

**GR-4.2.1 Levels of Qualification.** There are four levels of qualification for Quality Inspector’s Delegate. Examination personnel qualifications are not covered in this section but shall be in accordance with ASME B31.3, para. 342.

(a) **Trainee.** An individual who is not yet certified to any level shall be considered a trainee. Trainees shall work under the direction of a certified Quality Inspector’s Delegate and shall not independently conduct any tests or write a report of test results.

(b) **Quality Inspector’s Delegate 1 (QID-1).** This individual shall be qualified to properly perform specific calibrations, specific inspections, and specific evaluations for acceptance or rejection according to written instructions. A QID-1 may perform tests and inspections according to the capabilities’ requirements under the supervision of, at a minimum, a QID-2.

(c) **Quality Inspector’s Delegate 2 (QID-2).** This individual shall be qualified to set up and calibrate equipment and to interpret and evaluate results with respect to applicable codes, standards, and specifications. The QID-2 shall be thoroughly familiar with the scope and limitations of the inspection they are performing and shall exercise assigned responsibility for on-the-job training and guidance of trainees and QID-1 personnel. A QID-2 may perform tests and inspections according to the capabilities’ requirements.

(d) **Quality Inspector’s Delegate 3 (QID-3).** This individual shall be capable of establishing techniques and procedures; interpreting codes, standards, specifications, and procedures; and designating the particular inspection methods, techniques, and procedures to be used. The QID-3 shall have sufficient practical background in applicable materials, fabrication, and product technology to
(b) 3 yr of documented relevant experience in inspection, examination, or testing activities of high-purity/hygienic systems

(2) receive a minimum of 40 additional hr of relevant documented training (minimum total = 80 hr), including as a minimum the requirements shown in Table GR-4.2-1

(3) pass a written test and practical performance examination, including as a minimum the requirements shown in Table GR-4.2-1 for this level

22) GR-4.2.3 Certification. The employer is responsible for training, testing, and certification of employees. The employer shall establish a written practice in accordance with the guidelines of ASNT SNT-TC-1A including

(a) the requirements listed in Table GR-4.2-1
(b) training programs
(c) certification testing requirements
(d) eye examinations as follows:
   (1) Near Vision Acuity. The individual shall have natural or corrected near distance acuity in at least one eye such that the individual is capable of reading a minimum of a Jaeger Number 2 or equivalent type and size letter at a distance designated on the chart but no less than 12 in. (305 mm). This test shall be administered initially and at least annually thereafter.
   (2) Color Contrast. The individual shall demonstrate the capability of distinguishing and differentiating contrast among colors. This test shall be administered initially and, thereafter, at intervals not exceeding 3 yr.

   These examinations shall be administered by an ophthalmologist, optometrist, medical doctor, registered nurse or nurse practitioner, certified physician assistant, or other ophthalmic medical personnel, and the documentation shall include the state or province (or applicable jurisdictional) license number.

(e) certification documentation
   The owner/user is responsible for verifying the requirements of this section are met.

GR-4.2.4 Recertification. A QID-1, QID-2, or QID-3 whose employment has been terminated may be recertified to their former level of qualification by a new or former employer based on examination, provided all of the following requirements are met:

(a) The employee has proof of prior certification.
(b) The employee was working in the capacity to which certified within 6 months of termination.
(c) The employee is being recertified within 6 months of termination.

If the employee does not meet the listed requirements, additional training as deemed appropriate by the owner’s Inspector shall be required.

GR-4.3 Responsibilities

The responsibilities of inspection personnel are defined in GR-4.3.1 and GR-4.3.2.

GR-4.3.1 Pressure Vessels. The responsibilities of the owner’s Inspector shall be the same as the inspector in ASME Piping and Tubing.

GR-4.3.2 Piping, Tubing, and Non-Code Vessels. The responsibilities of the owner/user’s Inspector shall be in accordance with ASME B31.3, para. 340.2.

GR-4.4 Access for Inspectors

Manufacturers of bioprocessing equipment and components shall allow free access to owner/user and authorized inspection personnel at all times while work on the equipment or components is being performed. The notification of an impending inspection should be mutually agreed to by the manufacturer and the inspector. Access may be limited to the area of the manufacturer’s facility where assembly, fabrication, welding, and testing of the specific equipment or components are being performed. Inspectors shall have the right to audit any examination, to inspect components using any examination method specified in the Design Specification (including Purchase Order), and to review all certifications and records necessary to satisfy the requirements of GR-5. The manufacturer shall provide the Inspector with work progress updates.

GR-5 DOCUMENTATION

GR-5.1 General

Documentation requirements shall be agreed to at the beginning of a design project and shall be made available upon request or submitted at the agreed-upon time to support the requirements of this Standard, as agreed to by the owner/user and manufacturer/contractor.

GR-5.2 Document Requirements

Material Test Reports (MTRs) for all metallic process components shall be verified to be in conformance to the applicable specification. Certificates of Conformance (C of Cs) for all polymeric and other nonmetallic process components shall be provided. In addition, the following documentation shall be provided to the owner/user or their designee.

GR-5.2.1 General List of Documents

GR-5.2.1.1 Metallic Materials

(1) Materials Documentation
   (a) Material Test Reports
   (b) Certificates of Conformance for Multiuse Systems
Material Examination Logs

Identification of the filler metal or consumable insert used.

Welding, Inspection, and Examination Qualification Documentation (not required for standard fittings, valves, and components unless specifically required by the owner/user). The following documentation shall be provided to the owner/user or their designee:

(1) Procedure Qualification Records (PQRs)
(2) Welding Procedure Specifications/Parameters (WPS/P)
(3) Welder Performance Qualifications (WPQs)
(4) Welding Operator Performance Qualifications (WOPQs)
(5) Examiner qualifications
(6) Documentation of approval of (1) by the owner/user’s representative prior to welding
(7) Inspector qualifications
(8) Documentation of the approval of (7) by the owner/user prior to welding
(c) Weld Documentation (not required for standard fittings, valves, and components unless specifically required by the owner/user)
(1) weld maps
(2) weld logs
(3) weld examination and inspection logs
(4) coupon logs
(d) Testing and Examination Documentation (as applicable)
(1) passivation reports
(2) spray device coverage testing
(3) pressure testing
(4) final slope check documentation
(5) calibration verification documentation
(6) purge gas certifications
(7) signature logs
(8) number of welds — both manual and automatic
(9) number of welds inspected expressed as a percentage (%)
(10) heat numbers of components that must be identified, documented, and fully traceable to the installed system
(11) surface finish C of Cs
(12) NDE (nondestructive examination) reports
(c) Material Test Reports/Certificates of Conformance

Material Test Reports/Certificates of Conformance

- Technical Support Information to support the design, operation, and maintenance of equipment may include, but is not limited to, the following:
  (a) material handling procedures
  (b) mechanical and electropolishing procedures
  (c) shop passivation procedures

GR-5.3 Material Test Reports/Certificates of Conformance

Metallic Materials. The combination of documents, including C of Cs and MTRs, for all valves and fittings having process contact surfaces shall include the following information, as a minimum:
(a) ASME BPE Standard, including year
(b) material type
(c) heat number or code traceable to the original heat
(d) chemical composition
(e) AWS classification of filler metal, if used
(f) alloy designation and material specification of insert, if used
(g) postweld heat treatment documentation, if applicable
(h) mechanical properties are not required, but if included must be accurate to the raw material specification

MTRs for other components made to a material specification shall contain the minimum information specified by the material specification incorporated by reference. MTRs for tubing shall also state the year edition of the ASME BPE Standard.

Polymeric and Other Nonmetallic Material Components. The manufacturer of polymeric and other nonmetallic components shall issue a Certificate of Conformance that the components meet requirements as shown in Table PM-2.2.1-1. Additional agreements may be required.

GR-5.3.2.1 Seal Documentation. Seal manufacturers shall provide, upon owner/user request, documentation (test report) of the USP <88> Biological Reactivity Test In Vivo, Class VI and the USP <87> Biological Reactivity Test In Vitro testing on final manufactured seals. A Certificate of Conformance shall be issued by the seal manufacturer to certify conformance to this Standard when required by the owner/user. The Certificate of Conformance shall contain the information listed in Table PM-2.2.1-1. Additional agreements may be required.

GR-5.3.2.2 Sealed Unions. The seal manufacturer shall provide, upon request of the owner/user, a certificate of design conformance that the sealed union meets the intrusion requirements of MC-4.2.

GR-5.3.3 Electropolishing. The electropolishing vendor, if requested by the owner/user, shall provide a Certificate of Conformance with each type of component(s) that shall include, but is not limited to, the following:
...
GR-5.3.4 Passivation. The passivation service provider shall provide documentation for each type of component, type of process equipment (e.g., vessel, filter housing) or process system including, but not limited to, the following information:

(a) service provider company name
(b) description of component(s), process equipment or process system
(c) identification of component(s), process equipment or process system
(d) identification of the qualified passivation procedure used
(e) final surface finish report ($R_a$ if required by the owner/user)

The passivation service provider shall provide a Certificate of Conformance for each system or set (type) of component(s) that shall include, but not be limited to, the following:

(a) owner/user’s name
(b) description of system or component(s)
(c) service provider’s company name
(d) qualified passivation method used
(e) documentation of passivation process, as follows:
   (1) written qualified procedure
   (2) documentation of process control of essential variables
   (3) instrument calibration records
   (4) certificates of analysis for all chemicals used
   (5) process testing and verification
(f) postpassivation verification method(s) used
(g) for material manufacturers/suppliers of components whose surfaces have been electropolished and/or passivated, a Certificate of Conformance for Passivation and/or Electropolishing stating that standard industry practices, such as ASTM A967 or ASTM B912, as applicable, have been used. If required by the owner/user, the manufacturer or supplier may be required to demonstrate the effectiveness of their procedure by a method mutually agreed upon.

GR-5.5 Records Retention

GR-5.5.1 Vessel Documentation. For all Bioprocessing ASME Code-stamped vessels, National Board registration is recommended to maintain vessel data on file. Manufacturing documentation shall be maintained throughout the design and manufacture for each component, assembly, part, or unit.

All documentation shall be retained by the owner/user. As agreed to by the owner/user and manufacturer, documentation from the manufacturer will be retained for the agreed-upon duration of time but not less than 3 yr after manufacture.

GR-5.5.2 Welding Documentation

(a) Piping and Tubing. Records and retention of records associated with piping and tubing shall be in accordance with ASME B31.3.
(b) Pressure Vessels and Tanks. Records and retention of records for code vessels shall be in accordance with ASME BPVC, Section VIII.

GR-5.5 Document Requirements for Polymeric and other Nonmetallic Materials. The manufacturer of polymeric and other nonmetallic components shall issue a Certificate of Conformance that the components meet requirements as shown in Table PM-2.2.1-1. In addition, the following documentation shall be provided to the owner/user or their designee.

GR-5.5.1 Seal Documentation. Seal manufacturers shall provide, upon owner/user request, documentation (test report) of the USP <88> Biological Reactivity Test In Vivo, Class VI and the USP <87> Biological Reactivity Test In Vitro testing on final manufactured seals. A Certificate of Conformance shall be issued by the seal manufacturer to certify conformance to this standard when required by the owner/user. The Certificate of Conformance shall contain the information listed in Table PM-2.2.1-1. Additional agreements may be required.
GR-5.5.2 Sealed Unions. The seal manufacturer shall provide, upon request of the owner/user, a certificate of design conformance that the sealed union meets the intrusion requirements of MC-4.2.

GR-6 PRODUCT IDENTIFICATION AND PACKAGING
Manufacturers shall use a combination of marking, labeling, and primary packaging for identification and protection of components, equipment and assemblies.

GR-6.1 Marking and Labeling
Marking and labeling shall provide traceability for process contact components, equipment, and assemblies. Specific marking and labeling requirements are addressed in the applicable Parts.

GR-6.2 Packaging
Components or single-use assemblies shall be packaged by the manufacturer to protect against damage and contamination that may result from routine shipping and subsequent handling and storage in order to maintain the "as manufactured" condition. Additional packaging that may be necessary for shipping and subsequent handling and storage is not addressed in this Standard except when necessary to maintain sterility or integrity. Specific packaging requirements are addressed in the applicable Parts.

GR-7 PROCESS COMPATIBILITY

GR-7.1 Materials.
Process contact surfaces of components shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the product given the following requirements:
(a) Materials shall be capable of withstanding process, cleaning, and sanitization conditions (e.g., temperature, pressure) and shall be chemically compatible with those conditions.
(b) For a metallic material to be acceptable for hygienic service, it shall meet the requirements in Part MM. For a polymeric or other non-metallic material to be acceptable for hygienic service it shall meet the requirements in Part PM.

GR-7.2 Animal Derived Ingredients
Process contact surfaces of components, equipment, and systems shall be constructed from and processed with materials that are free from animal-derived ingredients/products (ADI/ADP), or shall be manufactured with materials that meet the conditions of the Committee for Medicinal Products for Human Use (CHMP, formerly known as CPMP) Note for Guidance (EMEA/410/01 rev 3).

GR-8 CONTAMINATION CONTROL

GR-8.1 Closed Systems.
Components, equipment, and systems of closed processes shall be designed to mitigate the risk of contamination within the process zone, including the risk of ingress of contaminants during bioprocessing. Functionally closing a system is a two-step process:
(a) Removal of latent viable and nonviable contaminants within the process zone prior to process or product contact (e.g., CIP, SIP, ionizing irradiation)
(b) Prevention of ingress of viable and non-viable particulates during product contact

GR-8.2 Open systems.
Components, equipment, and systems of open processes shall be designed to mitigate the risk of bioburden proliferation within the process zone.

GR-6 U.S. CUSTOMARY AND SI UNITS

This Standard uses standard units listed in Mandatory Appendix II. Nonmandatory Appendix U has been provided as a guide and SI unit conversion.

GR-7 REFERENCES

Material specifications for metallic materials are listed by product form in Part MM. For this Standard, the most recent approved version of the following referenced standards shall apply:

3-A, Sanitary Standards
Publisher: 3-A Sanitary Standards, Inc., 6888 Elm Street, Suite 2D, McLean, VA 22101 (www.3-a.org)

ANSI/FCI Standard 70-2, Control Valve Seat Leakage
ASME BPE-2022

ASTM D624, Standard Test Method for Tear Strength of Conventional Vulcanized Rubber and Thermoplastic Elastomers
ASTM D1599, Standard Test Method for Resistance to Short-Time Hydraulic Pressure of Plastic Pipe, Tubing, and Fittings
ASTM D2240, Standard Test Method for Rubber Property — Durometer Hardness
ASTM D2657, Standard Practice for Heat Fusion Joining of Polyolefin Pipe and Fittings
ASTM E112, Test Methods for Determining Average Grain Size
ASTM E220, Standard Test Method for Calibration of Thermocouples by Comparison Techniques
ASTM E499, Standard Practice for Leaks Using the Mass Spectrometer Leak Detector in the Detector Probe Mode
ASTM E515, Standard Practice for Leaks Using Bubble Emission Techniques
ASTM E644, Standard Test Methods for Testing Industrial Resistance Thermometers
ASTM E1003, Standard Practice for Hydrostatic Leak Testing

ASME A923, Standard Test Methods for Detecting Detrimental Intermetallic Phase in Duplex Austenitic/Ferritic Stainless Steels

ASME A924, Standard Test Methods for Detecting Susceptibility to Intergranular Attack in Austenitic Stainless Steels

ASME A3.0M/A3.0, Standard Welding Terms and Definitions
ASME B2.4, Specification for Welding Procedure and Performance Qualification for Thermoplastics
ASME D18.2, Guide to Weld Discoloration Levels on Inside of Austenitic Stainless Steel Tube
ASME QC1, Standard for AWS Certification of Welding Inspectors

ASME B31.3, Process Piping
ASME B46.1, Surface Texture (Surface Roughness, Waviness, and Lay)
ASME Boiler and Pressure Vessel Code, Section VIII, Rules for Construction of Pressure Vessels
ASME Boiler and Pressure Vessel Code, Section IX, Welding, Brazing, and Fusing Qualifications

ASME CA-1, Conformity Assessment Requirements
ASME MFC-22, Measurement of Liquid by Turbine Flowmeters

ASME PTC 19.3 TW, Thermowells
ASME PVHO-1, Safety Standard for Pressure Vessels for Human Occupancy

ASTM A380, Practice for Cleaning, Descaling, and Passivation of Stainless Steel Parts, Equipment, and Systems
ASTM A967, Standard Specification for Chemical Passivation Treatments for Stainless Steel Parts

ASTM A1015, Standard Guide for Videoborescoping of Tubular Products for Sanitary Applications

ASTM B912, Standard Specification for Passivation of Stainless Steel Tubing

ASTM D2657, Standard Practice for Heat Fusion Joining of Polyolefin Pipe and Fittings

ASTM A1059, Sampling Procedures and Tables for Inspection of Metal Fabrication Equipment

ASTM A262, Standard Practices for Detecting Susceptibility to Intergranular Attack in Austenitic Stainless Steels


ASTM E1593, Standard Test Method for Leakage Testing of Empty Rigid Containers by Vacuum Method

DVS 2202-1, Imperfections in Thermoplastic Welding Joints; Features, Descriptions, Evaluation

EN 12266-1, Industrial valves — Testing of metallic valves

European Hygienic Engineering & Design Group (EHEDG), Document No. 18 — Passivation of Stainless Steel

FDA, 21 CFR, Parts 210 and 211, Current Good Manufacturing Practices
GMP: Current Good Manufacturing Practices, Title 21 of the Food and Drug Administration

FDA, 21 CFR, Part 177.1520 Olefin Polymers
FDA, 21 CFR, Part 177.2510 Polyvinylidene Fluoride Resins
FDA, 21 CFR, Part 177.2600 Rubber Articles Intended for Repeated Use
animal-derived ingredients (ADI): products or ingredients derived from tissues or secretions of animals susceptible to transmissible spongiform encephalopathies (TSEs), primarily cattle’s bovine spongiform encephalopathy (BSE).

animal-derived products (ADP): products made from animal-derived ingredients (ADI).

annealing: a treatment process for steel for reducing hardness, improving machinability, facilitating cold working, or producing a desired mechanical, physical, or other property.
anomaly: a localized surface area that is out of specifications to the surrounding area, and is classified as abnormal.

arc gap: for orbital GTAW, the nominal distance, measured prior to welding, from the tip of the electrode to the surface of the weld joint or insert.

arc strike: a discontinuity consisting of any localized remelted metal, heat-affected metal, or change in the surface of the weld or insert.

aseptic: free of pathogenic (causing or capable of causing disease) microorganisms.

aseptic processing: operating in a manner that prevents contamination of the process.

audit: an ASME Certificate Holder’s documented evaluation of a supplier performed to verify, by examination of objective evidence, that those selected elements of a previously approved quality management system have been developed, documented, and implemented in accordance with specified requirements. A surveillance is not an audit.

audit (as performed by ASME or their designee on ASME BPE Certificate Holders and Applicants): see ASME CA-1.

autogenous fillet weld: a fillet weld that is produced without the addition of filler metal. (See also seal weld.)

autogenous weld: a weld made by fusion of the base material without the addition of filler. [See also gas tungsten-arc welding (GTAW).]

automatic welding: welding with equipment that performs the welding operation without adjustment of the controls by a welding operator. The equipment may or may not perform the loading and unloading of the work. (See also machine welding.)

barrier fluid: a fluid used to separate environment from product such as water or condensate in a dual mechanical seal.

bioburden: the number of viable contaminating organisms per product unit.

biofilm: a film of microorganisms or cell components adhering to surfaces submerged in or subjected to fluid environments.

biologics: therapeutic or diagnostic products generated and purified from natural sources.

biopharmaceuticals: pharmaceuticals manufactured by biotechnology methods, with the products having biological sources, usually involving live organisms or their active components. Biopharmaceuticals generally include recombinant proteins, (monoclonal) antibodies, vaccines, blood/plasma-derived products, nonrecombinant culture-derived proteins, and cultured cells and tissues.

bioprocessing equipment: equipment, systems, or facilities used in the creation of products utilizing living organisms.

blind weld: a weld joint by design that cannot feasibly be visually examined internally.

blister (polymeric): a localized imperfection on a polymer surface, containing a pocket of fluid.

blistering (metallic): a localized delamination within the metal that has an appearance of chipped or flaked-off areas. Per SEMI F019-0304, section 4.2.1.

borescope: generic term for a group of optical instruments for visual examinations. This includes rigid borescopes and flexible borescopes (fiberscopes). Often a camera chip is mounted to the borescope. (See also videoscope.)

break: a discontinuity in the face of a fitting.

buffing: a metal finishing process for smoothing the surface using a grease-suspended abrasive.

burn-through: excessive melt-through or a hole through the root bead of a weld.

burr: excess material protruding from the edge typically resulting from operations such as cutting or facing.

butt joint: a joint between two members lying approximately in the same plane.

cartridge seal: a self-contained seal assembly.

cavitation: a condition of liquid flow where, after vaporization of the liquid, the subsequent collapse of vapor bubbles can produce surface damage.

Certificate: a Certificate of Authorization or Quality System Certificate issued by ASME.

Certificate Holder: an organization holding a Certificate of Authorization or a Quality System Certificate issued by the Society upon satisfactory completion of evaluation of its capability to conform to the requirements of this Standard.

Certificate of Authorization: a document issued by ASME that authorizes the application of the ASME Single Certification Mark with the BPE certification designator for a specified time and for a specified scope of activity.

certification: documented testimony by qualified authorities that a system qualification, calibration, validation, or revalidation has been performed appropriately and that the results are acceptable.

NOTE: The term burn through is not used in this Standard.
**cGMPs:** current Good Manufacturing Practices. Current design and operating practices developed by the pharmaceutical industry to meet FDA requirements as published in the Code of Federal Regulations, Chapter 1, Title 21, Parts 210 and 211.

**chromatography:** the purification of substances based on the chemical, physical, and biological properties of the molecule.

**clean:** a condition achieved by removal of dirt, residues, detergents, or other surface contaminants.

**cleaning:** operations by which dirt, residues, detergents, or other surface contaminants are removed to achieve predetermined surface attributes.

**clean-in-place (CIP):** cleaning of process contact surfaces of a system or component without disassembly beyond the removal of single-use components.

**clean steam:** see pure steam.

**closed head:** for orbital GTAW, a welding head that encapsulates the entire circumference of the tube/pipe during welding, and other high-temperature operations such as performing a function or operation in a recognized way to abide by a law or legislative requirement such as complying with the Code of Federal Regulations (CFR). Compliance is externally imposed. Noncompliance is the failure to adhere to an act or law or regulation.

**compression set:** permanent deformation of rubber after subscription in compression for a period of time, as typically determined by ASTM D395.

**concavity:** a condition in which the surface of a welded joint is depressed relative to the surface of the tube or pipe. Concavity is measured as a maximum distance from the outside or inside diameter surface of a welded joint along a line perpendicular to a line joining the weld toes.

**conformity:** see conformity.

**conformity:** the state of meeting, acting, or behaving in accordance with a specification, procedure, method, stated rule, or standard such as the ASME BPE Standard. Nonconformity is the state when a process or action or system does not conform to a stated quality requirement, specification requirement, procedure, or standard such as the ASME BPE Standard.

**consumable insert:** a ring of metal placed between the two elements to be welded that provides filler for the weld when performed with fusion welding equipment. A consumable insert can also be used for the root pass in a multipass weld with the addition of filler wire (also called insert wire).

**convexity:** a condition in which the surface of a welded joint is extended relative to the surface of the tube or pipe. Convexity is measured as a maximum distance from the outside or inside diameter surface of a welded joint along a line perpendicular to a line joining the weld toes.

**corrosion:** a chemical or electrochemical interaction between a metal and its environment, which results in changes in the property of the metal. This may lead to impairment of the function of the metal, the environment, and/or the technical system involved.

**cracks:** fracture-type discontinuities characterized by a sharp tip and high ratio of length and width to opening displacement. A crack may not be detected with a stylus. A linear crack will produce a liquid penetrant indication during liquid penetration inspection, X-ray, or ultrasound.

**crater:** a depression at the termination of a weld bead.

**crater cracks:** cracks that form in the crater, or end, of the weld bead.

**creep:** a time-dependent permanent deformation that occurs under stress levels below the yield stress.

**dead leg:** a space where system design and operating conditions result in insufficient process fluid flow, presenting a risk for particulate, chemical, or biological contamination.

**defects:** discontinuities that by nature or accumulated effect (e.g., total crack length) render a part or product unable to meet minimum applicable acceptable standards or specifications. This term designates rejectability. (See also discontinuity.)

**deionized water:** a grade of purified water produced by the exchange of cations for hydrogen ions and anions for hydroxyl ions.

**delamination:** separation into constituent layers.

**demarcation:** a localized area that is dissimilar to the surrounding areas with a defined boundary.

**dent:** a large, smooth-bottomed depression whose diameter or width is greater than its depth and that will not produce an indication.

**descaling:** the removal of heavy, tightly adherent oxide films resulting from hot-forming, heat-treatment, welding, and other high-temperature operations such as in steam systems.
direct visual examination: a visual examination where there is an uninterrupted optical path from the observer’s eye to the area to be examined. This can be either unaided or aided via mirrors, lenses, etc.
dirty: a relative term indicating the condition of being contaminated.
discoloration: any change in surface color from that of the base metal. Usually associated with oxidation occurring on the weld and heat-affected zone on the outside diameter and inside diameter of the weld joint as a result of heating the metal during welding. Colors may range from pale bluish-gray to deep blue, and from pale straw color to a black crusty coating.
discontinuity: interruption of the typical structure of a weldment, such as a lack of homogeneity in the mechanical, metallurgical, or physical characteristics of the material or weldment. A discontinuity is not necessarily a defect.
distribution system: centralized system for the delivery of fluids from point of generation or supply to point of use.
downslope: that part of an automatic orbital weld sequence during which the welding current is gradually reduced prior to extinguishing of the welding arc. The downslope portion of a welded joint is seen as a tapering of the end of the weld bead with a reduction of penetration from the beginning to the end of the downslope so that the final weld bead is small with minimal penetration.
drainable: a designed characteristic of a component, equipment, or system that enables the removal of water by means of gravity except for that which remains due to surface adherence. Drain paths that become blocked due to surface-adhered water are not considered drainable.
duplex stainless steel: a group of stainless steels whose chemical composition is designed to produce a room-temperature microstructure that is a mixture of austenite and ferrite.
durometer: measurement of hardness related to the resistance to penetration of an indenter point in to a material as a material is compressed repeatedly and, upon immediate release of stress, will return to its approximate original size.
dynamic seal: seal with a component that is in motion relative to a second surface.
dynamic spray device: a moving device, designed to produce a nonstationary spray pattern.
elastomer: rubber or rubberlike material possessing elasticity. (See also elastomeric material.)
elastomeric material: a material that can be stretched or compressed repeatedly and, upon immediate release of stress, will return to its approximate original size.
electropolishing: a controlled electrochemical process utilizing acid electrolyte, direct current, anode, and cathode to smooth the surface by removal of metal.
end grain effect: a surface discontinuity of small diameter (or linear) cavities located perpendicular to the rolling direction of the material and appearing after electropolishing.
etching: the process of removing a layer of metal from its surface using a chemical and/or electrolytic process.
ethical pharmaceutical: a controlled substance for the diagnosis or treatment of disease.
examination: as it relates to pressure vessels, vessels not rated for pressure service, process piping, and process contact equipment, the quality control functions carried out by the manufacturer, fabricator, or erector in accordance with ASME BPVC, Section VIII.
excessive penetration: weld penetration that exceeds the acceptance limit for inside diameter convexity. (See also convexity.)
expiration date: the date after which the shelf life has been exceeded.
extractables (polymeric): chemicals that can be removed from polymeric articles using appropriate solvents.
fermentation: the biochemical synthesis of organic compounds by microorganisms or cultivated cells.
fermentor (fermenter): a vessel for carrying out fermentation.
finishing marks: any surface texture or pattern resulting from cutting, machining, forming, grinding, polishing, and/or other finishing methods.
fixture marks: an area on an electropolished component where the electrical connection was made for the processing of the component.
flash electropolish: an electrochemical process done for a very short duration of time with a low current density, which neither significantly alters the surface of the material nor meets the acceptance criteria as set forth in Nonmandatory Appendix H, Table H-3.3-1.
fluoropolymer: polymer material having a carbon chain either partially or completely bonded to fluorine atoms.
flushing (rinsing): the flowing of water over the process contact surfaces of system components for the removal of particulates or water-soluble contaminants.
full penetration: a weld joint is said to be fully penetrated when the depth of the weld extends from its face into the weld joint so that the joint is fully fused. For a tube-to-tube weld, no unfused portions of the weld joint shall be visible on the inside diameter of a fully penetrated weld.
fusion: the melting together of filler metal and base metal, or of base metal only, that results in coalescence.
fusion welding: welding in which the base material is fused together without the addition of filler material to the weld. [See also gas tungsten arc welding (GTAW).]
gas tungsten-arc welding (GTAW): an arc welding process that produces coalescence of metals by heating them with an arc between a tungsten (nonconsumable) electrode and the work. Shielding is obtained from a gas or gas mixture. (This process is sometimes called TIG welding, a nonpreferred term.) GTAW may be performed by adding filler material to the weld, or by a fusion process in which no filler is added.

GMP facility: a facility designed, constructed, and operated in accordance with cGMP guidelines established by the FDA.

grain boundary: an interface separating two grains, where the orientation of the lattice structure changes from that of one grain to that of the other. Per SEMI F019-0304, section 4.8.2.

harvesting: the separation of cells from growth media. This can be accomplished by filtration, precipitation, or centrifugation.

haze: a localized diminished surface brightness, commonly produced by gassing or variations of the essential variables during electropolishing.

heat-affected zone: that portion of the base metal or polymer that has not been melted, but whose microstructure or mechanical properties have been altered by the heat of welding or cutting.

heat number: an alphanumeric identification of a stated tonnage of metal obtained from a continuous melting in a furnace. (See also discoloration.)

heat tint: coloration of a metallic or polymer matrix, resulting from the surface treatment of a component during the manufacturing process. (See also discoloration.)

High Efficiency Particulate Air (HEPA) filter: a type of air filter that removes 99.97% of particles 0.3 μm and larger in diameter.

higher alloy: a metal containing various alloying constituents formulated to provide enhanced corrosion resistance and possibly improved mechanical properties beyond those that are typically observed in 316L-type stainless steel.

holdup volume: the volume of liquid remaining in a vessel or piping system after it has been allowed to stand. The specified holdup volume is determined by the applicable code.

hydrotest: a pressure test of piping, pressure vessels, or pressure-containing parts, usually performed by pressurizing the internal volume with water at a pressure determined by the applicable code.

hygienic: of or pertaining to equipment and piping systems that by design, materials of construction, and operation provide for the maintenance of cleanliness so that products produced by these systems will not adversely affect human or animal health.

hygienic clamp joint: a tube outside diameter union consisting of two neutered ferrules having flat faces with a concentric groove and mating gasket that is secured with a clamp, providing a nonprotruding, recessless process contact surface. Either with or without filler metal.

hygienic joint: a tube outside diameter union providing a nonprotruding, recessless process contact surface. Usually appear as long, narrow portions of weld metal on the weld underbead. (See also convexity and excessive penetration.)

inclusions: particles of foreign material in a metallic or polymer matrix.

incomplete fusion (or lack of fusion): a weld discontinuity in which fusion did not occur between weld metal and faces or between adjoining weld beads. Also, in welding of tubing, when the weld fully penetrates the wall thickness but misses the joint, leaving some portion of the inner (inside diameter) weld joint with unfused edges.

incomplete penetration (or lack of penetration): a groove weld in which the weld metal extends through the joint thickness and does not fill the joint.

indication: a condition or an anomaly of a localized area that has not been classified as being accepted or rejected.

inspection (as it relates to pressure vessels): functions or actions carried out by an ASME-accredited Authorized Inspector; normally a regular employee of an ASME-accredited Authorized Inspection Agency (or equivalent for other applicable codes or standards) in accordance with ASME BPVC, Section VIII.

inspection (as it relates to process piping, tubing, and process contact surfaces): functions performed by the owner’s Inspector to verify that all required examinations and testing have been completed and to evaluate the physical attributes of the piping to the extent necessary to be satisfied that it conforms to all applicable requirements.

interrupted electropolish: a break in the continuity of the electropolished surface appearance, due to a change of electropolishing conditions at the overlapping boundaries, which may occur when surfaces are electropolished by zones. It may be visible as haze, cloudiness, or variance in luster across these overlapping boundaries.

inclusion: an impurity or other foreign matter within a material.

joint penetration: the depth that a weld extends from its face into a joint, exclusive of reinforcement.

lack of fusion after reflow: a discontinuity in welding of tubing where, after a reflow or second weld pass has been made, the original joint has still not been consumed, the lower of the two base metal surfaces being joined.

lack of penetration (or fusion): evidence obtained from a nondestructive examination method.

leakage: liquid or gas that escapes from an assembly.

lektвор: localized regions of excessive penetration, which usually appear as long, narrow portions of weld metal on the weld underbead. (See also convexity and excessive penetration.)

material: the material used to construct or manufacture something.

melted: solid material that has been converted into a liquid.

metallic: of or pertaining to metals.

metallographic: pertaining to metallography, the study of the microstructure and properties of metals.

microstructure: the arrangement of grains and phases within a material, as observed at a microscopic scale.

miscellaneous: various items or objects that are not included in a specific category.

miscible: capable of dissolving in another substance without forming a separate phase.

miscibility: the ability of two substances to dissolve in each other.

monomer: a small molecule that can polymerize to form a polymer.

nadir: the lowest point or level.

neutered: having been altered so as to provide a nonprotruding process contact surface.

offset: a deviation from a specified location or position.

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leaving the weld joint with unfused edges on the inner surface.

*lamellar tears:* terrace-like fractures in the base metal with a basic orientation parallel to the wrought surface; caused by the high stress in the thickness direction that results from welding.

*laminations:* elongated defects in rolling, resulting from the rolling of a metal containing a blowhole; actually, the out-of-plane direction of rolling.

*leachables (polymeric):* typically a subset of extractables, these chemicals migrate from polymeric articles into the product or process fluid.

*linear porosity:* porosity that occurs in a linear pattern. Linear porosity generally occurs in the root pass from inadequate joint penetration.

*liquid penetrant indication:* refer to ASME BPVC, Section V, T-600, for testing an anomaly or an indication.

*looped header:* a piping ring with multiple branches for inlet or outlet. The branches on the ring can be closed by valves, caps, or other means of flow isolation.

*luster:* the state or quality of shining by reflecting light. (See also variance in luster.)

*machine welding:* welding with equipment that performs the welding operation under the constant observation and control of a welding operator. The equipment may or may not perform the loading and unloading. (See also automatic welding.)

*manual welding:* welding in which the operation is performed and controlled.

*material manufacturer:* an organization responsible for the production of products meeting the requirements of the material specification(s).

*Material Test Report (mill test report or mill test report)* in which the results of tests, examinations, repairs, or treatments required by the material specification are recorded. This document may be combined with a Certificate of Conformance as a single document.

*material type:* a commercial designation for a given chemistry range.

*maximum allowable leakage limit (MALL) (single-use):* the greatest leakage rate (or leak size) tolerable for a given single-use system to maintain its barrier properties under its use-case conditions (e.g., prevent any risk to product safety, product quality or operator and environmental safety), in accordance with ASTM E3336.

*meandering:* of or pertaining to a weld bead that deviates from side to side across the weld joint rather than tracking the joint precisely.

*mechanical polishing:* a process by which abrasive media is applied to a surface until the specified surface roughness \( R_a \) is achieved.

*mechanical seal:* a device used for sealing fluids with rotating shafts. A mechanical seal is a prefabricated or packaged assembly that forms a running seal between flat surfaces.

*micron (1 μ) or micrometer (1 μm):* one-millionth of a meter.

*misalignment (mismatch):* axial offset of the joint members.

*mitter:* two or more straight sections of tube matched and joined in a plane bisecting the angle of junction so as to produce a change of direction.

*mold seal:* a seal that is manufactured by forming in a mating cavity.

*mold flash:* excess material that is greater than the designed geometry of a part that is formed in the molding process.

*multiuse:* a term describing process contact components, equipment, and systems that are designed to be cleaned, sanitized, or sterilized and used multiple times (also referred to as repeated use).

*nick:* a surface void anomaly caused by material removal or compression from the surface, whose bottom surface is usually irregular.

*nominal outside diameter:* a numerical identification of outside diameter to which tolerances apply.

*nominal wall thickness:* a numerical identification of wall thickness to which tolerances apply.

*nonsliding seal:* a seal that does not have transverse or rotational movement between the seal and mating surface(s).

*nonuniform mechanical polishing marks:* a localized surface polishing pattern that is dissimilar to the surrounding area.

*off angle:* a measurement of face-to-face squareness.

*off plane:* a measurement of the offset between part centerlines or two planes.

*open head:* for orbital GTAW, a welding head that is open to the atmosphere external to the tube/pipe being welded and that does not enclose the shielding gas, which is still provided through the torch.

*orange peel:* large-featured, roughened type of surface visible to the unaided eye whose surface appearance pattern is like that of an orange peel.

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**NOTE:** The terms lamellar tears, laminations, and linear porosity are not used in this Standard.
orbital welding: automatic or machine welding of tubes or pipe in-place with the electrode rotating (or orbiting) around the work. Orbital welding can be done with the addition of filler material or as a fusion process without the addition of filler.

O-ring: ring seal of circular cross section.

outboard seal: a seal that is outside the product area in the outermost part of a mechanical seal assembly.

overlap: the protrusion of weld metal beyond the weld toes or weld root. Also, in an orbital weld, that amount by which the end of the weld bead overlaps the beginning of the weld bead (not including the downslope) on a single-pass weld.

owner/user: the body on which final possession or use rests.

oxidation: a common form of electrochemical reaction that is the combining of oxygen with various elements and compounds.

oxide island: a concentration of nonmetallic impurities (often oxides or nitrides) that may form in the weld pool and solidify on the underbead or weld top surface.

oxide layer: an area usually located in the heat-affected zone of the weldment where an oxidation reaction has taken place.

packing: a type of shaft seal formed into coils, spirals, or rings that is compressed into the seal cavity.

particulates (single-use): small, solid, and mobile matter.

passivation: removal of exogenous iron or iron from the surface of stainless steels and higher alloys by means of a chemical dissolution, most typically by a treatment with an acid solution that will remove the surface contamination and enhance the formation of the passive layer.

passive layer: a chromium-enriched oxide layer on a stainless steel surface that improves the corrosion resistance of the base metal.

process zone - area to which the product is potentially exposed during manufacturing (e.g., interior of bioreactor after SIP; manufacturing suite environment would not be in the process zone, unless system is open).

penetration: see full penetration, incomplete penetration, and joint penetration.

personal care products: products used for personal hygiene or cosmetic care.

PFA: fluoropolymer, copolymer of tetrafluoroethylene and perfluorovinyl ether.

pharmaceutical: relating to the use and/or manufacture of medical drugs or compounds used to diagnose, treat, or prevent a medical condition.
chromatography columns, vessels, and recirculating segments of CIP systems.

**profilometer**: an instrument for the measurement of the degree of surface roughness.

**progressive polishing**: a mechanical grinding procedure where a coarse grit material is used first and the successive operations use a finer and finer grit until the desired surface roughness is achieved.

**PTFE**: polytetrafluoroethylene, homopolymer material of tetrafluoroethylene.

**pure steam**: also known as clean steam, steam that is produced by a steam generator that, when condensed, meets requirements for water-for-injection (WFI).

**purified water (PW)**: a classification of water according to compendial standards.

**PVD**: polyvinylidene fluoride, homopolymer, and/or copolymer material composed of carbon, hydrogen, and fluorine.

**pyrogen**: a fever-producing substance.

**Quality Inspector’s Delegate**: a person who is delegated by an owner’s Inspector to perform inspection functions as referenced in ASME B31.3, para. 340.4(c).

**Quality System Certificate**: a document issued by ASME that authorizes the use of an ASME Certificate number on Certificates of Conformance for a specified time and that authorizes the inspection functions as referenced in ASME B31.3, para. 340.4(c).

**Ramax.**: the highest value of a series of Ra readings.

**RND**: log of the arithmetic mean of the surface profile.

**R_{max}**: the highest value of a series of R_n readings.

**reinforcement**: see convexity.

**remote visual examination**: a visual examination where there is an interrupted optical path from the observer’s eye to the area to be examined. This covers the use of photography, video systems, videoscopes, and borescopes.

**repeated use**: see multiuse.

**rouge**: a general term used to describe a variety of discolorations in high-purity stainless steel biopharmaceutical systems. It is composed of metallic (primarily iron) oxides and/or hydroxides. Three types of rouge have been categorized. **Class I rouge**: a rouge that is predominantly particulate in nature that tends to migrate downstream from its origin point and can deposit on process contact surfaces. It is generally orange to red-orange in color. These particles can be wiped off a surface and are evident on a wipe. Surface composition under the rouge remains unchanged. **Class II rouge**: a localized form of active corrosion. It occurs in a spectrum of colors (orange, red, blue, purple, gray, black). It can be the result of chloride or other halide attack on the surface of the stainless steel. **Class III rouge**: a surface oxidation condition occurring in high-temperature environments such as pure steam systems. The system’s color transitions to gold, to blue, to various shades of black, as the layer thickens. This surface oxidation initiates as a stable layer and is rarely particulate in nature. It is an extremely stable form of magnetite (iron sesquioxide, Fe_{3}O_{4}).

**sanitary**: see hygienic.

**sanitary (hygienic) weld**: generally considered to be a groove weld in a square butt joint made by the GTAW (or plasma) process as a fusion weld without the addition of filler material. A sanitary weld must be completely penetrated on the weld inside diameter (I.D.), with little or no discoloration due to oxidation, and be otherwise without defects that would interfere with maintenance in a clean and sterile condition.

**schedule**: dimensional standard for pipe as defined by ASTM.

**scratch**: an elongated mark or groove cut in the surface by mechanical means, not associated with the predominant surface texture pattern.

**SDR**: standard dimension ratio, a sizing system for polymer piping systems that relates wall thickness to pressure rating as defined by ISO.

**seal chamber**: see stuffing box.

**seal face**: surface point on which a seal is achieved. **seal point**: location of process boundary created by components in contact (seal), having sufficient contact stress/load to create media or environmental isolation.

**seal weld**: a weld used to obtain fluid tightness as opposed to mechanical strength. (See also autogenous fillet weld.)

**service life**: the life expectancy or number of cycles for which the unit will maintain its performance.

**shelf life**: the duration, under specified storage conditions, from the date of manufacture to the last date the product can be placed in service without having an unacceptable effect on performance.

**shell泄漏**: a quantity of test fluid passing from the inside of a component externally to atmosphere under the defined test conditions.

**NOTE**: Since sanitary is defined as "see hygienic," and hygienic is defined, there is no need for a definition for sanitary weld.
significant change (polymeric): a change that may affect form, fit, or function.

single-use: a term describing process contact components, assemblies, and systems that are designed to be used once, and not to be cleaned or sterilized for reuse.

size classification: the size of surface deficits is classified in two groups as follows:

(a) macro: referring to indications that can be seen in adequate lighting without magnification.
(b) micro: referring to indications that can be seen only with the aid of magnification.

slag: a nonmetallic product resulting from the mutual dissolution of flux and nonmetallic impurities in some welding and brazing operations.

sliding seal: a seal that has transversal or rotational movement between the seal and mating surface(s).

slope: an incline or deviation from the horizontal. A tube or pipe installed in the horizontal plane is said to slope if one end is positioned higher than the other.

sparger: a device used to agitate, oxygenate, or aerate a liquid by means of compressed air or gas.

spatter: the metal particles expelled during welding that do not form part of a weld.

special process: a process, the results of which are highly dependent on the control of the process or the skill of the operators, or both, and in which the specified quality cannot be readily determined by inspection or test of the product.

spot electropolishing: a localized electrochemical process that is capable of producing the correct Cr to Fe ratios on the surface of a material and meeting the requirements of Nonmandatory Appendix H, Table H-3.3-1.

spray device: device for the directed distribution (delivery) of liquids to defined process contact surfaces of equipment. (See also dynamic spray device and static spray device.)

square cut: a tube end cut perpendicular to the tangent plane.

squareness: face-to-face perpendicularity.

static seal: a stationary sealing device.

static spray device: a stationary device designed to produce a fixed directional spray pattern.

steam-in-place (SIP): the use of steam to sanitize or sterilize a piece of equipment without the use of an autoclave.

stem seal: a seal element that is used on a shaft.

sterile: free from living organisms.

sterility: the absence of all life forms.

strainer: a component that mechanically separates and retains suspended solid particulates from a process fluid. (See also strainer body and strainer element.)

strainer body: the subcomponent of a strainer that holds or houses the strainer element. A strainer body can be part of the process piping in which the strainer is installed (e.g., gasket strainer).

strainer element: the subcomponent of a strainer with openings (e.g., perforations, slots). This subcomponent provides the straining of suspended solid particulates.

stringer indication: a linear void resulting from the removal of an elongated nonmetallic inclusion or secondary phase.

stuffing box: in shaft seals, the casing containing the sealing material; seal chamber for shaft seals. (See also packing.)

superaustenitic stainless steel: a subgroup of austenitic stainless steels having elevated levels of nickel, chromium, and molybdenum compared with standard austenitic stainless steels (e.g., UNS S31603) and that may have other additions (e.g., nitrogen and/or copper) to increase strength and resistance to pitting corrosion and stress corrosion cracking in the presence of chlorides.

super duplex stainless steel: those duplex stainless steels whose chemical composition is designed to result in a pitting resistance equivalent number (PREN) of at least 40.

surface finish: all surfaces as defined by Part SF of the current ASME BPE Standard and/or the owner/user or manufacturer and expressed in Ra inches or meters.

surface inclusion: particles of foreign material in a metallic matrix. The particles are usually compounds such as oxides, sulfides, or silicates, but may be a substance foreign to and essentially insoluble in the matrix.

surface residual: a foreign substance that adheres to a surface by chemical reaction, adhesion, adsorption, or ionic bonding (e.g., corrosion, rouging, and staining).

surveillance: the act of an ASME Certificate Holder’s monitoring or observing a supplier’s in-process production activities at the location of work to verify whether an item conforms to specified requirements.

survey: an ASME Certificate Holder’s documented evaluation of a supplier’s ability to supply items to meet specified requirements as verified by a determination of the adequacy of the organization’s quality management system for the items to be procured and by review of the implementation of that quality management system at the location of work.

system volume: total volume of liquid in the system, including equipment, piping, valving, and instrumentation.

tack weld: a weld made to hold parts of a weldment in proper alignment until the final welds are made.
testing (as it relates to pressure vessels): a function of the manufacturer or fabricator, as witnessed by the examiner or ASME Authorized Inspector and verified or witnessed by the owner’s Inspector or the Quality Inspector’s Delegate including written documentation in accordance with ASME BPVC, Section VIII (or equivalent for other applicable codes or standards).

testing (as it relates to process contact equipment): a function of the manufacturer, fabricator, or erector, as witnessed by the examiner and may be verified or witnessed by the owner’s Inspector or the Quality Inspector’s Delegate including written documentation in accordance with ASME BPE.

testing (as it relates to process piping): a function of the manufacturer, fabricator, or erector, as witnessed by the examiner or Inspector and verified or witnessed by the owner’s Inspector or the Quality Inspector’s Delegate including written documentation in accordance with ASME B31.3.

testing (as it relates to vessels not rated for pressure service): a function of the manufacturer, fabricator, or erector, as witnessed by the examiner and verified or witnessed by the owner’s Inspector or the Quality Inspector’s Delegate including written documentation.

thermoplastic: long-chain polymers that are usually not connected by crosslinks. Once formed, these materials can be reshaped.

thermoset: long-chain polymers that are usually connected by crosslinks. Once formed, these materials cannot be reshaped.

transfer panel: a panel to which process and/or utilities are piped that mechanically precludes erroneous cross-connections.

tube: tube is sized by its nominal outside diameter. For bioprocessing equipment, tube does not include pipe.

tungsten inclusions: tungsten particles transferred into the weld deposit by occasional touching of the tungsten electrode used in the gas tungsten-arc process to the work or to the molten weld metal. These inclusions are often considered defects that must be removed and the weld repaired prior to final acceptance. Tungsten inclusions may be invisible to the unaided eye, but are readily identified in a radiograph.

Ultra-Low Particulate Air (ULPA) filter: a type of air filter that removes 99.999% of particles 0.1 μ and larger in diameter.

unacceptable leakage: leakage level above which the system performance is considered unacceptable by the system user and applicable regulating body.

undercut: a groove melted into the base metal adjacent to the weld toe or weld root and left unfilled by weld metal.

underfill: a depression on the weld face or root surface extending below the adjacent surface of the base metal. (See also concavity.)

uniformly scattered porosity: porosity that is distributed in a weldment in a uniform pattern.

user: see owner/user.

validation: establishing documented evidence that the system does what it purports to do.

variance in luster: the appearance of a different shine or reflectivity resulting from the examination or inspection technique or from the preconditioning or conditioning of the electropolished surface.

videoscope: a type of borescope with a camera chip mounted to the instrument for taking photos or videos of the area of examination.

waviness: undulations or rippling of the surfaces.

welding operator: one who operates machine or automatic welding equipment.

weld joint design: the shape, dimensions, and configuration of the weld joint.

weld whitening: a difference in appearance of grain structure between weld metal and base metal after electropolishing.

WFI: water-for-injection, a classification of water according to compendial standards.

GR-9 NOMENCLATURE

Dimensional and mathematical symbols used in this Standard are listed in Mandatory Appendix IV with definitions for each symbol given in addition to their point-of-use location(s) within the Standard. Uppercase and lowercase English letters are listed alphabetically, followed by Greek letters.
New Table CR-1-1 per record 23-236

<table>
<thead>
<tr>
<th>Component</th>
<th>Certificate of Authorization</th>
<th>Quality System Certificate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metallic fittings</td>
<td>X</td>
<td>..........................</td>
</tr>
<tr>
<td>Metallic tubing</td>
<td>X</td>
<td>..........................</td>
</tr>
<tr>
<td>Metallic valves</td>
<td>X</td>
<td>..........................</td>
</tr>
<tr>
<td>Polymetric seals</td>
<td>..........................</td>
<td>X</td>
</tr>
</tbody>
</table>

Note: (1) Valve Certificate Holders may issue a Certificate of Conformance for polymeric seals they manufacture within the scope of their authorization.

CR-2 GENERAL

(a) To obtain, maintain, and renew an ASME Certificate, applicants and Certificate Holders shall conform with the conformity assessment requirements addressed in ASME CR-1.

(b) An ASME BPE Certificate Holder shall have a QMS in conformance with the ASME BPE Standard. Any changes in conformance with the ASME BPE Standard shall be documented in a QMS Manual. The QMS Manual shall be reviewed, updated, and if necessary, withdrawn, and/or revised by ASME based upon surveys, audits, and investigations conducted by an ASME team. A list of ASME BPE Certificate Holders can be found on the ASME website.

(c) ASME surveys are conducted by an ASME team to evaluate the capability of an organization to manufacture components in conformance with the requirements of the QMS and the ASME BPE Standard. Surveys are conducted as part of the ASME decision process for the issuance or renewal of an ASME Certificate. ASME Certificates are issued and renewed with an expiration date by which time the Certificate Holders shall have their QMS Manual and its implementation surveyed by ASME.

(d) Additional audits may be conducted based upon the results of past surveys and audits or complaints.

(e) Certificate Holders who manufacture components under a Certificate of Authorization shall provide designated oversight of their activities and the proper
(d) ASME BPE Certificate Holders shall be authorized, under a valid Certificate of Authorization, to mark components, documentation traceable to the components, or both, with the ASME Single Certification Mark with the BPE certification designator and their Certificate number.

(e) When an ASME BPE Certificate Holder supplies documentation for a manufactured component that includes material supplied by another organization, it is not mandatory for the Certificate Holder to add their ASME Single Certification Mark with BPE certification designator to the documentation received from the original organization. However, if the Certificate Holder chooses to add their ASME Single Certification Mark with BPE certification designator in addition to that on the existing documentation from the original organization, the additional markings shall be clearly identified and traceable to the Certificate Holder.
(3) have knowledge of the Certificate Holder’s QMS
(4) have training commensurate with the scope, complexity, or special nature of the activities to which oversight is to be provided
(b) The individual meeting the established competency requirements under the Certificate Holder’s qualification and certification program shall be certified by the Certificate Holder to be able to perform the duties of a GI.
(c) The Certificate Holder shall maintain a record of the certifications and training of the GI.

CR-2.3.2 Duties of the Certified Individual. The duties of the GI shall include, but are not limited to:

(a) verifying that each component to which the ASME Single Certification Mark with the BPE certification designation is applied conforms with both the QMS set file with ASME and the applicable requirements of the ASME BPE Standard. Verification activities include, but are not limited to, ensuring the component is manufactured in accordance with:

(1) the scope of the ASME Certificate of Authorization
(2) a valid and current ASME Certificate of Authorization
(3) the QMS Manual on file with ASME
(b) certifying the appropriate documentation, Certificate of Conformance, or both prior to the release of the BPE component. This certification shall attest to the component being in conformance with the ASME BPE Standard and shall be by signature or other means as described in the organization’s QMS.
### Table MM-2.1-1

**Wrought Stainless Steels: Nominal Compositions (wt. %)**

<table>
<thead>
<tr>
<th>UNS Number [Note (1)]</th>
<th>EN Designation</th>
<th>JIS Designation</th>
<th>C</th>
<th>Mn</th>
<th>N</th>
<th>Cr</th>
<th>Ni</th>
<th>Mo</th>
<th>Cu</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Austenitic Stainless Steels</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>S30400</td>
<td>...</td>
<td>...</td>
<td>0.07</td>
<td>2.00</td>
<td>0.10</td>
<td>17.5–19.5</td>
<td>8.0–10.5</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>...</td>
<td>1.4301</td>
<td>...</td>
<td>0.07</td>
<td>2.00</td>
<td>0.10</td>
<td>17.5–19.5</td>
<td>8.0–10.5</td>
<td>...</td>
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</tr>
<tr>
<td>...</td>
<td>SUS304</td>
<td>0.08</td>
<td>2.00</td>
<td>...</td>
<td>18.0–20.0</td>
<td>8.0–10.5</td>
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<td></td>
</tr>
<tr>
<td>S30403</td>
<td>...</td>
<td>...</td>
<td>0.030</td>
<td>2.00</td>
<td>0.10</td>
<td>17.5–19.5</td>
<td>8.0–12.0</td>
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</tr>
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<td>2.00</td>
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<td>0.10</td>
<td>16.0–18.0</td>
<td>10.0–14.0</td>
<td>2.00–3.00</td>
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<tr>
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<td>0.07</td>
<td>2.00</td>
<td>0.10</td>
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<td>0.10</td>
<td>16.0–18.0</td>
<td>10.0–14.0</td>
<td>2.00–3.00</td>
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<td>2.00</td>
<td>0.10</td>
<td>16.5–18.5</td>
<td>10.0–14.5</td>
<td>2.00–2.50</td>
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<td>2.00</td>
<td>0.10</td>
<td>17.0–19.0</td>
<td>12.5–15.0</td>
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<td>...</td>
<td>SUS316L</td>
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<td>2.00</td>
<td>...</td>
<td>16.0–18.0</td>
<td>12.0–15.0</td>
<td>2.0–3.0</td>
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<tr>
<td><strong>Superaustenitic Stainless Steels</strong></td>
<td></td>
<td></td>
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<td>23.0–28.0</td>
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<td>1.0–2.0</td>
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<td>19.0–21.0</td>
<td>24.0–26.0</td>
<td>4.0–5.0</td>
<td>1.20–2.00</td>
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<td>...</td>
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<td>2.00</td>
<td>0.15–0.25</td>
<td>19.0–21.0</td>
<td>24.0–26.0</td>
<td>4.0–5.0</td>
<td>1.15–2.00</td>
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<td>17.5–18.5</td>
<td>6.0–6.5</td>
<td>0.50–1.00</td>
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<td>24.0–26.0</td>
<td>6.0–7.0</td>
<td>0.5–1.5</td>
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<td><strong>Duplex Stainless Steels</strong></td>
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<td>0.10–0.80</td>
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<td>21.0–22.0</td>
<td>1.35–1.70</td>
<td>0.10–0.80</td>
<td>0.10–0.80</td>
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<td>0.14–0.20</td>
<td>22.0–23.0</td>
<td>4.5–6.5</td>
<td>3.0–3.5</td>
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<td>21.0–23.0</td>
<td>4.5–6.5</td>
<td>2.50–3.5</td>
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</tr>
</tbody>
</table>

**GENERAL NOTES:**

(a) Maximum, unless range or minimum is indicated.

(b) Values listed in this Table are primary elements only and are not complete chemical compositions as listed in specific product type material specifications. Alloy composition is typically at the low end of the ranges indicated above. Refer to appropriate product type material specification for complete material composition requirements.

(c) Alloys listed between horizontal lines are not equivalent, but comparable.

NOTE: (1) For cross-referencing of the UNS numbers listed above to common alloy names, refer to SAE Metals and Alloys in the Unified Numbering System, latest edition.
## Table MM-2.1-3
Stainless Steel and Nickel Alloy Cast Designations

<table>
<thead>
<tr>
<th>UNS Designation</th>
<th>ACI Designation</th>
<th>EN Designation</th>
<th>JIS Designation</th>
<th>Approximate Wrought Equivalent</th>
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</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>UNS Designation</td>
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<td><strong>Austenitic Stainless Steels</strong></td>
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<td>J92600</td>
<td>CF8</td>
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<td>S30400</td>
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<td>SCS 13A</td>
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<td>J92900</td>
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<td>SCS 16A</td>
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<td><strong>Superaustenitic Stainless Steels</strong></td>
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| **GENERAL NOTE:** Alloys listed between horizontal lines are not equivalent, but comparable.
Table MM-2.1-4  
Wrought Copper: Nominal Compositions (wt. %)  
(Cleaned for Oxygen Service)

<table>
<thead>
<tr>
<th>UNS Number</th>
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<th>Cu + Ag</th>
<th>P</th>
<th>O</th>
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<td>C10200</td>
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<td>99.95</td>
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<td>99.90</td>
<td>0.008-0.012</td>
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<td>CW024A</td>
<td>99.90</td>
<td>0.015-0.040</td>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>

GENERAL NOTES:
(a) Minimum, unless range or maximum is indicated.
(b) Copper grades listed between horizontal lines are not equivalent, but comparable.

MM-3.5 Reclaimed Materials

Reclaimed process components, equipment, or both may be used with owner/user authorization, provided they are properly identified as conforming to a published specification listed in MM-4.6 or to a Standard Specification in those paragraphs from which requirements of austenitic or duplex stainless steel or MM-5.2.1.2 or MM-5.2.1.3 are adopted.

MM-3.6 Designation of Alloy and Fluid Services

DELETED

MM-4 REFERENCED SPECIFICATIONS

MM-4.2 Tubing, Piping, and Hollow Bar

Tubing, piping, and hollow bar manufactured in accordance with the following specifications may be used:

- ASTM A269/A269M, Standard Specification for Seamless and Welded Austenitic Stainless Steel Tubing for General Service
- ASTM A270/A270M, Standard Specification for Seamless and Welded Austenitic and Ferritic/Austenitic Stainless Steel Sanitary Tubing
- ASTM A312/A312M, Standard Specification for Seamless, Welded, and Heavily Cold Worked Austenitic Stainless Steel Pipes
- ASTM A511/A511M, Standard Specification for Seamless Stainless Steel Mechanical Tubing and Hollow Bar
- ASTM A789/A789M, Standard Specification for Seamless and Welded Ferritic/Austenitic Stainless Steel Tubing for General Service
- ASTM A790/A790M, Standard Specification for Seamless and Welded Ferritic/Austenitic Stainless Pipe
- ASTM B626, Specification for Welded Nickel and Nickel-Cobalt Alloy Tube
- ASTM B673, Specification for UNS N08367 Welded Pipe
- ASTM B676, Specification for UNS N08367 Welded Tube
- ASTM B819, Standard Specification for Seamless Copper Tube for Medical Gas Systems
- DIN 17744, Wrought nickel alloys with molybdenum and chromium — Chemical composition
- DIN 17751, Tubes of wrought nickel alloys — Properties
- EN 10216-5, Seamless steel tubes for pressure purposes — Technical delivery conditions — Part 5: Stainless steel tubes
- EN 10217-7, Welded steel tubes for pressure purposes — Technical delivery conditions — Part 7: Stainless steel tubes
- EN 10312, Welded stainless steel tubes for the conveyance of water and other aqueous liquids — Technical delivery conditions
- EN 13348, Copper and copper alloys — Seamless, round copper tubes for medical gases or vacuum
- JIS G 3447, Stainless steel sanitary pipes
- JIS G 3459, Stainless steel pipes
- JIS G 4903, Seamless nickel-chromium-iron alloy pipes
(22) **MM-4.3 Castings**

Castings manufactured in accordance with the following specifications may be used:

- ASTM A351/A351M, Standard Specification for Castings, Austenitic, for Pressure-Containing Parts
- ASTM A995/A995M, Standard Specification for Castings, Austenitic-Ferritic (Duplex) Stainless Steel, for Pressure-Containing Parts
- EN 10213, Steel castings for pressure purposes
- EN 10283, Corrosion resistant steel castings
- JIS G 5121, Corrosion-resistant cast steels for general applications

(22) **MM-4.4 Forgings**

Forgings manufactured in accordance with the following specifications may be used:

- ASTM A182/A182M, Standard Specification for Forged or Rolled Alloy and Stainless Steel Pipe Flanges, Forged Fittings, and Valves for High-Temperature Service
- ASTM B462, Standard Specification for Forged or Rolled Nickel Alloy Pipe Flanges, Forged Fittings, and Valves and Parts for Corrosive High-Temperature Service
- ASTM B564, Standard Specification for Nickel Alloy Forgings
- EN 10222-5, Steel forgings for pressure purposes — Part 5: Martensitic, austenitic, and austenitic-ferritic stainless steels
- EN 10250-4, Open die steel forgings for general engineering purposes — Part 4: Stainless steels
- JIS G 3214, Stainless steel forgings for pressure vessels
- JIS G 4319, Stainless steel blooms and billets or forgings

(22) **MM-4.5 Plate, Sheet, and Strip**

Plate, sheet, and strip manufactured in accordance with the following specifications may be used:

- ASTM A240/A240M, Standard Specification for Chromium and Chromium-Nickel Stainless Steel Plate, Sheet, and Strip for Pressure Vessels and for General Applications
- ASTM A666, Standard Specification for Annealed or Cold-Worked Austenitic Stainless Steel Sheet, Strip, Plate, and Flat Bar
- DIN 17744, Wrought nickel alloys with molybdenum and chromium — Chemical composition
- DIN 17750, Strip and sheet of nickel and wrought nickel alloys — Properties
- EN 10028-1, Flat products made of steels for pressure purposes — Part 1: General requirements
- EN 10028-7, Flat products made of steels for pressure purposes — Part 7: Stainless steels
- EN 10088-2, Stainless steels — Part 2: Technical delivery conditions for sheet/plate and strip of corrosion resisting steels for general purposes
- EN 10095, Heat resistant steels and nickel alloys
- JIS G 4304, Hot-rolled stainless steel plate, sheet and strip
- JIS G 4305, Cold-rolled stainless steel plate, sheet and strip
- JIS G 4312, Heat-resisting steel plate, sheet and strip
- JIS G 4902, Corrosion-resisting and heat-resisting super-alloy plates and sheets

(22) **MM-4.6 Shapes, Rods, and Bars**

Shapes, rods, and bars manufactured in accordance with the following specifications may be used:

- ASTM A276/A276M, Standard Specification for Stainless Steel Bars and Shapes
- ASTM A479/A479M, Standard Specification for Stainless Steel Bars and Shapes for Use in Boilers and Other Pressure Vessels
- ASTM B649, Standard Specification for Ni-Fe-Cr-Mo-Cu-N Low-Carbon (UNS N08925, UNS N08031, UNS N08034, UNS N08354, and UNS N08926), and Cr-Ni-Fe-N

ASTM A1049/1049M, Standard Specification for Stainless Steel Forgings, Ferritic/Austenitic (Duplex), for Pressure Vessels and Related Components

JIS G 4305, Cold-rolled stainless steel plate, sheet and strip
JIS G 4312, Heat-resisting steel plate, sheet and strip
JIS G 4902, Corrosion-resisting and heat-resisting super-alloy plates and sheets
Low-Carbon Alloy (UNS R20033) Bar and Wire, and Ni-Cr-Fe-Mo-N Alloy (UNS N08936) Wire
DIN 17744, Wrought nickel alloys with molybdenum and chromium — Chemical composition
DIN 17752, Wrought nickel and nickel alloy rods and bars — Requirements and testing
EN 10088-3, Stainless steels — Part 3: Technical delivery conditions for semi-finished products, bars, rods, wire, sections and bright products of corrosion resisting steels for general purposes
EN 10095, Heat resistant steels and nickel alloys
EN 10272, Stainless steel bars for pressure purposes
JIS G 4303, Stainless steel bars
JIS G 4308, Stainless steel wire rods
JIS G 4311, Heat-resisting steel bars and wire rods
JIS G 4901, Corrosion-resisting and heat-resisting superalloy bars
JIS H 4553, Nickel and nickel alloy bars
JIS H 4554, Nickel and nickel alloy wire and drawing stock

(22) MM-4.7 Copper Alloy Fittings
DELETED

MM-5 BASE METALS AND FILLER MATERIALS

MM-5.1 General
This section provides requirements and recommendations for the base metals listed in Tables MM-2.1-1 through MM-2.1-4. The use of base metals other than those listed in this section is permitted with the owner/user’s written approval (see MM-3.3).

MM-5.2 Base Metals
(22) MM-5.2.1 Stainless Steels

MM-5.2.1.1 Austenitic Stainless Steels
(a) Weld Ends of Process Components. Weld ends of process components that are to be autogenously welded shall have a sulfur content between 0.005 wt. % and 0.017 wt. % [see also MJ-2.1.1(a)]. This requirement applies to the austenitic stainless steels listed in Tables MM-2.1-1 and MM-2.1-3. This requirement does not apply to materials used in the manufacture of process components only to the weld ends of process components in their final form.

(b) Delta Ferrite. If specific delta ferrite levels in austenitic stainless steels are deemed necessary to maintain certain properties, the owner/user shall specify required delta ferrite ranges separately for the base metal, for welds in the solution-annealed condition, and for welds left in the as-welded condition. As a general rule, material with low Cr-to-Ni ratios show lower delta ferrite levels in the base metal and subsequent to welding. See Table MM-5.2.1.1-1 for predicted ferrite number ranges for various austenitic stainless steel product forms. These are not acceptance criteria. The listed ferrite numbers refer to as-solidified austenitic stainless steels and therefore indicate predicted delta ferrite levels of the respective autogenous welds, welds with filler metal, or castings. Additional information regarding delta ferrite can be found in Nonmandatory Appendix G.

Table MM-5.2.1.1-1
Predicted Ferrite Number (FN) Ranges for Various Austenitic Stainless Steel Product Forms and Welds

<table>
<thead>
<tr>
<th>Product Form</th>
<th>Expected FN</th>
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</thead>
<tbody>
<tr>
<td>Wrought product forms with sulfur levels less than 0.005%</td>
<td>0.5 to 4</td>
</tr>
<tr>
<td>Wrought product forms with a sulfur range of 0.005% to 0.017%</td>
<td>1.0 to 6</td>
</tr>
<tr>
<td>GMAW/GTAW using ER316L [Note (1)]</td>
<td>4 to 12</td>
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<tr>
<td>SMAW using E316L [Notes (3), (4)]</td>
<td>4 to 10</td>
</tr>
<tr>
<td>CF8M and CF3M castings</td>
<td>5 to 15</td>
</tr>
</tbody>
</table>


NOTES:
(1) SFA 5.9/5.9M, Specification for Bare Stainless Steel Welding Electrodes and Rods.
(2) Nitrogen pickup or weld metal dilution could result in a 3 FN to 4 FN loss in the as-deposited weld metal.
(3) SFA 5.4/5.4M, Specification for Stainless Steel Electrodes for Shielded Metal Arc Welding.
(4) Electrodes with a restricted FN usually require a special order, with the exception of 2 FN maximum product for cryogenic temperatures.
(5) FN in the as-deposited weld is influenced by welding technique and is lowered by nitrogen pickup or weld metal dilution.
desirable to keep exposure time within this temperature range to a minimum.

Exposure time to undesirable temperatures reached during high-temperature service, heat treatment, or joining should be minimized. The material manufacturer should be consulted for specific instructions regarding heat treatment.

**MM-5.2.1.3 Duplex Stainless Steels.** The corrosion resistance and mechanical properties of duplex stainless steels listed in Tables MM-2.1-1 and MM-2.1-3 are based on having roughly equal amounts of ferrite and austenite in the microstructure at room temperature while also avoiding undesirable secondary phases.

The UNS S32101 grade listed in Table MM-2.1-1 may be prone to the precipitation of undesirable nitrides and carbides when exposed to temperatures in the range of 1,200°F to 1,570°F (650°C to 850°C). Similarly, the duplex stainless steel, UNS S32205, may be prone to the precipitation of undesirable secondary intermetallic phases such as sigma and chi. This precipitation occurs continually in the range of 1,200°F to 1,830°F (650°C to 1,000°C). Exposure time to undesirable temperatures reached during high-temperature service, heat treatment, or joining should be minimized. The material manufacturer should be consulted for specific instructions regarding heat treatment.

**MM-5.2.2 Nickel Alloys.** The nickel alloys listed in Tables MM-2.1-2 and MM-2.1-3 may be prone to precipitation of secondary phases such as mu and P. Such secondary precipitation typically occurs when the material is subjected to temperatures in the range of 1,500°F to 1,800°F (820°C to 980°C) and can create a detrimental effect on the material's corrosion resistance. Exposure time to undesirable temperatures reached during high-temperature service, heat treatment, or joining should be minimized.

**MM-5.2.3 Castings.** When cast alloys discussed in this section solidify, microsegregation of chromium and molybdenum occurs. Segregation reduces corrosion resistance and is corrected in castings by a full solution anneal as specified by the material specification or as recommended by the material manufacturer. All cast materials shall be supplied in the solution-annealed condition, and the solution-anneal procedure shall meet the time and temperature requirements of the product specification. Any weld repair by the casting manufacturer shall meet the requirements of the specification or shall be as specified by the owner/user.

**MM-5.2.4 Copper Alloys.** In applications allowed in Part SD or approved by the owner/user, copper tubing, as listed in Table MM-2.1-4, may be used for process gas distribution systems.

**MM-5.2.5 Special Alloys.** When specified by the owner/user, alloys listed in Table MM-5.2.5-1 may be used for process contact surfaces in unique applications, such as original equipment manufacturer (OEM) process instrumentation, pump internals, etc.

<table>
<thead>
<tr>
<th>UNS Number</th>
<th>EN Designation</th>
<th>Common Name</th>
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<tr>
<td>R50250</td>
<td>Ti — Grade 1</td>
<td>Platinum (coating)</td>
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<tr>
<td>R50400</td>
<td>Ti — Grade 2</td>
<td>Gold (coating)</td>
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<tr>
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<td>Ti — Grade 3</td>
<td>Silver (coating)</td>
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<td>R56400</td>
<td>Ti — Grade 4</td>
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<td>Inconel 600</td>
<td>Inconel 718 [Note (2)]</td>
</tr>
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<td>Inconel 718</td>
<td>Inconel 600 [Note (2)]</td>
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<tr>
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<td>Inconel 718</td>
<td>17-4 PH [Note (3)]</td>
</tr>
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</table>

GENERAL NOTE: Alloys listed between horizontal lines are not equivalent, but comparable.

NOTES:
(1) Hastelloy C-2000 is a registered trademark of Haynes International, Inc.
(2) Inconel is a registered trademark of Special Metals Corp.
(3) 17-4 PH is a registered trademark of AK Steel.

NOTE TO EDITORS: The registered company name on the trademark is "Cleveland-Cliffs Steel Corporation." After approval of record 18-2271, the correction from "Cleveland-Cliffs Inc." to "Cleveland-Cliffs Steel Corporation" was made as an editorial change.
<table>
<thead>
<tr>
<th>Base Metal Alloy [Note (1)]</th>
<th>SMAW</th>
<th>Filler Metal</th>
<th>GTAW/GMAW/SAW/PAW</th>
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**GENERAL NOTE:** The use of AWS/UNS filler metal is recommended for welding of UNS base metal; the use of EN filler metal is recommended for welding of EN base metal.

**NOTES:**
(1) Alloys listed between horizontal lines are not equivalent, but comparable.
(2) Filler metal designation as per ISO 3581-A.
(3) Filler metal designation as per ISO 14343-A.
### Table MM-5.3-3

**Filler Metals for Duplex Stainless Steels**

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<th>Base Metal Alloy</th>
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</table>

**GENERAL NOTE:** The use of AWS/UNS filler metal is recommended for welding of UNS base metal; the use of EN filler metal is recommended for welding of EN base metal.

**NOTES:**
1. Alloys listed between horizontal lines are not equivalent, but comparable.
2. Any super duplex stainless steel filler metal can be used to weld any duplex stainless steel.
3. Addition of up to 5% of nitrogen to the shielding gas is recommended to aid in obtaining ferrite/austenite balance.
**Table MM-5.3-5**

**Consumable Inserts for Superaustenitic and Duplex Stainless Steels**

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GENERAL NOTE: The use of UNS consumable inserts is recommended for welding of UNS base metal; the use of EN consumable inserts is recommended for welding of EN base metal.

NOTES:
(1) Alloys listed between horizontal lines are not equivalent, but comparable.
(2) See MM-4 for listed rod, bar, or plate specifications from which these consumable inserts may be manufactured.
Resistance to corrosion is an essential characteristic of the materials used to fabricate the systems governed by this Standard. Corrosion testing is recommended when specific production performance characteristics must be determined. The owner/user shall have the final responsibility for proper material selection.

**MM-8.2 Corrosion Testing**

Corrosion testing may be performed for the following reasons:

(a) To determine the compatibility of an alloy in an atmosphere defined by characteristics such as temperature, pressure, and concentration of corrosive agent or condition.

(b) To determine the effects of process variables on material performance.

(c) To evaluate the performance of materials in various environments.

(d) To determine the effectiveness of protective coatings or surface treatments.

(e) To compare the performance of different materials or to assess the impact of a change in material.

(f) To establish performance criteria for new or existing applications.

The results of corrosion testing may be used to determine the suitability of materials for specific applications. It is important to consider the environment in which the material will be used, as well as the expected service conditions, when selecting materials.

**MM-9 MINIMUM REQUIREMENTS FOR ALLOYS IN PART MM**

**MM-9.1 General**

Metallic materials shall meet the requirements of this section as a minimum.

For materials to be added to Part MM, the information in MM-9.1.1 or MM-9.1.2, as applicable, shall be provided to the ASME BPE Staff Secretary.

**MM-9.1.1 Wrought, Cast, and Welded Fabricated Applications**

(a) Listing of the alloy in an industry-recognized specification or standard including tensile strength properties.

(b) Evidence that the proposed material, in both the wrought and welded conditions, will have corrosion resistance equal to or greater than 304L stainless steel (UNS S30403) in a service environment within the scope of this Standard. Materials that will not be welded (e.g., some castings) do not require corrosion testing in the welded condition.

(c) Welded austenitic stainless steel tube shall be capable of passing the weld decay test in ASTM A249/A249M, Supplement S7 and the intergranular corrosion test in either ASTM A270/A270M, Supplement S1 or ISO 3651-2 Method B. See Nonmandatory Appendix F for additional information.

**MM-9.1.2 Specialty OEM Material Applications**

(a) Listing of the alloy in an industry-recognized specification or standard. Tensile strength properties shall also be included unless the material is used only as a coating.

(b) Evidence that the material surface can be mechanically polished, electropolished, or passivated to meet the applicable requirements of Part SF.

(c) Recommended welding process(es), filler metal(s), and evidence showing that the combination of base metal, filler metal(s), and recommended welding process(es) meets the applicable requirements of Parts MJ and SF. Special restrictions, exceptions, or guidance shall be noted.

**Table MM-5.4-1 Solution Anneal Heat Treatment Requirements for Superaustenitic and Duplex Stainless Steels**

<table>
<thead>
<tr>
<th>Base Metal Alloy [Note (1)]</th>
<th>Solution Anneal Temperature, °F (°C)</th>
<th>Notes (2), (3), and (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNS Designation</td>
<td>EN Designation</td>
<td>Base Metal Alloy [Note (1)]</td>
</tr>
<tr>
<td>N08904</td>
<td>2,000 (1095)</td>
<td></td>
</tr>
<tr>
<td>S31254</td>
<td>2,100 (1150)</td>
<td></td>
</tr>
<tr>
<td>N08367</td>
<td>2,025 (1105)</td>
<td></td>
</tr>
<tr>
<td>N08926</td>
<td>2,010 (1100)</td>
<td></td>
</tr>
<tr>
<td>S32101</td>
<td>1,870 (1020)</td>
<td></td>
</tr>
<tr>
<td>S32205</td>
<td>1,870–2,010 (1020–1100)</td>
<td></td>
</tr>
<tr>
<td>S32750</td>
<td>1,880–2,060 (1025–1125)</td>
<td></td>
</tr>
</tbody>
</table>

NOTES:

(1) Alloys listed between horizontal lines are not equivalent, but comparable.

(2) Minimum solution anneal temperature unless range is specified.

(3) No minimum anneal time is specified, however, very short anneal times can result in inadequate time at temperature to restore the corrosion resistance of autogenous welds.

(4) Post-solution anneal cooling shall be achieved by a water quench or rapid cooling by other means.

**ASME BPE-2022**

(a) For wrought, cast and welded fabricated materials to be added to Part MM, the following information shall be provided to the ASME BPE Staff Secretary:

(b) Welded austenitic stainless steel tubing shall be capable of passing the weld decay test in ASTM A249/A249M, Supplement S7 and the intergranular corrosion test in either ASTM A270/A270M, Supplement S1 or ISO 3651-2 Method B. See Nonmandatory Appendix F for additional information.

(c) Welded austenitic stainless steel tube shall be capable of passing the weld decay test in ASTM A249/A249M, Supplement S7 and the intergranular corrosion test in either ASTM A270/A270M, Supplement S1 or ISO 3651-2 Method B. See Nonmandatory Appendix F for additional information.

(d) Evidence that the material surface can be mechanically polished, electropolished, or passivated to meet the applicable requirements of Part SF.

(e) Recommended welding process(es), filler metal(s), and evidence showing that the combination of base metal, filler metal(s), and recommended welding process(es) meets the applicable requirements of Parts MJ and SF. Special restrictions, exceptions, or guidance shall be noted.

**MM-8.2.1 Corrosion Testing**

Corrosion testing may be performed for the following reasons:

(a) To determine the compatibility of an alloy in a specific environment.

(b) To determine the effects of process variables on material performance.

(c) To evaluate the performance of materials in various environments.

(d) To determine the effectiveness of protective coatings or surface treatments.

(e) To compare the performance of different materials or to assess the impact of a change in material.

(f) To establish performance criteria for new or existing applications.

The results of corrosion testing may be used to determine the suitability of materials for specific applications. It is important to consider the environment in which the material will be used, as well as the expected service conditions, when selecting materials.
commercially supplied parts. See Nonmandatory Appendix F for additional information.

(3) Evidence that the material surface can be mechanically polished, electropolished, or passivated to meet the applicable requirements of Part SF.

(4) For sprayed or vapor deposited coatings, a recommended spraying process(es) or vapor deposition process(es). Special restrictions, exceptions, or guidance shall be noted.

(5) For welded coatings, recommended welding process(es), filler metal(s), and evidence showing that the combination of base metal, filler metal(s), and recommended welding process(es) meets the applicable requirements of Parts MJ and SF. Special restrictions, exceptions, or guidance shall be noted.
PART PM
POLYMERIC AND OTHER NONMETALLIC MATERIALS

PM-1 PURPOSE AND SCOPE
The purpose of this Part is to provide the basis for selecting and using polymeric and other nonmetallic materials.

This Part describes the types of polymeric and other nonmetallic materials and identifies different ways to characterize materials.

PM-2 MATERIALS
Polymeric and nonmetallic materials have found widespread use in bioprocessing equipment because of their broad range of physical and chemical properties, their ability to be formed into complex shapes, and their biocompatibility. Polymeric materials may be used in a range of applications including static and dynamic seals, hoses, pumps, tubing, barrier coatings, diaphragms, valves, and filters. The choice of material class depends on the design requirements and material performance, both as installed and during use.

For in-depth discussion and guidance on polymeric and nonmetallic materials, see Nonmandatory Appendix O.

PM-2.1 Materials of Construction
Materials of construction shall be selected to maintain the purity and integrity of the product/process fluid. It is the owner/user’s responsibility to select the appropriate materials of construction for the conditions of use. Materials should be compatible with the stated processing conditions, cleaning solutions (where appropriate), and sterilizing conditions (where appropriate), etc., as specified by the owner/user.

The following sections outline the major classes of polymeric and nonmetallic materials and their requirements for use in bioprocessing equipment.

PM-2.1.1 Thermoplastic Polymers. Thermoplastic polymers will melt and flow to form desired shapes when sufficiently heated. They can be melt-processed into a wide variety of shapes by molding, extruding, thermoforming, etc., and can be re-formed and shaped with heat and/or pressure.

Thermoplastic materials are often used for fittings, tubing, piping, diaphragms, seals, liners for vessels, column tubes, filter media and capsules, etc. Examples of thermoplastic polymers are shown in Table PM-2.1.1.
## Table PM-2.1.1-1
### Common Thermoplastic Polymers and Applications

<table>
<thead>
<tr>
<th>Type of Polymer</th>
<th>Example Polymers</th>
<th>Example Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>General thermoplastics</td>
<td>Polyester (PET)</td>
<td>Fittings, connectors, filter housings, piping and rigid tubing, column tubes, filter media</td>
</tr>
<tr>
<td></td>
<td>Polyamide (nylon)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polycarbonate (PC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polysulfones (PSU, PPS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polyether ether ketone (PEEK)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic polyolefins</td>
<td>Polypropylene (PP)</td>
<td>Fittings, connectors, piping and rigid tubing, filter media and capsules, bolts, vessels, vessel linings, and coatings</td>
</tr>
<tr>
<td></td>
<td>Ultra-low-density polyethylene (ULDPE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low-density polyethylene (LDPE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High-density polyethylene (HDPE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ultra-high-molecular-weight polyethylene (UHMWPE)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic fluoropolymers</td>
<td>Fluorinated ethylene propylene (FEP)</td>
<td>Fittings, piping and tubing, flexible hose, filter media and capsules, diaphragms, pumps, vessels, vessel linings, and coatings</td>
</tr>
<tr>
<td></td>
<td>Perfluoroalkoxy (PFA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polytetrafluoroethylene (PTFE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethylene tetrafluoroethylene (ETFE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polyvinylidene fluoride (PVDF)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic elastomers (TPE)</td>
<td>Blends of EPDM with polypropylene</td>
<td>Tubing, bags</td>
</tr>
<tr>
<td></td>
<td>Styrene-isoprene-styrene block polymers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copolymers of ethylene and octane</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethylene-vinyl acetate copolymer (EVA)</td>
<td></td>
</tr>
</tbody>
</table>

## Table PM-2.1.2-1
### Common Thermoset Polymers and Applications

<table>
<thead>
<tr>
<th>Type of Polymer</th>
<th>Example Polymers</th>
<th>Example Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermoset elastomers</td>
<td>Ethylene propylene diene (EPDM)</td>
<td>Tubing, seals, gaskets, diaphragms, and hoses</td>
</tr>
<tr>
<td></td>
<td>Ethylene propylene rubber (EPR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Silicone (VMQ)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluoroelastomers (FKM)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perfluoroelastomer (FFKM)</td>
<td></td>
</tr>
<tr>
<td>Rigid thermosets</td>
<td>Fiber-reinforced polymer (FRP/GRP) composites</td>
<td>Tanks and pipes</td>
</tr>
</tbody>
</table>
PM-2.2 General Requirements

Materials shall be selected to not affect the purity or integrity of the drug product. The owner/user is responsible for the qualification of materials for the intended use. The requirements for conformance are summarized in PM-2.2.1. The requirements relate to identification, traceability, biocompatibility, and marking.

Polymeric materials exposed to process fluids and/or that have a high probability of exposure shall comply to the USP directive with regard to USP <87> (or ISO 10993-5) and USP <88> Class VI (or ISO 10993-6, -10, and -11) on biological reactivity (see PM-3.1). Examples of materials that may come into direct contact with process fluids include tubing, pipe, fittings, filters, bags, gaskets, O-rings, diaphragms, pinch tubes, and valve stem seals.

PM-2.2.1 Certificate of Conformance. A Certificate of Conformance shall be issued by the manufacturer to certify conformance to this Standard when required by the end-user. Additional certification documentation may be required. The Certificate of Conformance shall contain the information summarized in Table PM-2.1.3-1.

PM-2.2.2 Labeling and Marking. Manufacturers shall mark the package containing polymer components or assemblies with the manufacturer’s name, part number, and lot number or unique identifier (see Table PM-2.1-1) to enable the manufacturer to trace back to the raw material(s) and processing conditions used to fabricate the component/assembly. Manufacturers should mark the component/assembly itself to avoid potential loss of traceability and to aid in positive identification of components/assemblies after use.

PM-2.1.3 Other Nonmetallic Materials. Solid single-phase nonmetallic materials can be divided into amorphous nonmetallic materials (e.g., glass, amorphous carbon) and crystalline nonmetallic materials (e.g., sintered silicon carbide, graphite).

If manufactured by heating and subsequent cooling, these materials are often referred to as ceramics. Materials may consist of a mixture of an amorphous and a crystalline phase (e.g., glass-ceramics). To improve performance, nonmetallic materials may be combined with other materials such as metals or polymers to form multiphase mixtures. Examples of such materials are metal-matrix composites such as cemented tungsten carbide with an alloyed nickel binder matrix and resin-impregnated carbon-graphites. Some of the more commonly used nonmetallic materials are listed in Table PM-2.1.3-1.

See next pages.
PM-2.1.1 Reference Specifications

This section provides limitations and requirements for rigid thermoplastic piping and fitting materials based on their properties. Use of these materials in piping systems is also subject to requirements and limitations in other parts of this Standard.

Standards and specifications adopted by reference in this Standard are listed by product form in this Part. When preparing a Material Test Report (MTR), a manufacturer may transcribe data produced by other organizations, provided they accept responsibility for the accuracy and authenticity of the data.

PM-2.1.2 Piping and Fittings

Piping and fittings manufactured in accordance with the following specifications may be used:

- ASTM D5575 Standard Classification System for Copolymers of Vinylidene Fluoride (VDF) With Other Fluorinated Monomers
- ASTM D6713 Standard Specification for Extruded and Compression Molded Shapes Made From Polyvinylidene Fluoride (PVDF)
- ASTM D4101 Standard Specification for Polypropylene Injection and Extrusion Materials
- ASTM F2389 Standard Specification for Pressure-Rated Polypropylene (PP) Piping Systems

PM-2.1.2.1 Listed Materials

In this section, listed materials are materials that conform to one or more specifications as defined in this Standard for piping and fitting manufactured in accordance with PM-2.

(a) Polyvinylidene Fluoride (PVDF):
PVDF material selected for the construction of pipe and fittings shall be virgin and unpigmented. All PVDF resin shall be tested in conformance with the United States Code of Federal Regulations (CFR) Title 21 Chapter 1, Part 177.2510 or 2600, Title 21 Chapter 1 Part 177.1520, USP 25 Class VI.

(b) Polypropylene (PP):
Polypropylene (PP) material selected for the construction of pipe or fittings should be either virgin (unpigmented) or pigmented. All polypropylene (PP) resin shall be of the same type and class as described in ASTM D4101 and tested in conformance with the United States Code of Federal Regulations (CFR) Title 21 Chapter 1, Part 177.1520.
(c) Other Materials: Material that is not specifically prohibited by this Standard and meets one of the following requirements shall be considered listed and acceptable:

(1) Thermoplastic materials:
   - (a) when referenced in other parts of this Standard, the material shall be used only within the scope of use in the product form permitted by the referencing text or,
   - (b) when used for pressure pipe, the material shall be documented suitable for the design pressure and temperature and conform with the requirements of this Standard.

PM-2.1.3 Limitations on Thermoplastic Materials

A thermoplastic material for pressure pipe applications should not be used at a design temperature above the maximum temperature at which the allowable stress value has been determined for the material or below the minimum temperature recommended by the manufacturer of the thermoplastic. If used outside of these limits, the designer shall have test results at the design temperature to ensure that the thermoplastic material is suitable for the intended application at the design temperature. Consult material manufacturers’ technical documentation for specific details or see ASME NM.3.3.

PM-2.1.3.1 Size or Thickness

Materials within the size or thickness limits given in this Standard should be used. If outside the limits, the material shall be in conformance with the other requirements of the specification and the designer has documented the owner/user’s acceptance for use of the material for the application.

PM-2.1.4 Marking of Thermoplastic Materials or Products

Thermoplastic materials or products marked as meeting the requirements of a material specification or multiple specifications shall be acceptable provided:

(a) one of the markings includes the thermoplastic material specification
(b) the type of thermoplastic material is permitted by this Standard
(c) all other requirements of this Standard are satisfied

PM-2.1.5 Unlisted Materials

Thermoplastic materials other than those meeting the requirements of this Standard shall be considered unlisted thermoplastic materials. Unlisted thermoplastic materials shall be used only if they satisfy all of the following requirements:

(a) The designer shall document the owner/user’s acceptance for the use of an unlisted thermoplastic material for the application.
(b) All other requirements of this Standard are satisfied.
(c) Unlisted materials shall meet a published specification covering chemistry, physical and mechanical properties, method and process of manufacture, and quality control.
(d) Unlisted materials shall be qualified for service within a stated range of minimum and maximum temperature and pressure based upon data associated with successful experience, tests, or analysis, or a combination thereof.

PM-2.1.6 Unknown Thermoplastic Materials

Thermoplastic materials of unknown specification shall not be used for piping systems or components.

PM-2.1.7 Filler Materials

Filler materials may be utilized with the materials listed above to enhance properties for uses such as gaskets and seals. Final fabricated products made with filler materials shall be in conformance with the requirements of this Standard.
testing is required, specific fluids should be used to expose test samples for the necessary time and temperature.

PM-3.9 Polymeric Surface Finish
Polymeric materials that contact surface classifications are found in Part SF.

PM-4 APPLICATIONS

PM-4.1 Single-Use Components and Assemblies
See Part SC, Part SJ, or Part SK.

PM-4.2 Piping
The following shall be considered in the design of polymeric rigid piping and tubing:

PM-4.2.1 Sizing Comparisons. Thermoplastic piping systems are available in a variety of sizing standards. Table PM-4.2.1-1 is a reference that compares the outside and inside dimensions of these standards. It is important to consider these standards when performing system sizing calculations to enhance dimensional alignment of pipe/tube inner diameters to enable stability, cleanliness, and drainability. Tube inside dimensions are critical for alignment to stainless steel systems.

PM-4.2.2 Pressure Ratings. Polymeric piping systems have varying pressure ratings depending on material and sizing standards. Valves and mechanical connections such as sanitary adapters, flanges, or thread may carry pressure ratings independent of pipe and fittings. Elevated operating temperatures will decrease overall system rating. Consult material manufacturers for specific details.

PM-4.2.3 Thermal Expansion. Polymeric materials will expand and contract with changing temperature conditions. The effect of thermal expansion shall be considered and designed for in every thermoplastic system. To compensate for thermal expansion, it is recommended to use loops, offsets, and changes in direction by using the pipe itself to relieve the stress, the integrity of the pipe system is maintained. The use of bellows or pistons is not recommended due to the formation of pockets and gaps where liquids may be held up. The amount of thermal expansion growth in a pipe system is generally calculated by the following formula:

\[
\Delta L = 12 \times L \times \alpha \times \Delta T
\]

where
\[
\Delta L = \text{change in length, in.}
\]
\[
\Delta T = \text{temperature change, } ^\circ F
\]

(U.S. Customary Units)

where
\[
L = \text{length of the pipe run, ft}
\]
\[
\alpha = \text{coefficient of thermal expansion, in./in./}^\circ F
\]

Material and temperature dependent

Typical coefficients of thermal expansion at room temperature by material type are found below. Consult the manufacturer for exact coefficient values.

(U.S. Customary Units)

FVDF 6.6 \times 10^{-5}, \text{in./in./}^\circ F
FPA 7.0 \times 10^{-5}, \text{in./in./}^\circ F
FP 8.33 \times 10^{-5}, \text{in./in./}^\circ F

(SI Units)

FVDF 1.2 \times 10^{-5}, \text{mm/m/}^\circ C
FPA 1.2 \times 10^{-5}, \text{mm/m/}^\circ C
FP 1.5 \times 10^{-5}, \text{mm/m/}^\circ C

\Delta T is the maximum (or minimum) temperature minus the installation temperature. If the installation temperature or time of year is unknown, it is practical to increase \Delta T by 15% for safety. It is not necessary or practical to use the maximum temperature minus the minimum temperature unless it will truly be installed in one of those conditions.

PM-4.2.4 System Support Criteria

PM-4.2.4.1 Support Distances. Supports shall be placed based on the spacing requirements provided by system manufacturers. Hanger distances are based on system material and as well as the specific gravity and temperature of the process media. Operating conditions of all applicable processes, including CIF and SIP, shall also be considered. Hanger spacing generally increases with system operating temperature. The placement of hangers, guides, and anchors is critical in systems exposed to thermal cycling. Hanger locations should be identified by the system engineer and laid out to allow for expansion and contraction of the pipe over its life of operation.

PM-4.2.4.2 Hanger and Clamp Types. Avoid using hangers that place a pinpoint load on the pipe when tightened. A U-bolt hanger is not recommended for thermoplastic piping. Hangers that secure the pipe 360 deg around the pipe are preferred. Thermoplastic clamps are also recommended over metal clamps, as they are less likely to scratch the pipe in the event of movement. Clamps should be evaluated to avoid rough edges that

INSERT:
Manufacturers shall provide technical documentation regarding pressure ratings per ASME NM.3.3.

See next page

REPLACE WITH INSERT #2
See next page

REPLACE WITH INSERT #3
See next page
**PM-4.2 and 4.2.1 revision**

**PM-4.2.1 Sizing Comparison.** Thermoplastic piping systems are produced in a variety of dimensional sizing standards. Schedule (e.g., 40, 80) and Standard Dimensional Ratio (e.g., SDR 11, SDR 21) are some of the most common standards used (refer to ASTM D2122, ISO 10931 and ISO 15494). Table X2-1 in Nonmandatory Appendix X2 is a reference that compares the outside and inside dimensions of these standards. It is important to consider these standards when performing system sizing calculations to enhance dimensional alignment of inner pipe diameters to enable sterility, cleanability, and drainability. Tube inside dimensions are critical for alignment to stainless steel systems.

**NOTE:** NMA X2 refers to new NMA X2 in this manuscript

**PM-4.2.4 revision**

**PM-4.2.4.1 Support Distances.** Nonrestrictive supports, which allow for axial movement and expansion and contraction of the pipe, shall be placed based on the spacing requirements provided by system manufacturers according to load, material, temperature, pipe wall thickness and diameter. Operating conditions of all applicable processes, including CIP and SIP, shall also be considered. Hanging criteria generally increase with system operating temperatures. The placement of hangers, guides, and anchors is critical in systems exposed to thermal cycling. Hanger locations should be identified by the system engineer in conformance with the recommendations found within the material manufacturers’ technical documentation, and laid out to allow for expansion and contraction of the pipe over its life of operation.
<table>
<thead>
<tr>
<th>Nominal Size System</th>
<th>SXS Tube O.D.</th>
<th>SXS Tube I.D.</th>
<th>Sch 40 O.D.</th>
<th>Sch 40 I.D.</th>
<th>Sch 80 O.D.</th>
<th>Sch 80 I.D.</th>
<th>SDR 11 O.D.</th>
<th>SDR 11 I.D.</th>
<th>SDR 21 O.D.</th>
<th>SDR 21 I.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2</td>
<td>0.5</td>
<td>0.84</td>
<td>0.61</td>
<td>0.53</td>
<td>1.05</td>
<td>0.74</td>
<td>0.79</td>
<td>0.55</td>
<td>0.74</td>
<td>0.64</td>
</tr>
<tr>
<td>3/4</td>
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<td>0.81</td>
<td>0.74</td>
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<td>1</td>
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<td>1 1/4</td>
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<td>1.36</td>
<td>1.26</td>
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<td>2.27</td>
<td>1.57</td>
<td>1.26</td>
<td>1.57</td>
<td>1.26</td>
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<td>1 1/2</td>
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<td>2.25</td>
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<td>2.29</td>
<td>5.25</td>
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<td>5.14</td>
</tr>
</tbody>
</table>
PM-4.2.5 Hose Materials. Hose assembly materials shall conform to applicable sections of SD-2.4.1.2 and PM-2.1.

(a) Biocompatibility. The biocompatibility and proper material selection shall be the responsibility of the end-user. Biocompatibility testing of candidate hose assemblies for qualification requires USP <87> (or ISO 10993-5) and USP <88> Class VI (or ISO 10993-6, -16, and -11) tests on all polymeric process contact materials. Failure of either test indicates unacceptable biocompatibility of the candidate hose assembly.

(b) Surface Finish. Surface finish of metallic and fittings shall conform to the requirements of Part 3.2.

(c) Particle Generation. Hose assembly designs should minimize wear that generates particles that could enter the process.

(d) Extractables. Hose assembly materials shall conform to the requirements of PM-3.2.

PM-4.3.3 Hose Assembly Performance. The equipment supplier should be informed of all the conditions under which the hose assembly may be expected to operate. This should include the methods, frequency, and length of cleaning and sterilization procedures. In addition to the service temperature and pressure, any parameters that may affect the hose assembly performance should be provided. The equipment supplier should inform the end-user of the life cycle expectancy and the methods that will ensure that the hose assembly operates within its design specification (e.g., routine maintenance).

PM-4.3.3.1 Service Temperatures and Pressures. Hose assemblies shall be capable of withstanding thermal and pressure cycling between the rated upper and lower temperature and pressure limits.

PM-4.3.3.2 Nonroutine Events. The complete procedure for nonroutine events such as passivation, derouging, and postconstruction cleaning should be supplied by the end-user. The supplier should inform the end-user whether the hose assembly will perform as specified during these events. The end-user should perform a risk assessment to determine if a new hose assembly is required after nonroutine events.

PM-4.3.3.3 Cleaning Systems

(a) Clean-in-Place (CIP). Hose assemblies shall be designed in accordance with SD-3.1. The hose assembly shall be installed to enable drainability (see SD-3.2).

(b) Clean-out-of-Place (COP). External surfaces of hose assemblies subject to COP shall be compatible with cleaning agents and be nonabsorbent. Hose assemblies...
PM-4.2.5 Joining of Pipe Lengths and Fittings. Design of piping layouts should minimize the number of mechanical (hygienic) connections. Fusion welded connections (e.g., noncontact infrared [IR], beadless welding) shall conform to MJ-9.3. Hygienic design of connections shall conform to SD-3.1.
PM-4.3 moved to Part MC

(Record 22-1253) PM-4.4 moved to Part MC
CHAPTER 4
DESIGN FOR MULTIUSE

PART SD
SYSTEMS DESIGN FOR MULTIUSE

SD-1 PURPOSE AND SCOPE

The purpose of Part SD is to establish design guidelines applicable to bioprocessing equipment. Wherever “equipment” is stated in this Part, it shall mean all bioprocessing equipment, components, assemblies, and systems.

The purpose of this Part is to provide requirements for the specification, design, fabrication, and verification of process equipment and systems that are fit for intended use, and to minimize risk to the product. Part SD also provides design guidelines that should be applied at the discretion of the owner/user on the basis of assessed risk to the product. Figures in this Part are intended to illustrate accepted applications of general design principles and are not intended to limit alternate designs.

The scope of Part SD encompasses requirements for equipment, process systems, and utilities that could potentially impact product quality. Specific guidance is provided for bioburden control in manufacturing processes, including design requirements for cleaning, sanitization, and sterilization of bioprocess systems.

SD-2 GENERAL GUIDELINES

All equipment and systems shall be designed according to the bioprocessing application, requirements, and specifications of the owner/user. It shall be the responsibility of the owner/user to specify the requirements for cleaning or sanitization of the equipment or system.

Following installation, to remove construction debris or foreign bodies, process contact liquid-service systems should be flushed with deionized or better-quality water or chemically cleaned, per specifications provided by the owner/user, before being placed into service. This does not apply to single-use or precleaned components.

The design shall provide for the removal of components (e.g., pumps, control valves, spray devices, instrumentation) that may be damaged by construction debris during flushing. If removal is not practical, the design shall allow for a temporary strainer installed upstream of the component, sized to catch the debris.

The pipe design and the flushing sequence, including associated variables (e.g., velocity), shall meet specifications provided by the owner/user.

SD-2.1 Containment

The containment level of the system or individual pieces of equipment should be specified and communicated by the owner/user.

The owner/user shall determine the containment level for the particular type of equipment or system, in accordance with the Centers for Disease Control and Prevention (CDC) and guidelines of the National Institutes of Health (NIH) or directives of the European Union and other applicable local codes or environmental regulations.

SD-2.2 Bioburden Control

Part SD provides recommended design features of components and equipment that should be incorporated into hygienic systems. These design elements, properly implemented and in conjunction with proper bioburden reduction measures such as CIP/SIP, enable hygienic systems to control bioburden.

It is the owner/user’s responsibility to provide the following information for the designer to determine the design features required to maintain bioburden control:

(a) the acceptable level of bioburden before, during, and at completion of a process step or sanitization interval
(b) the duration that bioburden control needs to be maintained whether in a closed-process or open-process system

This Part does not address self-sanitizing processes but does address features of continuously operated systems such as hot water-for-injection and pure steam that control bioburden by continuous heat and are considered self-sanitizing process utility systems.

SD-2.3 Bioburden Reduction

Bioburden reduction is an activity performed with the purpose of achieving a measured reduction in bioburden levels, in the equipment or product, to allowable levels.
Depending on the chosen methodology or goal, the activity may be performed prior to equipment use, between process steps, or during a process step.

(a) For process operations in multiuse systems, bioburden reduction is typically accomplished by, but not limited to

1. cleaning (with or without chemicals)
   -a) clean-in-place (CIP)
   -b) clean-out-of-place (COP)
2. steaming
   -a) steam-in-place (SIP)
   -b) autoclaving
3. dry heat
4. process heating
   -a) batch heating
   -b) pasteurization
   -c) high-temperature short-time (HTST)
   -d) ultra-high-temperature (UHT)
5. process filtration
6. chemical sanitization
   -a) ozone
   -b) vaporized hydrogen peroxide (VHP)
   -c) chlorine dioxide
   -d) other acids, bases, or solvents
7. ultraviolet light

(b) For single-use systems, where sanitization/sterilization occurs prior to product contact, bioburden reduction is typically accomplished by, but not limited to

1. gamma-sterilization
2. electron beam (E-beam)
3. ultraviolet light
4. ozone
5. ethylene oxide (ETO)

SD-2.3.1 Thermal Sanitization. This section specifies the design requirements for equipment that is sterilized or sanitized by the application of heat. Thermal sanitization includes dry heat treatment, SIP for sanitization, SIP for sterilization, steam out of place (autoclaving), hot liquid sterilization, and hot liquid sanitization.

SD-2.3.1.1 Steam-in-Place. Equipment parts and components subject to SIP should be designed and constructed to withstand continuous exposure to saturated steam at a minimum temperature of 266°F (130°C; representing 24 psig/1.65 bar under saturated steam conditions) for a duration of at least 100 hr under continuous steady-state conditions. All process contact surfaces subject to SIP shall reach the required temperatures, under the required saturated steam pressure conditions, during the SIP cycle. Executing SIP operations at temperatures exceeding 266°F (130°C) may cause degradation of elastomers or damage to other components, resulting in reduction of overall equipment life. SIP conditions that are more stringent may be imposed by the owner/user. The use of elastomers (within a piece of equipment or certain process instrumentation) that could thermally degrade during SIP shall be evaluated by the owner/user.

SD-2.3.1.1.1 Requirements. Process systems subject to SIP shall be designed to

(a) provide for air removal within the SIP boundary
(b) provide for removal of condensate within the SIP boundary
(c) be drainable in conformance with SD-2.4.3
(d) have provisions in place for verification of SIP performance
(e) have no dead legs within the SIP boundary

SD-2.3.1.1.2 Recommendations. Process systems subject to SIP should be designed to

(a) avoid concurrent steam supplies from alternate locations to prevent stagnant zones/entrained air
(b) monitor temperature and pressure at appropriate locations (e.g., vessels) that confirm saturated steam conditions within the SIP boundary
(c) monitor temperature at every SIP boundary point during performance verification
(d) enable continuous verification or periodic confirmation of the validated state
(e) maintain the integrity of the system post-SIP
(f) maintain monitored temperature points within 2°C (assuming ±0.5°C accuracy of the RTD) of each other during dwell within the SIP boundary
(g) maintain monitored temperature points within 2°C (assuming ±0.5°C accuracy of the RTD) of the corresponding saturated steam temperature for the system pressure during dwell
(h) maintain monitored temperature points above the minimum specified SIP temperature and in accordance with SD-2.3.1.1 within the SIP boundary during dwell

SD-2.3.1.2 Depyrogenation. [Reserved for future content]

SD-2.3.2 Chemical Sanitization. [Reserved for future content]

SD-2.4 Fabrication

Fabrication shall be performed in facilities where the process contact surfaces are protected from contamination. During field welding and assembly, surface contamination shall be prevented.

Systems, equipment, and components shall be cleaned with a suitable cleaning agent and covered for protection before shipment. The use of preservative fluids is not recommended.

Any process contact surfaces that require shipment with preservatives or coatings shall be

(a) mutually agreed to, in advance, by the owner/user and manufacturer
(b) clearly identified to all parties
(c) in conformance to FDA or other applicable regulations, as appropriate for the process
Following installation, to remove construction debris or foreign bodies, process contact liquid-service systems should be flushed with water or chemically cleaned, per specifications provided by the owner/user, before being placed into service. The minimum acceptable quality of water used for flushing is non-compendial purified water (e.g., reverse osmosis or de-ionized water.)

The system design should provide for the removal of components (e.g., control valves, spray devices, instrumentation) and equipment (e.g., pumps) that may be damaged by construction debris during flushing. If removal is not practical, the design shall allow for a temporary strainer/screen installed upstream of the component. Temporary strainers/screens shall be removed prior to the system being put into service.

The as-built layout of piping (e.g., pipe diameter change, blocked branches, low points, direction of slope) should be considered while specifying the flushing sequence and flushing parameters (e.g., velocity, volume, time).

The flushing procedure should specify inspection points (e.g., low points, Valve diaphragms, hygienic clamp unions, system elastomers, strainers, spray devices, temporary screens) and acceptance criteria to confirm the procedure is complete.
SD-2.4.1 Materials of Construction

(22) SD-2.4.1.1 General. Generally, materials such as stainless steels (e.g., 316-type and 316L-type alloys), duplex stainless steels, and higher alloys have proven to be acceptable. The owner/user shall be responsible for the selection of the appropriate materials of construction for the specific process. Metallic materials of construction are listed in Part MM.

When nonmetallic materials are used (e.g., polymeric materials or adhesives), the owner/user shall specify which one of these materials shall carry a Certificate of Conformance. The conformance of material shall be explicitly stated (e.g., conforming to FDA 21 CFR 177 and USP Section <88> Class VI). Polymeric materials and other nonmetallic materials of construction are listed in Part PM.

SD-2.4.1.2 Process Compatibility

(a) Materials of construction shall be capable of withstanding the temperature, pressure, and chemical corrosiveness of the process.

(b) Materials shall be compatible with the stated bioprocessing conditions, cleaning solutions, and SIP conditions, etc., as specified by the owner/user.

(c) Surfaces exposed to bioprocessing fluids, cleaning, and SIP conditions must be

(1) homogeneous in nature
(2) impervious
(3) inert
(4) nonabsorbent
(5) nontoxic
(6) insoluble by process or cleaning fluids
(7) resistant to corrosion, scratching, scoring, and distortion

(d) Materials that are in contact with bioprocessing fluids shall be identified by an industry-recognized standard (see MM-4).

SD-2.4.1.3 Surface Coatings. Clad or electroplated surface coatings, plating, and surface preparatory chemicals may be used provided approval from the owner/user has been obtained. All surface coatings shall remain intact and be tolerant to the process, SIP and CIP fluids, and temperatures, without peeling or cracking.

SD-2.4.1.4 Transparent Materials

(a) Transparent materials (e.g., glass, polymer) that are used in viewing ports shall be rated for the applicable pressure, temperature range, and thermal shock.

(b) Internally coated glass shall only be used if the coating complies with FDA regulations or another regulatory authority’s regulations and is approved by the owner/user.

(22) SD-2.4.2 Cleanability

(a) The following provisions are applicable to tubing, equipment, or systems intended to be cleaned:

(1) All surfaces shall be cleanable. Surface imperfections (e.g., crevices, gouges, obvious pits) should be eliminated whenever feasible.

(2) All surfaces shall be accessible to the cleaning solutions and shall be accessible to establish and determine efficacy of the cleaning protocol.

(3) Fasteners or threads shall not be exposed to the process, steam, or cleaning fluids. The use of threads within the process requires owner/user agreement. Bolted attachments should be eliminated whenever possible.

(4) No engraving or embossing of materials (for identification or traceability reasons) should be made on the process contact side. When markings are required on process contact surfaces, other methods of identification shall be used.

(b) The following provisions are applicable to tubing, equipment, or systems intended to be cleaned in place:

(1) Internal horizontal surfaces should be minimized.

(2) The equipment should be drainable or capable of having energy applied (e.g., pressurized gas, vacuum, heat) to remove liquid. The equipment shall be free of areas where soil or contaminants could collect. The equipment should be free of areas of low flow and velocity or impact where soil or contaminants could collect.

(3) Design of corners and radii should meet the following requirements: All internal angles of 135 deg or less on surfaces shall have the maximum radius possible for ease of cleanability. Where possible, these surfaces shall have radii of not less than \( \frac{1}{16} \text{ in.} \) (3.2 mm) except where required for functional reasons, such as the bonnet/body connection. For special cases, the radii may be reduced to \( \frac{1}{32} \text{ in.} \) (1.6 mm) when agreed to by the owner/user. When the \( \frac{1}{16} \text{ in.} \) (1.6 mm) radii cannot be achieved for essential functional reasons such as flat sealing surfaces and flow control apertures, the surfaces of these internal angles shall be readily accessible for cleaning and examination.

SD-2.4.3 Drainability

SD-2.4.3.1 General. For the purpose of bioburden control and cleaning, gravity is an effective way to enable draining. For drainability, lines should be pitched to designated points at a specific slope. Refer to Nonmandatory Appendix C for suggested method of slope measurement. For drainable piping/tubing systems, the owner/user may define the system slope in accordance with one of the designations listed in Table SD-2.4.3.1-1. Drainable piping/tubing systems shall have a continuous pitch that is equal to or greater than the slope designation. Line sections up to 10 in. (25 cm) in length (or longer with advance approval of the owner/user) that are level or have a positive slope less than the slope designation are acceptable if the section is fitting-bound.
**SD-2.4.3.1-1**

**Slope Designations for Drainable Lines**

<table>
<thead>
<tr>
<th>Slope Designation</th>
<th>Minimum Slope, in./ft</th>
<th>Minimum Slope, mm/m</th>
<th>Minimum Slope, %</th>
<th>Minimum Slope, deg</th>
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<tr>
<td>GSD0</td>
<td>Line slope not required</td>
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<td></td>
</tr>
</tbody>
</table>

**SD-2.4.3.2 Drainability Design Considerations.** The system’s process requirements should be considered in the selection of slope designation.

(a) Process contact lines exposed to liquid should be sloped to minimize pooling in the system.

(b) Lines that are steam sterilized in place should be sloped to enable condensate removal.

(c) Lines that are cleaned in place should be sloped to enable removal of cleaning fluids.

The physical characteristics of the system (e.g., line size, materials, fluid viscosity, fluid surface tension) will influence drainability at a given slope and should also be considered. The owner/user may apply additional criteria in the selection of slope designation to address issues such as product recovery or maintenance. Fluid retention due to surface tension and surface adherence should be considered when using tubing less than 3/4 in. (19 mm). System leveling should be considered for mobile equipment that is designed to be drainable.

**SD-2.4.3.3 Slope Considerations.** The recommended minimum slope designation for drainable process contact lines is GSD2.

**SD-2.4.3.4 Drain Points**

(a) Piping and equipment should be installed with designated low-point drains and high-point vents for drainability. The number of drain points and vents should be minimized. The equipment manufacturer shall indicate the proper orientation to optimize drainability. The owner/user shall ensure that proper orientation is achieved.

(b) Systems of equipment that cannot be drained should be capable of having energy applied (e.g., pressurized gas, vacuum, heat) to be drained.

**SD-2.4.4 Miscellaneous Design Details**

**SD-2.4.4.1 Lubricants**

(a) Grease and other lubricating fluids that are used in gearboxes, drive assemblies, etc., shall be contained to prevent leakage of the lubricants or process, either directly or indirectly (e.g., through seepage, seal leaks).

(b) The equipment manufacturer shall specify the type of lubricants that are to be used for maintenance. If the specified lubricant is not accepted by the owner/user, the choice of an alternative shall be agreed to by the owner/user and the equipment manufacturer.

(c) The owner/user shall give his approval for the lubricants that could come in contact with the process. These lubricants shall be identified by name, manufacturer, and grade and shall conform to FDA or other applicable regulatory codes.

**SD-2.4.4.2 Exterior Design.** Equipment located in clean areas should be periodically cleaned by wash-down or manually cleaned by wipe-down with harsh cleaning solutions. Such equipment shall conform to the following:

(a) Materials of construction should be corrosion resistant, easily maintained, cleaned, and sanitized without flaking or shedding.

(b) Finishes shall be compatible with the area/room classification as agreed to by the owner/user and manufacturer.

(c) Components shall be capable of being chemically cleaned, steam cleaned, or pressure washed.

(d) All burrs or weld marks shall be removed.

(e) Hinges should be easily removable or cleanable.

(f) Equipment mounted on cabinets that are exposed to the environment should be mounted flush.

(g) Skids should have no openings in the frame allowing water retention. Supporting skid frame structures and modules should be constructed from fully sealed tubes or pipes, which are easily cleaned. Frames should have rounded rather than sharp edges.

(h) Motors, gearboxes, and similar equipment should not retain fluids or cleaning solutions on their external surfaces.

(i) Nameplates for tagging equipment should be constructed from corrosion-resistant material, such as stainless steel or polymeric material, and should have minimal crevices. The nameplates should be cleaned and sealed or attached with a corrosion-resistant wire loop.

(j) There should be adequate clearance below or under the equipment for cleaning, and clearance for discharge should be provided. Elevated equipment under open frames should have a minimum clearance of 6 in. (150 mm) for wash-down and cleaning. In other cases a minimum of 4 in. (100 mm) would be adequate.

(k) Joints and insulation materials shall be sealed and impervious to moisture and cleaning agents.

(l) Electrical enclosures and conduit should be cleanable and use materials of construction that are compatible with cleaning agents.

(m) Painted surfaces shall be identified by the fabricator and have the advance approval of the owner/user. All painted systems shall be FDA compliant.
**SD-2.4.4.3 Surface Finishes.** The finishes of process contact surfaces shall be specified by the owner/user in accordance with the definitions of Part SF in this Standard.

**SD-2.5 Hygienic System Design**

The hygienic design of the system shall incorporate the applicable functionality for passivation, cleaning, sanitization, steam-in-place, process fluid distribution, and process parameter measurement and control. The system’s hygienic physical (general arrangement) design shall be integral with its operations including, but not limited to, valve sequencing, parameter measurement, and controls. The owner/user and designer should evaluate the design across all operations to confirm that the design mitigates contamination risk to the product and to identify installation, operational, and performance verification testing requirements.

**SD-2.5.1 Tube/Pipe Branches.** Tube/pipe branches that are closed (e.g., closed valve, capped branch tee) during an operation should be designed and installed to mitigate contamination risk. Tube/pipe branches closed during CIP/SIP operations, designed to meet the minimal dimensional and orientation criteria detailed in SD-3.1.2.2, are not dead legs if they are operated, cleaned, or sanitized under specified conditions (e.g., velocity, temperature, time). Tube/pipe branches that are open during CIP/SIP shall be designed to enable flow of cleaning/sanitizing fluids under specified conditions. Tube/pipe branches with valves that are cycled during processing operations should be designed to mitigate cross-contamination risk and are not dead legs if they are toggled, cleaned, or sanitized under specified conditions (e.g., flow/impingement, steam penetration, temperature, time).

**SD-2.5.2 Tube/Pipe Instruments.** Process tubing/piping instrumentation and associated connection points should be designed to mitigate the risk of contamination due to extended ferrule connections and any annular space around the sensor. Instrument tees or short-outlet tees conforming to DT-4.1.2 should be used wherever feasible, maintaining $L/A < 2$ [see Figure SD-3.4.3-1, illustration (a)]. When an instrument tee or short-outlet tee is not used, the tee should be oriented such that cleaning and sanitization fluids circulate into the branch and annular space around the instrument sensor, and air is not trapped, to avoid the formation of a dead leg. The system designer shall identify instrument locations where $L/A$ or $L/d < 2$ is not met.

**SD-2.5.3 Equipment Nozzles.** Equipment nozzles used to accommodate agitators, controls, instrumentation, or process fluid transfer should be designed to mitigate contamination risk due to extended connections or the annular space around the inserted appurtenance by meeting the dimensional and orientation criteria detailed in SD-3.5.1 and SD-3.4.3. Equipment nozzles closed during CIP/SIP operations shall be designed to meet the minimal dimensional and orientation criteria detailed in SD-3.4.2 and are not dead legs if they are cleaned or sanitized under specified conditions (e.g., flow/impingement, steam penetration, temperature, time).

**SD-2.6 Animal-Derived Ingredients**

Process contact surfaces of components, equipment, and systems shall be constructed from and processed with materials that are free from animal-derived ingredients/products (ADI/ADP), or shall be manufactured with materials that meet the conditions of the Committee for Medicinal Products for Human Use (CHMP, formerly known as CPMP) Note for Guidance (EMEA/410/01 rev 3).

**SD-3 PROCESS COMPONENTS AND EQUIPMENT**

**SD-3.1 Connections, Fittings, and Piping**

**SD-3.1.1 General**

(a) Design of equipment or systems shall meet the number of connections. Butt-welded connections should be used wherever practical.

(b) Connections to equipment shall use acceptable hygienic design connections, mutually agreeable to the owner/user and manufacturer.

(c) All connections shall be capable of CIP and SIP.

(d) Ferrules and ferrule connections should not constitute a dead leg. The use of short welding ferrules should be incorporated into the design to promote enhanced cleanliness or bioburden reduction of the system.

(e) Process contact fittings exposed to liquid should be drainable when properly installed.

(f) Threaded fittings, exposed to process fluid, are not recommended (see Figure MC-2.2.2-5).

(g) The use of flat gaskets may be acceptable, when agreed to by the owner/user and manufacturer, for applications where it is considered self-sanitizing (i.e., in pure steam distribution systems).

(h) The centerline radius of factory-bent tubes shall be in accordance with Table DT-3-1, CLR, (R).

(i) Piping systems described in Part SD refer to hygienic tubing systems. Caution should be exercised if using pipe (instead of tube) to ensure that the requirements of this Standard are met. The requirements of hygienic tubing (e.g., surface finish, dimensions, and tolerances) are not typically met by pipe.
SD-3.1.2 System Design

SD-3.1.2.1 General

(a) Product holdup volume in the system should be minimized.

(b) Bioprocessing piping and tubing design should have routing and location priority over process and mechanical support systems.

(c) Piping and connections to in-line valves should be of all-welded construction where feasible, practical, and agreed to by the owner/user and manufacturer. To ensure the highest degree of hygienic design, the piping systems should use welded connections except where make-break connections are necessary.

SD-3.1.2.2 Closed Tube/Pipe Branches. Closed tube/pipe branches will be measured by the term \( L/d \), where \( L \) is the leg extension from the I.D. wall normal to the flow pattern or direction, and \( d \) is the I.D. of the extension or leg of a tubing fitting or the nominal dimension of a valve or instrument. For valves, \( L \) shall be measured to the seal point of the valve. Tables SD-3.1.2.2-1 and SD-3.1.2.2-2 indicate \( L/d \) values based on the BPE definition for various tubing geometries and configurations.

There is evidence that an \( L/d \) of 2 or less may prevent the branch from being a dead leg; however, the size and shape of the branch are also important in determining if the branch could lead to contamination. With sufficient flow through a primary pipeline, a branch may not constitute a dead leg.

The orientation of a branch is critical to the cleanability of the system. The branch shall be oriented to avoid a dead leg (e.g., a vertical branch with an \( L/d \) of 2 or less may still result in a dead leg with trapped gas or residual materials).

For high-purity water systems, an \( L/d \) of 2 or less is attainable with today’s manufacturing and design technology. For other bioprocessing systems, such as purification, filtration, and fermentation having cluster, block, and multiport valves, an \( L/d \) of 2 or less is achievable. However, it may not be achievable with certain equipment and process configurations as they are currently manufactured. An \( L/d \) of 2 or less is recommended but shall not be construed to be an absolute requirement. The system designer and manufacturer shall make every attempt to eliminate system branches with an \( L/d \) greater than 2. It will be the responsibility of the system manufacturer or designer to identify where exceptions exist or where the \( L/d \) of 2 or less cannot be met.

An \( L/d \) of 2 or less may not be achievable for weir-type valves clamped to tees and certain sizes of close welded point-of-use valves, as shown in Figure SD-3.1.2.2-1, illustrations (a), (d), (e), and (f). For the header and valve size combinations where the \( L/d \) of 2 cannot be met using these configurations, a specific isolation valve design, as shown in Figure SD-3.1.2.2-1, illustrations (b) and (c), may be required to achieve the desired ratio.

### Table SD-3.1.2.2-1

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<th>Nominal Size, in.</th>
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<th>I.D. (( d ))</th>
<th>Branch, ( L )</th>
<th>( L/d ) (Branch)</th>
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<td>0.109</td>
<td>5.782</td>
<td>4.24</td>
<td>0.73</td>
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</table>
Figure SD-3.1.2.2-1
Accepted Point-of-Use Designs

Notes:
(1) \(L/d\) of 2 or less.
(2) \(L/d = 0\) (preferred).

ASME BPE-2022
\( L/d \approx 0 \)
All process contact O-rings, gaskets, and shaft seals shall conform to Part MC.

If a pressure relief device is used, it shall be of hygienic design in conformance with SD-3.15.

**SD-3.4 Vessels**

**SD-3.4.1 General.** This section defines the requirements that are to be met in the design, fabrication, and supply of pressurized and nonpressurized biopharmaceutical vessels.

- **Design and fabrication of vessels and internal components shall ensure that surfaces are free of edges, crevices, pockets, and other surface irregularities.** If more restrictive tolerances are required, they shall be included as part of the fabrication specifications for the project.

- **All heat transfer surfaces should be drainable and ventable.**

- **Reinforcing pads, doubler plates, poison pads, etc., should be constructed of the same material as the vessel.** These components should be installed on non-process contact surfaces. No telltale holes are allowed on process contact surfaces.

- **Vessels that are to be exposed to temperatures above 80°C (e.g., SIP, hot water-for-injection, S. Pharmacopeia (USP) waters, and hot CIP solutions) should be designed for full vacuum service (maximum allowable working pressure—external of 15 psig (1 barg)).**

- **Top and bottom heads on vessels that are cleaned in place shall be drainable.** Dished heads such as torispherical (e.g., ASME flanged and dished (F&D), 80:10 F&D), elliptical, and hemispherical are the most common types. Flat or conical heads should slope at not less than \( \frac{1}{8} \) in./ft (10 mm/m) to a common drain.

- **Drain valves should be drainable, designed with a minimum branch \( \frac{L}{d} \), sized, and installed to enable vessel drainability for all operations.**

- **Sample valves shall be designed and installed in accordance with SD-3.11.**

- **All nozzles should be flush and radiused with the interior of the vessel except where projections are required to ensure additives are directed into the process fluid (e.g., chemical addition) (see Figure SD-3.4.2-5).**

- **Flanges for bottom, centerline-mounted agitators should be designed in accordance with Nonmandatory Appendix EE (see EE-3.3).**
Figure SD-3.4.2-2
Side and Bottom Connections

NOTES:
(1) If a flat gasket is used, mismatch of diameters can result in crevices.
(2) Telltale hole required.
**SD-3.4.3 Internal Components**

(a) Sparger and dip tubes shall be designed in accordance with SD-3.4.1(a), SD-3.4.1(d), SD-3.4.1(f), and SD-3.4.1(g). Sparger and dip tubes shall incorporate low-point drains [where applicable, i.e., horizontal lines should slope at not less than \(\frac{1}{8}\) in./ft (10 mm/m)] and be properly supported to ensure drainability. Refer to Table SD-2.4.3.1-1 to determine the appropriate slope designation.

(b) Dip tubes and spargers mounted in the nozzle neck should have an annular space between the O.D. of the dip tube or sparger and the I.D. of the nozzle neck in accordance with Table SD-3.4.3-1. An \(L/A\) of 2 or less is recommended (see Figure SD-3.4.3-1, illustration (a)). If a larger \(L/A\) exists, a method for cleaning this space shall be specified. In all cases, sufficient annular space to allow access for CIP coverage shall be provided.

(c) Dip tubes shall be designed for CIP or cleaning out of place (COP). Spargers should be designed for CIP. Where the sparging device cannot be CIP’d, the device shall be removable for COP or replaceable.

(d) Removable dip tubes and spargers shall be designed to ensure that the installation orientation conforms with the design intent.

(e) Spray devices shall meet the requirements of SD-3.9.

(f) Internal support members shall be solid, rather than hollow, because hollow support members have a higher risk of fatigue and contamination problems (see Figure SD-3.4.3-2).

(g) Mitered fittings for internal pipe work should be avoided. When mitered joints are used, they shall be designed and fabricated in accordance with the appropriate codes.

<table>
<thead>
<tr>
<th>Dip Tube Size Tube O.D.</th>
<th>Mount Nominal Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>in.</td>
<td>mm</td>
</tr>
<tr>
<td>(\frac{1}{2})</td>
<td>12.7</td>
</tr>
<tr>
<td>(\frac{3}{4})</td>
<td>19.1</td>
</tr>
<tr>
<td>1</td>
<td>25.4</td>
</tr>
<tr>
<td>1 (\frac{1}{2})</td>
<td>38.1</td>
</tr>
<tr>
<td>2</td>
<td>50.8</td>
</tr>
<tr>
<td>2 (\frac{1}{2})</td>
<td>63.5</td>
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<td>3</td>
<td>76.2</td>
</tr>
<tr>
<td>4</td>
<td>101.6</td>
</tr>
</tbody>
</table>

**SD-3.4.4 Fabrication**

(a) Weld joint designs shall conform to MJ-3.2. For process contact surfaces, butt joints should be used and the use of lap joints should be minimized. Intermittent welds shall not be used on process contact surfaces.

(b) Flanges are not recommended for process contact applications, and their use should be minimized. The bore of weld neck flanges shall be the same as the I.D. of the connected components to prevent ledges and nondrainable areas.

(c) Where slip-on flanges are used, the process contact fillet weld shall be designed for drainability and CIP.

**Table SD-3.4.3-1**

**Annular Spacing Recommendations for Hygienic Dip Tubes**

**SD-3.4.5 Finishes**

(a) Surface finishes shall be specified in \(R_a\) values (see Table SF-2.4.1-1).

(b) Process contact surface finish specifications shall pertain to all the wetted or potentially wetted surfaces (e.g., vapor space, nozzle necks, agitators, thermowells, dip tubes, baffles).

(c) The polishing of a connection face, body flange, etc., shall extend up to the first seal point.

**SD-3.4.6 Sight Glasses**

(a) Sight glasses on vessels should be designed with reference to SD-3.4.2(a). Sight glasses on vessels should be designed with the smallest \(L/d\) possible and incorporate cleanable O-ring designs when applicable (see Figure SD-3.4.6-1).

(b) Refer to PI-9.1.2.3 for additional sight glass requirements.

(c) Surface finish for the metal frame shall meet the requirements of Part SF in this Standard.

(d) Sight glasses shall be marked with the glass type, maximum pressure, and temperature rating per DT-11.1 and DT-11.1.1.

(e) Part MC requirements shall be met when mounting a sight glass.

(f) Preferred sight glass mountings are shown in Figure SD-3.4.6-1.

**SD-3.4.7 Portable Vessels**

(a) Casters shall be cleanable and compatible with cleaning solutions used for external cleaning.

(b) Casters should be designed for the environment in which the vessel will be used.

(c) Portable vessels should be designed to resist overturning during normal operating conditions.

(d) Flexible hoses used to connect portable vessels shall meet the requirements of SD-3.2.

(e) Provisions for static grounding should be evaluated and incorporated into the vessel design, if required. The connections for static grounding should be designed to be cleanable.
in use (e.g., chromatography system that is filled with sodium hydroxide solution between uses).

(c) The flow direction and required orientation for drainability should be clearly identified on the device. Where the valve is integral to equipment (e.g., diaphragm pumps, homogenizers), indication of the flow direction is not required.

(d) The use of check valves with springs in product contact should be avoided. The owner/user should determine whether check valves that use a spring are acceptable for other process contact applications. Applications where spring check valves are typically acceptable include condensate removal lines and dry process gases.

(e) Check valve design shall conform to MC-3.3.2.3.

SD-3.14 Orifice Plates

Orifice plates, when required and used in hygienic piping systems, shall be installed in a drainable position.

SD-3.15 Relief Devices

(a) Rupture disks (or other hygienic pressure relief devices approved by the owner/user) shall be installed in a hygienic manner without compromising the safety or efficiency of the system.

(b) The cleaning system design shall ensure that the rupture disk (or other hygienic pressure relief devices approved by the owner/user) will not be damaged by the cleaning process (e.g., mechanical forces, chemical compatibility).

(c) Rupture disk (or other hygienic pressure relief devices approved by the owner/user) installation shall conform to the $L/d$ ratios mentioned in SD-3.1.2.2.

(d) Rupture disks shall be installed in the manufacturer’s recommended holder to ensure proper functionality and cleanliness.

(e) Relief devices, including discharge piping, shall be installed in conformance to applicable codes (e.g., flammable liquids and combustibles in accordance with NFPA 30).

(f) Pressure relief valves that are used in product contact applications shall meet the requirements of MC-3.3.2.3(a) on both sides of the valve seat. Crevices and holdup volumes should be minimized.

(g) Safety pressure relief valves that are used in product contact applications shall meet the requirements of MC-3.3.2.3(a) up to the valve seat.

(h) Pressure and safety pressure relief valves shall be installed in a manner that permits draining on both the process and discharge sides of the valve seat.

(i) Pressure relief valves that are used in product contact applications shall be CIP capable. If required for CIP or SIP, an override that allows flow through the valve shall be included.

(j) Pressure relief valves that are used in product contact applications shall conform to MC-3.3.2.3.

SD-3.16 Liquid Pressure Regulators

(a) Regulators should be installed to be drainable through the outlet or inlet ports.

(b) There shall be no voids or crevices within the area wetted by the fluid. Regulator designs, where a portion of the valve stem penetrates the sensing diaphragm, shall be avoided unless provisions are made to avoid entrapment of foreign matter and any leakage through the interface between stem and diaphragm, especially after SIP.

(c) Due to the inherent design characteristics of self-contained regulators, manual means of override may be required to allow for cleaning and draining.
**SD-3.17 Strainers**

**SD-3.17.1 General.** Strainers as described in this section are intended for process component and equipment protection (see Figure SD-3.17.1-1) and are not designed for bioburden control. Strainers are permitted in locations where they reduce the risk of contamination of a process (e.g., CIP return line).

**SD-3.17.2 Design and Manufacture**

(a) Strainers intended for single-direction flow shall have the flow direction indicated on the strainer body.

(b) The strainer body should have the same surface finish as specified for the process piping or equipment in which it is being installed.

(c) Surface finish achievement or measurement may not be possible for all areas of straining surfaces (e.g., strainer element holes, openings, or mesh).

(d) For strainers in-line within process piping, the manufacturer should state the operating flow coefficient, \(C_v\), when free of solid particulate loading and maximum allowable pressure drop.

(e) Strainer body design features (e.g., sight glasses) shall not create a dead leg.

**SD-3.17.3 Selection, Installation, and Operation**

(a) Perforated strainer elements that are free of crevices are preferred for use in permanent hygienic installations. Where perforated strainers cannot be
used, the use of other types of strainers (e.g., wire mesh, wedgewire) is permitted if the risk of contamination to the process is mitigated.

(b) When specifying strainer elements, the owner/user should provide strainer element hole/mesh size and allowable pressure drop at a given flow across the strainer element and body when free of solid particulate loading.  

(c) Strainers shall have field tagging (e.g., ID tag, engraving) to ensure external visual identification post-installation.  

(d) The installed strainer shall allow for removal of the element for inspection or cleaning.  

(e) Strainers shall be drainable when free of solid particulate loading and installed in the recommended orientation.  

(f) The design or installation of the strainer within the system should enable detection and removal of captured solid particulates (e.g., visual inspection or pressure differential monitoring).  

(22) SD-3.18 Chromatography Columns

SD-3.18.1 General. This section defines typical design elements related to large-scale chromatography columns and includes columns that are intended for repeated use in processing. Although chromatography processes are not typically aseptic, design features for cleaning and/or sanitization should be considered. More information on chromatography columns can be found in Nonmandatory Appendix T.

SD-3.18.2 Pressure-Retaining Parts. The column tube is both a product contact surface and a pressure-retaining component. Chromatography columns are vessels operating under pressure and should meet the requirements of ASME PBVC, Section VIII, as referred to in GR-1, as applicable. If the column tube is acrylic, it shall comply with ASME PVHO-1, Case 14, Low UV. The owner/user is responsible for informing the manufacturer of the conditions under which the column may be expected to operate. This shall include the methods, frequency, and duration of cleaning and sanitization procedures. In addition to the service temperature and pressure, any parameters that may affect the column performance shall be provided.

SD-3.18.3 Design for Cleaning and Sanitization

SD-3.18.3.1 Cleaning. Columns should be designed in accordance with SD-2.4.2 with the exception of the bed supports and flow distributor. Cleaning of chromatography columns is achieved by control of contact time and concentration of the appropriate cleaning agents.

SD-3.18.3.1.1 Seals. All seals shall conform to Part MC.

SD-3.18.3.1.2 Exterior Surfaces. Exterior surfaces of columns shall be nonabsorbent and compatible with cleaning agents. Columns shall be designed to allow effective removal of cleaning agents from surfaces.

SD-3.18.3.2 Sanitization

SD-3.18.3.2.1 Chemical Sanitization. All product contact surfaces within the system shall be compatible with the sanitization agents selected.

SD-3.18.3.2.2 Thermal Sanitization. When thermal sanitization is used, all column product contact surfaces shall be designed to accommodate expansion and contraction during exposure and cooldown stages.

SD-3.18.4 Column Materials. Column materials for all product contact surface wetted parts shall conform to application sections of Parts SD, PM, and SF.

SD-3.18.5 Column Performance.

SD-3.18.5.1 Service Temperature and Pressure. Columns shall be capable of withstanding thermal and pressure cycling between the rated upper and lower temperature and pressure limits.

SD-3.18.5.2 Routine Maintenance. To ensure continued column performance, the accessibility of all column components for routine maintenance shall be considered.

SD-3.18.6 Conformance Requirements

SD-3.18.6.1 General Requirements. A unique identifier shall be indelibly marked on the column or the column’s support structure. The unique identifier shall enable the owner/user to identify the supplier and the supplier to identify the raw material and processing conditions used to fabricate the article.

SD-3.18.6.2 Certificate of Conformance. A Certificate of Conformance shall be issued by the column manufacturer to certify conformance to this Standard when required by the owner/user. The Certificate of Conformance shall contain the following information:

(a) manufacturer’s name
(b) unique identifier of the column
(c) material of process contact items
(d) compliance to USP <87> Class VI (or ISO 10993-5) and USP <88> (or ISO 10993-6, -10, and -11) Also see Table PM-2.2.1-1.
SD-3.19 Multi-Use Rigid Polymeric Vessels

SD-3.19.1 General

This section defines requirements for the design, fabrication, and use of multi-use rigid polymeric pressure and non-pressure rated vessels in process contact applications.

(a) Design and fabrication of polymeric vessels shall conform to the requirements of SD-3.4.1.

(b) Polymeric vessels are fabricated utilizing weldless technologies (e.g., molding) or material joining methods. The manufacturer shall select a material joining method that meets the specified design criteria. The acceptance criteria for polymeric vessel welds shall be agreed upon by the manufacturer and the owner/user.

SD-3.19.2 Polymeric Materials

Thermoplastic polymeric materials are described in PM-2.1.1. Examples of thermoplastic polymers commonly used in bioprocessing applications are listed in Table PM-2.1.1-1.

The polymeric material shall be selected with consideration for operating temperature, composition of all fluids in contact with the polymer including cleaning agents, purity requirements, sanitization, and sterilization techniques.

Polymeric vessels shall be constructed of materials that

(a) provide adequate strength and durability to withstand continuous or cyclic stressors (e.g., thermal, pressure) as specified for design.

(b) do not directly or indirectly affect the purity or integrity of the product.

(c) conform to the biocompatibility requirements described in PM-3.1.

The owner/user should assess the intended use of process contact materials, as outlined in PM-2.2.

SD-3.19.3 - Operating Conditions

Polymeric vessels shall be designed with consideration for

(a) Extractables and leachables, in accordance with PM-3.2.

(b) Chemical compatibility, in accordance with PM-3.3.

(c) Operating conditions of all applicable processes, including CIP and SIP.

(d) Physical and mechanical properties, in accordance with PM-3.3.

SD-3.19.4 – Surface Finish

The surface finishes for the process contact surface of the vessel, tubing, and internal components shall be measured as required by Part SF and conform to values designated in Table SF-3.4-1. Acceptance criteria shall conform to Part SF.

The non-process contact surface finishes of the vessels located in clean areas shall meet the requirements of SD-2.4.4.2.
(22) SD-4 PROCESS UTILITY SYSTEMS

SD-4.1 Compendial Water Systems

(a) Compendial water systems, such as USP Grade Water-for-Injection (WFI), USP Grade Purified Water (PW), and Highly Purified Water (HPW), shall be designed as looped circulatory systems, rather than noncirculating, dead-ended, branched systems.

(b) Loops shall be designed to provide fully developed turbulent flow in the circulating sections and to prevent stagnation up to the weir of each point-of-use valve.

SD-4.1.1 Compendial Water Generation

(a) All surfaces that shall come into direct contact with the compendial water, feed water, or condensate/blowdown produced by the units shall be constructed of 316- or 316L-type stainless steel or other material as specified by the owner/user.

(b) Connections to the compendial water, feed water, or condensate/blowdown compendial water by the units shall be made by the use of hygienic design fittings. All fittings should be constructed in such a manner as to avoid dead legs and crevices.

(c) Units should be drainable and should not contain areas where agents used to clean, descale, or passivate the units are trapped or not easily flushed during rinsing operations.

SD-4.1.2 Compendial Water Distribution Systems

SD-4.1.2.1 Point-of-Use Piping Design for Compendial Water Systems. Point-of-use (POU) can be defined as a location in a compendial water loop where water is accessed for processing or sampling. Typically, the point-of-use assemblies are composed of the following elements:

(a) piping associated with a compendial water loop at the physical POU

(b) POU valves, equipment, and instruments

Additional process components and equipment may be added to satisfy any application or system requirements and will be discussed further in this Part (see Figure SD-4.1.2.1-1).

SD-4.1.2.2 Critical Design Criteria for Point-of-Use Assemblies

(a) All point-of-use assemblies should be designed to enable draining through the POU valve.

(b) Assemblies shall be designed for sanitization (e.g., hot flush, SIP).

(c) Valves used in POU applications should be welded into the water distribution loop where possible. Current industry designs are available to achieve an L/d of 2 or less (see SD-3.1.2.2).

(d) Sample valves should be integral to the design of the primary valve and should not constitute dead legs.

(e) Sample valves should be installed only as needed on the main loop.

(f) Sample valves should be installed where water is used for the process to demonstrate water quality compliance to compendial monographs.

(g) Any valve used to provide clean utility services to the POU assembly (e.g., steam or clean gas) should be fabricated in such a manner as to achieve an L/d of 2 or less downstream from the primary POU valve [see Figure SD-4.1.2.1-1, illustrations (a) and (c)].

(h) The length of tubing from POU valves to process equipment should be minimized [see Figure SD-4.1.2.1-1, illustrations (a) and (b)].

(i) If evacuating the system is not possible, appropriate porting of the primary POU valve should be accomplished to facilitate sanitation.

(j) When heat exchangers are used as POU coolers [see Figure SD-4.1.2.1-1, illustration (c)], the design shall conform to SD-3.6.

(k) Physical breaks shall be employed between hoses, drain valves, or any other component leading to drains or sinks to avoid back-siphoning into the POU assembly [see Figure SD-4.1.2.1-1, illustrations (d) and (e)]. The distance H of the physical break should be at least twice the inner diameter of the hoses, drain valves, or any other component leading to drains or sinks to avoid back-siphoning into the POU assembly. The break shall be at least 1 in. (25 mm) for hoses, drain valves, or other components with internal diameters less than or equal to ½ in. (13 mm) (see Figure SD-4.1.2.2-1).

(l) Tubing and other piping materials should be a minimum of ⅜ in. (19 mm) in diameter to enable draining of water after use.

(m) POU assemblies shall be drainable as indicated in SD-2.4.3.

(n) A POU may include a venturi or orifice plate, if the restriction of water flow is required. Where used, the additions of these components will require a blowdown to enable drainability.

(o) When compendial water systems are reconstructed of metallic materials, the surface finish should be less than or equal to 25 μin. Rₐ or 0.6 μm (see Part SF) and may be internally electropolished. All 316L-type internal surfaces shall be passivated.

(p) When compendial water systems are constructed of polymer materials, the surface finish should be less than or equal to 25 μin. Rₐ or 0.6 μm.

SD-4.2 Clean/Pure Steam Systems

This section is applicable to both clean and pure steam systems.

SD-4.2.1 Clean/Pure Steam Generation

(a) All surfaces that come into direct contact with the clean/pure steam, feed water, or condensate/blowdown produced by the units shall be constructed of 316- or
Figure SD-4.1.2.1-1
Point-of-Use Piping

(a) Hard Piped to Equipment

(b) Direct Connect to Equipment

(c) Integral Heat Exchanger

(d) Sink

(e) Hose
316L-type stainless steel or other material as specified by the owner/user.

(b) Connections to the clean/pure steam, feed water, or condensate/blowdown produced by the units shall be made by the use of hygienic design fittings. All fittings should be constructed to be free of dead legs and crevices.

(c) Units should be drainable and should not contain areas where agents used to clean, de-scale, or passivate the units are trapped or not easily flushed during rinsing operations.

SD-4.2.2 Clean/Pure Steam Distribution System

(a) The distribution system shall have adequate provision to remove air during start-up and normal operations. The use of air vents installed at locations where air is likely to be trapped, such as at the ends of steam headers, can assist in this requirement.

(b) The horizontal distribution lines should be sloped in the direction of flow as indicated in SD-2.4.3. Where necessary, increases in height should be achieved by vertical risers (see Figure SD-4.2.2-1).

(c) Adequate provision should be made to allow for line expansion and to prevent sagging of the distribution lines, so that lines are drainable.

(d) Distribution systems shall not be directly connected to any nonhygienic steam systems (e.g., plant steam systems).

(e) Trap legs for the collection of condensate from the steam distribution system should be of equal size to the distribution line for sizes up to 4 in. (100 mm), and one or two line sizes smaller for lines of 6 in. (150 mm) or larger. These shall be trapped at the bottom. The line size reduction can be made after the branch to the trap leg (see Figure SD-4.2.2-2).

(f) Trap legs should be installed at least every 100 ft (approximately 30 m), upstream of control and isolation valves, at the bottom of vertical risers, and at any other low points.

(g) Condensate systems shall be designed to drain to and from steam traps. The use of overhead, direct-coupled, pressurized condensate return systems should be avoided (see Figure SD-4.2.2-2).

(h) Where possible, all components within the distribution system should be drainable.

(i) Dead legs should be avoided by design of runs and the use of steam traps to remove condensate (see Figures SD-4.2.2-1 and SD-4.2.2-2).

(j) Branches and points-of-use should be routed from the top of the steam header to avoid excessive condensate loads at the branch (see Figure SD-4.2.2-2).

(k) Sampling points for clean/pure steam should be located to collect representative sample(s) of the system (e.g., generator outlet, distribution header ends, critical points-of-use, autoclaves, or SIP stations).

SD-4.2.3 Clean/Pure Steam Valves. This paragraph covers isolation, regulation, and control valves that are part of the steam system and are subject to continuous steam service.

(a) Valves for steam service shall be drainable.

(b) Ball valves are an acceptable industry standard for isolation purposes on continuous steam service. Three-piece-body ball valves should be used instead of single-body designs for both cleanability and maintainability. The bore of the ball valve assembly shall match the inside diameter of the tube (see Figure MC-2.3.1.3-1).

(c) All components shall be suitable for continuous steam service at the temperatures and pressures specified by the owner/user.

(d) Requirements for operation under CIP and SIP conditions [see MC-3.3.2.3(a)(10) and MC-3.3.2.3(a)(12)] can be relaxed when agreed to by the owner/user.

(e) Secondary stem seals with telltale connections are not required for steam service.

(f) Valves shall be accessible for maintenance.

SD-4.3 Process Gases

SD-4.3.1 Process Gas Distribution Systems. For this section, a process gas distribution system is one that extends from the bulk supply source (including cylinders) to the points of use as defined by the owner/user.

(a) The installation of process gas delivery and distribution systems for use within the scope of this Standard requires appropriate selection of piping materials. All components shall be supplied or rendered both hydrocarbon free (e.g., oil free) and particulate free prior to installation and use.

(b) For materials of construction, the owner/user shall specify all materials. When copper is used, it should be hard drawn and installed in accordance with the...
Provide steam traps
(a) where line transitions from horizontal to vertical (at the bottom of the vertical riser)
(b) at least every 100 ft (30 m)
(c) at end of each header or branch
(d) at thermal expansion loops or transitions
(e) where steam is sampled
The current edition of NFPA 99, Chapter 5. When copper is specified in a clean room or area, the owner/user shall confirm that all planned cleaning and sanitizing agents are compatible with copper and all materials of construction. When stainless steel tubing is specified, the materials of choice are 304L-type or 316L-type alloys. Orbital welding is the recommended joining method. Inside clean rooms, the materials of choice are 304L-type or 316L-type stainless steel tubing and fittings. The owner/user and manufacturer shall agree on all joining methods, levels of inspection, and acceptance criteria for all joints prior to installation.

(c) Compression fittings may be used for valves, regulators, mass flow controllers, and other instrumentation systems at the source and within system boundaries.

(d) Gas systems are not designed or configured with the intent or provisions to be cleaned, passivated, or chemically treated after installation. Features such as slope, high-point vents, and low-point drains need not be incorporated into these systems.

(e) There shall be no nonvolatile residue. The system design shall ensure that gas will remain pure throughout its delivery.

(f) It is important to select appropriate prefilters and final system filters. The final point-of-use gas purity shall conform to the process requirements.

(g) Gas systems testing and sampling shall conform to 21 CFR 211 and ICH Q7 (International Conference on Harmonization, Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients).

SD-4.4 Process Waste Systems

This section addresses process waste systems because the reliable function of the waste system can reduce the risk of contamination to the process. By designing systems that can be cleaned and rendered safe for access and preventive maintenance, reliable operation may be achieved.

SD-4.4.1 General. The manufacturing of biologics generates liquid waste in various quantities that may or may not contain viable microorganisms. The liquid waste comes directly from the process fluids and may include cleaning solutions mixed with product components, buffers, or media.

The performance of process waste treatment systems may benefit from the sanitary design requirements of Part SD. The design of the process waste transfer line(s) shall prevent process waste backflow to the process system(s), reducing the risk of contamination.

The effectiveness and safety of process waste treatment systems have been shown to benefit from incorporating the design principles of Part SD. This is true of bio-
inactivation systems where heat or chemical dosing is used, or where biosafety containment is required.

SD-4.4.2 Bio-Inactivation Systems. Depending on the type of waste, the treatment method is chosen based on effectiveness, efficiency, and jurisdictional requirements. The owner/user shall define the inactivation conditions and verify the effectiveness of the system with respect to these requirements. Bio-inactivation may be designed to be continuous or batch type and is achieved using one or more of the following methods:

(a) thermal
(b) chemical
(c) radiation

The system design should minimize fouling and buildup of solids and films. Bio-inactivation systems should be cleanable to allow safe disassembly and maintenance. Where biosafety containment is a requirement, the system shall be sanitizable.

In bio-inactivation systems, piping design features specified in SD-2 and SD-3 may help in achieving proper and repeatable operation of these process waste systems.

SD-5 PROCESS SYSTEMS

SD-5.1 Bioreactors and Fermentors

SD-5.1.1 General. For this section, the terms “fermentors” and “bioreactors” are interchangeable. A bioreactor or fermentor shall be defined as a vessel-based system used in the growth of microorganisms or plant, mammalian, or insect cells.

SD-5.1.4 System Design

SD-5.1.4.1 Inlet Gas Assembly. The inlet gas assembly shall be defined as a piping assembly that has the ability to deliver controlled amounts of filtered gases to a bioreactor vessel. The assembly shall include but is not limited to the items in SD-5.1.4.2 through SD-5.1.4.5.

SD-5.1.4.2 Flow Control Devices

(a) Flow control devices (e.g., rotameters, mass flow controllers, and modulating control valves) shall be installed outside of the sterile boundary; therefore, requirements within this section may not apply. However, provisions shall be included within the design to prevent instrumentation damage due to SIP procedures and backflow.

(b) Flow control devices should be sized to prevent a vacuum condition, or a provision to bypass the flow control device shall be provided to maintain positive pressure in the vessel.

SD-5.1.4.3 Inlet Filter Assembly

(a) For this section, an inlet filter shall be defined as a filter element installed in a housing of suitable material. The inlet filter assembly shall be defined as the filter(s) local to the bioreactor.

(b) Inlet filter assemblies shall be designed for SIP with provisions to remove entrapped air and condensate.

(c) If multiple inlet filters are used in series, then the filter assembly closest to the bioreactor shall be a sterilizing filter.

(d) Provisions shall be made for integrity testing of the inlet filter assembly in situ or out of place.

(e) If one or more inlet housings are included in a cleaning circuit, the filter element or elements shall be removed prior to introduction of cleaning solutions.

(f) Gas filters should be installed above the bioreactor liquid level.

SD-5.1.4.4 Gas Sparging Assemblies

(a) Spargers shall be defined as mechanical devices normally located below an impeller for introducing gases within a charged bioreactor. This section applies to sparge lances, wands, rings, and other devices (see Figures SD-5.1.4.4-1 through SD-5.1.4.4-4) that may be mounted in the bioreactor vessel to introduce various gas streams for process operations. Sparge device assemblies shall meet the requirements of SD-3.4.2.

(b) Spargers shall be designed for SIP with the vessel.

(c) Spargers should be designed for CIP. If the sparge element cannot be CIP’d, provisions shall be made to remove the sparge assembly from the bioreactor for replacement or cleaning out of place.

(d) The removable sparger shall be supplied with the means to ensure that the installation orientation is in conformance to design.

(e) If a check valve is installed in the sparge line within the sterile envelope, it shall be designed for CIP and SIP.

SD-5.1.4.5 Inlet Gas Piping

(a) Overlay piping is defined as piping that directs filtered gases to the vessel headspace.

(b) Inlet gas assembly piping (sparge and overlay) within the sterile envelope shall meet the requirements as defined in SD-3.1.2.

SD-5.1.4.6 Exhaust Gas Assembly.

The exhaust gas assembly is defined as a piping assembly that maintains the integrity of the sterile boundary with respect to sterility and pressure. The assembly shall include but is not limited to the items in SD-5.1.4.2 through SD-5.1.4.9.

SD-5.1.4.7 Exhaust Filter

(a) For this section, an exhaust filter shall be defined as a filter element (as described in Nonmandatory Appendix T) installed in a housing of suitable material.
Figure SD-5.1.4.4-1
Gas Sparging Assembly — Lance

Plan

Elevation

CIP drain hole at lowest point of cap

CIP spray hole (for mounting ferrule CIP)
Figure SD-5.1.4.2
Gas Sparging Assembly — Sintered

Sintered element removed for CIP

CIP spray hole (for mounting ferrule CIP)

CIP drain hole at lowest point of cap
Figure SD-5.1.4.4-4
Gas Sparging Assembly — Single Orifice
(b) Exhaust filters shall be designed for SIP. The housings shall be installed in such a way as to prevent the collection of condensate in the elements due to SIP.

(c) If redundant sterilizing-grade exhaust filters are used in series, then the filter farthest from the bioreactor shall have a maximum rating of 0.2 μm absolute. In addition, provisions shall be included for draining condensate from the piping between the filters.

(d) Consideration should be made for CIP or removal in the case of cleaning out of place.

(e) Provisions shall be made for integrity testing of the assembly.

(f) None or more exhaust filter housings are included in a cleaning circuit, elements shall be removed prior to introduction of a cleaning solution.

(g) To prevent the exhaust filters from becoming blinded by condensate saturation during operation, the exhaust gas assembly may include exhaust condensers (Figure SD-5.1.4.7-1), exhaust heaters (Figure SD-5.1.4.7-2), or steam jacketed or electrically heat traced filter housings (Figure SD-5.1.4.7-3). These items shall be designed for SIP and CIP.

SD-5.1.4.8 Exhaust Gas Piping

(a) The exhaust gas assembly within the sterile envelope shall meet the requirements as defined in SD-5.1.4.2.2.

(b) Gas heat exchangers shall be installed in the piping from the bioreactor to the no condensate condition.

(c) Back pressure control devices shall not hinder the bioreactor’s capability of being SIP’d and SIP, and SIP as appropriate.

SD-5.1.4.9 Back Pressure Control Devices

(a) If required, back pressure control devices (e.g., modulating control valves or regulators) should be installed outside of the sterile boundary.

(b) Back pressure control devices shall not hinder the bioreactor’s capability of being SIP’d and SIP.

(c) If a vapor-liquid separator is used in the exhaust within the sterile envelope, it shall be designed for CIP and SIP.

SD-5.1.4.10 Feed Lines. This section applies to bioreactor piping systems used to feed liquid ingredients (e.g., pH control reagents, antifoam reagents, media, nutrient, and inoculum). Feed lines shall be designed with the appropriate piping system to allow CIP and SIP of the bioreactor vessel and the feed line may be done independently or simultaneously with the bioreactor.

SD-5.1.4.11 Dip Tubes. This section applies to all bioreactor port tube-extensions within the vessel.

(a) Bioreactor dip tubes shall meet the requirements of SD-3.5.9.2.

(b) Removable dip tubes (see Figure SD-3.4.3-1) shall be inserted through a hygienic fitting. The removable dip tube shall be supplied with the means to ensure that the installation orientation is in conformance to design intent.

(c) Bioreactor dip tubes shall be designed for CIP or cleaning out of place (COP).

SD-5.1.4.12 Harvest Valves/Bottom Outlet Valves. This section applies to all valves installed in the vessel bottom head.

(a) Harvest valves shall meet the requirements of SD-3.5.9.2.

(b) Bioreactor harvest valves shall meet the requirements of MC-3.3.2.3.

(c) Bioreactor diaphragm valves shall be designed for SIP and SIP or COP.

SD-5.1.4.13 Agitation Assemblies. This section applies to mechanical agitator assemblies mounted in the bioreactor for achieving related unit operations (e.g., blending, mass transfer, heat transfer, and solids suspension).

(a) Agitators shall meet the requirements of SD-3.5.

(b) Agitators with dual mechanical seals (see Figure MC-2.3.2.3-2) or magnetic couplings (Figure SD-3.5.5-2) are recommended to isolate bioreactor contents from the environment.

(c) Agitator seal or magnetic coupling components shall be designed for CIP and SIP.

SD-5.1.4.14 Mechanical Foam Breaker Assemblies. This section applies to mechanical foam breaker assemblies that may be mounted in the bioreactor for reducing or eliminating foam accumulation in the vapor space of the bioreactor.

(a) Foam breaker assemblies shall meet the requirements of SD-3.5.

(b) Foam breaker assemblies with either dual mechanical seals (Figure MC-2.3.2.3-2) or magnetic couplings (Figure SD-3.5.5-2) are recommended to isolate bioreactor contents from the environment.

(c) Foam breaker seal or magnetic coupling components shall be designed for either CIP or for both CIP and SIP as appropriate.

SD-5.1.4.15 Internal Coils

(a) Internal coils should be avoided where possible.

(b) Product contact surfaces of internal coils require provisions for SIP of the bioreactor vessel for distribution of cleaning solution.

SD-5.1.4.16 Baffles. Baffle assemblies shall meet the requirements of SD-5.1.4.11 and SIP.

SD-5.1.4.17 Spray Devices. This section applies to sprayballs, wands, and other devices (see Figure SD-3.9.2.1-1) that may be mounted in the bioreactor vessel for distributing cleaning solution.

(a) Spray device assemblies shall meet the requirements of SD-3.4.2 and SD-3.9.
If not removed during processing, spray device assemblies shall be designed for SIP.

Instruments installed within the sterile envelope or boundary shall be designed for SIP. Consideration should be made in the design for instrument removal for calibration.

Instruments installed within the sterile envelope or boundary shall be designed for CIP or removed for COP.

Temperature-sensing elements should be installed in thermowells. Piping associated with in-line thermowells shall be sized to allow sufficient steam and condensate flow.

**SD-5.1.5 Design for Bioburden Control**

(a) The area within the bioreactor sterile envelope or boundary shall be designed for cleanability and bioburden control. As a minimum, the bioreactor sterile envelope or boundary shall include the following (see Figures SD-5.1.5-1 and SD-5.1.5-2):

1. vessel internals
2. inlet gas piping from the filter element(s) to the vessel and any installed isolation valving (If redundant sterilizing-grade filters are used in series, the inlet filter element farthest from the reactor vessel shall define the sterile boundary.)
3. exhaust gas piping from the vessel side of the exhaust filter(s) to the vessel and any installed isolation valving (If redundant sterilizing-grade filters are used in series, the exhaust filter farthest from the reactor vessel shall define the sterile boundary.)
4. agitation assembly including all internal surfaces of the impellers and the shaft up to the mechanical shaft seal in contact with the product
5. feed systems from the vessel to the seat of the isolation valve nearest to the bioreactor vessel or if the feed stream is being filter sterilized, the sterilizing-grade filter element
6. sampling system
7. product harvesting system from the vessel to the seat of the isolation valve nearest to the bioreactor vessel

(b) A bioreactor is made up of a number of subassemblies. Process-contacting subassemblies require special design consideration for cleaning and bioburden control.

(c) The bioreactor design for cleanability and sterility shall take into consideration the biosafety level requirement for the system. A bioreactor shall be designed in accordance with a biosafety level requirement as defined by the National Institutes of Health or equivalent organization (e.g., BSL-1, BSL-2, BSL-3, or BSL-4). The biosafety level requirement should be determined based on the organism, the process, the product being produced, and the owner/user’s preferences. To meet a specific biosafety level requirement, special operational considerations (e.g., steam blocks) may have to be addressed within the bioreactors’ subassembly designs. If the bioreactor has been used to grow an organism that requires biohazard containment, provision shall be made to decontaminate all surfaces that may have come in contact with the product prior to CIP, or to contain and decontaminate the fluids used for CIP.

**SD-5.1.5.1 Drainability**

(a) Inlet gas piping within the sterile envelope shall meet slope requirements as defined for GSD3 in Table SD-2.4.3.1-1.

(b) Exhaust gas piping within the sterile envelope shall meet slope requirements as defined for GSD3 in Table SD-2.4.3.1-1.
Multi-use centrifuges shall be cleaned and sanitized for storage (e.g., by CIP, COP, SIP).

Centrifuges shall be stored under the condition (e.g., flooded or dry) specified for bioburden control. Systems that are to be stored dry shall have design features (e.g., blowdown, venting) that maintain the bacteriostatic state.

When used in aseptic applications, centrifuges should be stored under positive pressure post-sterilization.

SD-5.3.5.3 Chemical Sanitization/Sterilization. [Reserved for future content]

SD-5.3.5.4 Thermal Sanitization/Sterilization. Centrifuges subject to SIP shall be designed in accordance with SD-2.3.1.1 and, in certain jurisdictions, may be considered pressure vessels (see GR-1). Saturated steam penetration across components that define the SIP boundary of the system shall be demonstrated.

SD-5.3.5.5 Post-Use Storage. The design shall meet the sterilization/sanitization and storage requirements (e.g., temperature, pressure, chemistry) and storage condition (e.g., flooded or dry) specified for bioburden control.

SD-5.3.6 Design for Serviceability, Examination, and Operation. [Reserved for future content]

SD-5.3.7 Testing. [Reserved for future content]

SD-5.4 Filtration

SD-5.4.1 General. Filtration systems are used for the purposes of product purification, product concentration, and reduction of bioburden. Filtration systems include the filter elements (see Part PM) and filter housings/holders, and may include pumps, vessels, piping, tubing, fittings, valves, and instrumentation.

The following sections describe the general design requirements for the operation, cleaning and sanitization of a multiuse filtration system.

SD-5.4.2 System Performance Requirements. The conditions and performance parameters under which the system will operate shall be defined. Typical items to consider include the following:

(a) type and mode of filtration
(b) inlet/outlet streams
   (1) inlet and outlet physical and chemical properties
   (2) flow rates required
   (3) pressure conditions
   (4) number of feed and outlet streams
   (5) recirculation streams for tangential flow filtration (TFF) systems
(c) operation
   (1) in-line dilution or formulation
   (2) diafiltration
   (3) measurement of fluid characteristics
   (4) control strategy (e.g., for TFF – transmembrane pressure (TMP) control, permeate flux control, permeate pressure control, retentate flow control)
(d) filtration element
   (1) preparation for operation
   (2) expected pressure drop at the indicated flow rates
(e) system
   (1) the fluids to which the system may be exposed
   (2) acceptable holdup volumes
   (3) temperature of operating area and process fluids
   (4) room classification
(f) automation
   (1) control system requirements
   (2) sensors and monitors for detection of system performance
(g) cleaning and sanitization requirements, including the following:
   (1) methods
   (2) frequency
   (3) duration

SD-5.4.3 Operating Capabilities and System Function. Filtration systems shall be designed to control and monitor filtrate (or tangential and permeate flow) according to process requirements. Multiuse systems shall be designed to allow for process cleaning and sanitization.

SD-5.4.4 System Design. The system should be designed to promote recovery of product (e.g., drainable branches and path-by-path air blows to recover product retained in lines and filter elements) and meet cleaning and sanitization requirements. The system should be designed to mitigate the risk of crossover of feed solutions, which could contaminate the process.

Filtration system designs should conform to SD-3.1. Where multiuse systems are not drainable, refer to SD-2.4.3.

When required by system function, components present in direct flow and tangential flow filtration systems shall include the following:

(a) feed and filtrate for direct flow; permeate and retentate for tangential flow
(b) valves
(c) pumps
(d) vessels (feed and filtrate collection)
(e) instruments (process monitoring and control)
(f) one or more filtration elements and element holders
transmembrane test to confirm absence of membrane fouling in tangential flow filtration systems
(c) salt rejection testing to confirm system integrity in reverse osmosis applications
(d) bubble point or forward flow diffusion tests in sterilizing-grade direct flow filtration systems used to verify bioburden control
(e) particle tests in viral filter systems employed to confirm specific viral removal

SD-5.5 Chromatography Systems

SD-5.5.1 General. Chromatography systems are used for product purification, concentration, and viral load reduction. Chromatography systems include pumps, piping, valves, instrumentation, and a stationary medium that is contained in a column, cartridge, or capsule. The stationary medium/phase may be a membrane adsorber or resin.

The chromatography system shall not contribute to the contamination of the product. This section describes operational, cleaning, and sanitization requirements of multiuse chromatography systems. This section does not address the requirements of systems intended for single-use. Chromatography systems used for analytical testing are not included in the scope of this section.

For the purposes of this section, “column” shall refer to any component (e.g., column, cartridge, capsule, membrane adsorber) housing the stationary medium.

A chromatography system may also include provisions for
(a) assisting with the packing of a column with the stationary phase
(b) evaluating the performance of a packed column
(c) performing in-line dilution and in-line formulation operations

For the purposes of this section, “gradient operation” refers to flow rates of two or more liquids to be adjusted such that the physical and chemical characteristics of the resulting chromatography feed solution change over time.

SD-5.5.3 Operating Capabilities and System Function. The chromatography system shall be capable of delivering a consistent flow of liquids through the stationary phase and mitigating the risk of introducing gas onto the column. Multiuse systems shall be designed to be cleaned and sanitized. If columns are stored packed with stationary phase, the systems shall be capable of maintaining a flooded bacteriostatic condition.

When gradient chromatography operations are required, gradient accuracy capability shall be defined. The chromatography system should be designed to provide an elution buffer flow path that minimizes axial dispersion.
SD-5.5.2 System Performance Requirements

The following operating conditions and performance parameters shall be specified to ensure proper design and function of a chromatography system:

(a) mode of operation (e.g., isocratic vs. gradient, in-line dilution or in-line formulation)
(b) inlet/outlet streams
   (1) physical and chemical properties of feeds and effluents
   (2) flow rate range
   (3) pressure conditions
   (4) number of feed and outlet streams
   (5) direction of flow

(c) operation
   (1) measurement of fluid characteristics
   (2) control strategy (e.g., gradients, product collection, flow rate control, inline dilution/formulation)

(d) chromatography column
   (1) preparation for operation
   (2) expected pressure drop at the indicated flow rates

(e) system
   (1) control of axial dispersion
   (2) acceptable holdup volumes
   (3) temperature of operating area and process fluids
   (4) room classification

(f) instrumentation and controls
   (1) control system requirements
   (2) sensors and monitors for detection of system performance

(g) cleaning and sanitization requirements
   (1) methods
   (2) frequency
   (3) duration
SD-5.5.5 Design for Bioburden Control

SD-5.5.5.2 Cleaning. Chromatography systems shall be designed for CIP. Systems should be designed in accordance with SD-3.1.

SD-5.5.5.3 Chemical Sanitization/Sterilization. Chemical sanitization processes are used to reduce bioburden. All process contact surfaces of system components shall either be compatible with the selected sanitization agents or be capable of being removed or isolated prior to the sanitization process.

SD-5.5.5.4 Thermal Sanitization/Sterilization. Chromatography systems may be designed for thermal sanitization. If a system is designed for thermal sanitization, components shall be designed for the specified conditions, or shall be removed or isolated prior to the sanitization process. Note that if items are removed for sanitization, they should be sanitized separately and reinstalled in a controlled environment to avoid contaminating the system.

SD-5.5.5.5 Post-Use Storage. Chromatography systems are typically stored flooded with a sanitizing solution to maintain bioburden control.

SD-5.6 Lyophilizers/Freeze Dryers

SD-5.6.1 General. For the purpose of this section, the terms “lyophilizer” and “freeze dryer” may be used synonymously. This section describes the requirements for cleanability and bioburden control of lyophilizers that are used for biopharmaceutical processing. This section applies to lyophilizers in which product is loaded onto shelves. Other designs that use methods and components not described in this section should be evaluated and agreed on by the owner/user. A lyophilizer comprises a number of interconnected components. Components with process contact surfaces shall be designed for cleanability and bioburden control.

Lyophilizer surfaces of components, piping, equipment, or systems that are isolated by design from both product and process fluids are not process contact surfaces and are not required to be designed for cleanability or bioburden control. Examples of surfaces that are not process contact surfaces include the exterior surfaces of equipment, piping lines, vacuum lines, and systems containing hydraulic fluids.

SD-5.6.2 System Performance Requirements. The following system performance requirements shall be defined:

(a) vacuum integrity requirements
(b) product capacity (vial quantity or required shelf area)
(c) condensing capacity (liters)
(d) minimum shelf temperature
(e) shelf heating and cooling rate (clean, dry, and empty)
(f) shelf temperature uniformity requirements
(g) evaporation rate
(h) minimum vacuum level

SD-5.6.3 Operating Capabilities and System Function. The lyophilizer should be capable of the following functions:

(a) shelf and condenser temperature control
(b) vacuum pressure control
(c) condenser defrost
(d) loading and unloading (when specified)
(e) stoppering (when specified)
(f) vacuum integrity testing
(g) filter integrity testing
(h) cleaning
(i) sterilization/sanitization

SD-5.6.4 System Design. A lyophilizer is comprised of functional components/systems, as shown in Figure SD-5.6.4-1, which are designed for isolation, cleanability, and bioburden control. All components shall be specified for the applicable pressure, vacuum, temperature range, thermal shock, and exposure to sanitizing agents [e.g., vaporized hydrogen peroxide (VHP)] when applicable.

Process contact surfaces made from nonmetallic material shall conform to SD-2.4.1.1, SD-2.4.1.2, SD-2.4.1.4, and Part PM. Components that require service or inspection shall be accessible. When required for packing and unpacking of the resin, the system shall be designed to allow access to service the columns, by the owner/user using equipment

SD-5.6.7 Testing
Pre-use integrity and performance tests are often required in a cGMP environment. Chromatography system testing should be based upon evaluation of process risks and may include verification of:

(a) feed delivery performance (e.g., gradient, inline dilution/formulation)
(b) column packing quality
(c) system integrity
Where integrity and performance tests are required, the system shall be designed to enable performance of these tests.

Chamber
The interior surfaces of the lyophilizer chamber are considered process contact surfaces. The lyophilizer chamber includes all necessary doors, bellows, isolation valves. The chamber floor shall be drainable.

The chamber internal surfaces (e.g., walls, ceiling, floor) shall be specified using the designations in Table SF-2.4.1-1. The surfaces of the lyophilizer chamber interfaces with the clean room shall meet the owner/user’s specification.

Vessel
The condenser vessel, used to contain the condenser heat exchanger, is connected to the chamber by a main isolation valve. The vessel is separated by a main isolation valve from the vacuum pumps, the condenser vessel is downstream of the vacuum pump, and the condenser vessel surfaces are not process contact surfaces and do not have surface finish requirements.
SD-5.5.4 System Design
Chromatography systems may include the following components, as required by system function:

(a) product feed, buffer feeds, eluate, and waste connections
(b) valves
(c) pumps
(d) filters
(e) vessels (feeds, eluate, and other collection)
(f) instruments (process monitoring and control)
(g) one or more chromatography columns
(h) air trap

The system should prevent leakage and minimize carryover of residual product, cleaning and buffer solutions to subsequent steps.

SD-5.5.4.1 Flow Control
A pump, a control valve or both shall be provided to control the process stream flow rate. The system should control the flow rate to the required set point at the expected operating pressure. The equipment should be selected so the turndown range meets process requirements including holding pulsation to within an acceptable limit when applicable.
If the chromatography system has integral pumps, they shall be selected to support CIP flow requirements.

SD-5.5.4.2 Mobile Phase Composition
When multiple liquid streams are blended into a feed solution, properties that confirm the composition should be monitored.

SD-5.5.4.3 Air Entrapment
The system should be designed to prevent the introduction of air into the chromatography column(s). The use of air traps upstream of the columns is acceptable.

SD-5.5.4.4 Instruments for Column Effluent Analysis
Instrumentation shall be provided to monitor properties of the column effluent. The properties monitored should be chosen to enable the system to monitor and control the performance of the chromatography process.

SD-5.5.4.5 Chromatography System Outlet
The system shall control the eluate flow path. The product outlet shall interface with downstream collection vessels or other unit operations and shall be of hygienic design.

SD-5.5.4.6 Additional System Components and Equipment
A chromatography process may require inclusion of additional components. Typical components often include:
(a) a static or dynamic mixer to ensure homogeneity of the system feeds
(b) one or more filter assemblies to allow liquid components to be filtered prior to entering the columns.
(c) a heat exchanger to regulate the temperature of the process liquids.
**SD-5.5.4.7 Seals**

Seal design should facilitate routine and non-routine operations (e.g., recovery from upset conditions, restarting equipment after maintenance).
SD-5.5.5 Design for Bioburden Control
This section provides requirements for the drainability, cleaning, and chemical and thermal sanitization/sterilization of chromatography systems for the purpose of bioburden reduction.

SD-5.5.5.1 Drainability
The chromatography system should have a low point drain to facilitate cleaning of the system and for chromatography column changeouts. Components, equipment, and systems that are not drained for storage shall be stored under bacteriostatic conditions.

Process piping systems that require draining shall be sloped to drain. Drain valves shall be installed at low points. Liquid holdup volume should be minimized in components, equipment and piping when drained. Where liquid removal is required but draining is not possible or practical, a method of forced expulsion of liquids (e.g., by clean compressed air), shall be provided. Drain points shall not create dead legs. A common drain port on the system is preferred.

SD-5.5.5.2 Cleaning
Chromatography systems requiring non-manual cleaning operations shall be designed for CIP using TACT criteria (see SD-6.3.1) to mitigate the risk of contamination from the environment, from product to product carry-over, or from cross-contamination.

SD-5.5.5.3 Chemical Sanitization/Sterilization
Process contact surfaces shall be compatible with the sanitization agents selected.

SD-5.5.5.4 Thermal Sanitization/Sterilization
Where a system is designed for thermal sanitization, components that are not capable of withstanding the specific conditions shall be removed or isolated prior to the sanitization process. Typically, chromatography columns are not designed for thermal sanitization.
Elastomers shall conform to MC-3.1 through MC-3.3. Elastomers shall be resistant to corrosion and to chemical and thermal degradation. Elastomers used in autoclave applications shall be capable of withstanding pressures of a minimum of 25 psig at 266°F (1.7 barg at 130°C). Seals should meet the testing requirements specified in MC-4.2.

**SD-6.2.4.1 Chamber.** Autoclave chambers are pressure vessels and shall be pressure and temperature rated per the owner/user’s design criteria with a minimum pressure rating of 25 psig at 266°F (1.7 barg at 130°C). The chambers shall also be vacuum rated.

For systems used in the processing of materials used in the European market, autoclaves may also be required to comply with relevant EU codes [e.g., Pressure Equipment Directive (PED) and EN-285].

**SD-6.2.4.2 Doors.** Autoclave door(s) shall be accessible, cleanable, and replaceable, and should be capable of undergoing inspection without dismantling. The door seal shall be resistant to clean steam and clean steam condensate. The door on the nonsterile side shall be capable of reopening after closing without undergoing a cycle. The door(s) shall not be capable of opening during a sterilization cycle. The doors shall be constructed of materials that are resistant to clean steam and clean steam condensate. For multiple-door systems, the doors shall be interlocked to allow the opening of only one door at a time. The unloading ("sterile-side") door shall remain sealed in standby mode. Refer to Part MC for specifications of seals used in bioprocessing.

**SD-6.2.4.3 Sterile Air/Vent Filters.** Where the sterilization cycle requires admission of air into the chamber, the air should be filtered with a sterilizing filter (0.22 µm or less). The filter element shall be replaceable. Provisions for the steam in place of the vent filter elements should be provided.

**SD-6.2.4.4 Steam Traps.** Refer to SD-3.12 for requirements of steam traps.

**SD-6.2.4.5 Loading Carts/Trays.** Carts and trays exposed to clean steam shall be constructed of materials resistant to clean steam and clean steam condensate. Carts, trays, and chamber shall be accessible or removable and cleanable.

**SD-6.2.4.6 Valves.** Valves and sealing materials located within the sterile boundary shall conform to MC-3.3.2.3. Valves within the sterile boundary are typically only exposed to clean steam service and chemical(s) used during passivation. Exposure to these conditions should be considered when selecting a valve type for this application.

**SD-6.2.4.7 Check Valves.** Provisions to prevent back-siphoning into the service feed systems should be considered.

**SD-6.2.4.8 Jacket.** The jacket shall be constructed using materials that are resistant to corrosion and degradation from steam or clean steam and clean steam condensate, as applicable.

**SD-6.2.4.9 Instrumentation.** Autoclave pressure and temperature shall be displayed at all doors. All instruments within the sterile boundary should be of hygienic design. Instruments shall be capable of being calibrated and replaced. The instrumentation shall include the following:

(a) **Temperature.** Independent temperature elements (one or two for monitoring and recording and an independent one for controlling temperature) shall be provided. The chamber temperature recording element should be located in the chamber drain. Each temperature element shall be accurate to ±0.18°F (0.1°C) with a sensor response time <5 sec. The element installation shall not affect the maximum leak rate. The temperature elements shall be temperature and clean steam resistant.

(b) **Pressure/Vacuum.** Pressure/vacuum instruments shall be provided. The pressure instruments shall monitor the chamber and jacket pressures. Provisions for recording chamber pressure during active autoclave cycles shall be included.

(c) **Date/Time.** Provisions for recording the date and time during an autoclave cycle shall be included.

(d) **Recording.** Recording may be achieved by paper or 21 CFR Part 11–compliant electronic means.

**SD-6.2.4.10 Interfaces**

(a) **Drain Temperature.** Waste to drain temperature shall conform to owner/user specifications. The owner/user shall specify discharge temperature requirements to the manufacturer.

(b) **Insulation.** External surfaces should be insulated to minimize heat transmission.

(c) **Biocontainment.** Special conditions such as bioseals may be required for autoclaves used in BSL-3 and BSL-4 applications. Please refer to the Biosafety in Microbiological and Medical Labs (BMBL) and Centers for Disease Control (CDC) guidelines for these special conditions.

**SD-6.3 CIP Systems**

**SD-6.3.1 General.** This section addresses CIP systems used to clean and reduce bioburden on process contact surfaces. CIP systems include the CIP skid and the CIP distribution system. The system shall be self-cleaning and capable of distributing CIP fluids (e.g., cleaning solutions, rinse water, compressed air) to the targeted process contact surfaces of a CIP client.

The following terms are defined for this section:

(a) **CIP path:** the specific route contacted with CIP fluids during a CIP cycle (e.g., spray device path, inoculum line path, addition line path). Multiple paths within a circuit may be cleaned simultaneously or sequentially.
(b) **CIP client**: system or equipment (e.g., bioreactor, buffer hold vessel) targeted for cleaning by a CIP system.

(c) **CIP circuit**: the sum of CIP paths within CIP clients that are cleaned as part of a CIP cycle, as well as the CIP skid, CIP supply, and return distribution system.

(d) **CIP phase**: a process-oriented action within a CIP cycle, such as a rinse, wash, or air blow, that can be subdivided into steps and transitions.

(e) **CIP cycle**: the executed recipe of sequential CIP phases established to provide CIP fluids to the CIP circuit, e.g., rinses, washes, and air blows.

(f) **TACT**: an acronym for the cleaning process parameters time, action, chemistry, and temperature. The term “action” refers to kinetic energy that drives breakdown and suspension of residues from the process contact surface.

### SD-6.3.2 System Performance Requirements

The following technical requirements or parameters that are essential for design development shall be defined:

- **(a)** rinse and wash duration range
- **(b)** flow rate and pressure ranges
- **(c)** cleaning agents and their wash concentration ranges
- **(d)** rinse and wash temperature ranges
- **(e)** final rinse water quality (e.g., TOC, conductivity)
- **(f)** air blow requirements
- **(g)** sampling locations
- **(h)** drain limitations

Refer to SD-5 for CIP client cleaning requirements.

### SD-6.3.3 Operating Capabilities and System Function

The CIP system shall be capable of controlling the following:

- **(a)** TACT
- **(b)** multiple water/solution feeds when required

#### SD-6.3.3.1 Rinse

The CIP system shall be designed with the capability to provide rinse solutions at the specified flow, pressure, and temperature to the CIP client.

#### SD-6.3.3.2 Wash

When a formulated wash step is required, the CIP system shall be designed to mix cleaning agents to prepare wash solutions. The CIP system shall be capable of supplying the wash solution at the specified cleaning agent concentration and wash temperature.

#### SD-6.3.3.3 Drain

The CIP system shall be drainable. The CIP system should support the use of multiple drain paths if required (e.g., biowaste inactivation system, waste neutralization system). Where the CIP skid or CIP client cannot be drained, provisions for a motive force such as a pump or pressurized gas (air blow) shall be included for removal of residual liquid.

#### SD-6.3.3.4 Air Blow

The CIP system should be designed to provide pressurized air as a motive force, if required, to assist in removing liquid from the CIP circuit. Air blows should be sequenced through the individual CIP paths of a CIP circuit.

### SD-6.3.3.5 Surface Treatment Cycles

If the CIP system is designed for surface treatment (e.g., derouging or passivation cycles) of CIP clients, the CIP system should have provisions to introduce and remove associated chemicals.

### SD-6.3.3.6 Self-Cleaning Cycle

If a self-cleaning cycle of the CIP skid is required (e.g., to clean the CIP skid after maintenance), the skid design should have piping that meets recirculation/cleaning requirements.

### SD-6.3.4 System Design

(a) Process contacting portions of the CIP system shall be of hygienic design and fabricated as per SD-3.1.2 and SD-2.4.3.

(b) Recirculating portions of the CIP system shall be considered process contact and may be considered product contact if used to clean product contact surfaces. Risks (e.g., cross contamination and containment) associated with recirculating CIP systems should be evaluated and addressed.

(c) **CIP system materials of construction shall be compatible with the process and CIP fluids.**

#### SD-6.3.4.1 CIP Skid

A CIP skid is a system that prepares, delivers, controls, and monitors CIP solutions.

(a) The following parameters shall be monitored and controlled:

- **(1)** rinse, wash, air blow, or drain duration
- **(2)** flow rate: CIP supply flow rate
- **(3)** chemistry: CIP wash solution concentration of cleaning agents (e.g., by conductivity)
- **(4)** temperature: CIP supply temperature

(b) The following parameters shall be monitored:

- **(1)** CIP return temperature
- **(2)** final rinse water quality (e.g., conductivity, TOC)

(c) The following parameters should be monitored:

- **(1)** temperature verification

**CIP circuit piping should be designed with low point drain valves that can be opened between each phase of the CIP cycle.**

#### SD-6.3.4.1.1 Wash/Rinse Vessels

(a) A CIP system can include one or more vessels (e.g., separate wash and rinse vessels). Vessels can be used to provide a physical separation between the water supply and the CIP solutions.
The rinse vessel should be sized to ensure uninterrupted delivery of rinse solution during the rinse phases of the CIP cycle.

The wash vessel should be sized to provide adequate volume for the duration of the wash step. Sizing factors to consider are holdup volume for recirculation steps, total wash volume for once-through steps, and wash solution losses.

Where recirculation of wash solutions is required, a no-foam inlet, tangential inlet, or dip tube should be used for the return of wash solutions to the wash vessel to reduce the risk of foaming.

The vessels should be provided with vortex breakers and adequate outlet sizes. Vessels should also be located close to the CIP supply pump to ensure that the available net positive suction head (NPSH) is greater than required NPSH. If removable vortex breakers are installed, the design shall account for the effect of vibrations and forces on the vortex breaker and vessel wall.

Air entrainment in the CIP return liquid can impact CIP pump performance. CIP return systems using eductors or liquid ring pumps often have a high percentage of air in the CIP liquid. Wash vessels should be designed to enhance gas/liquid separation and provide adequate NPSH, as well as to reduce CIP circuit volume. An example of a vessel having those features is a conical tank with a tangential inlet and cylindrical reduced diameter bottom section (i.e., tulip tank; see Figure SD-6.3.4.1.1-1).

Vent filters on CIP skid vessels should be designed to mitigate the risk of foam or moisture blinding the filter element (e.g., heating the filter housing, bypassing the filter during filling).

The CIP skid vessel used for final rinsing should be provided with a sterilizing-grade vent filter if the vessel is vented into unclassified space.

**SD-6.3.4.1.2 Heat Exchanger.** Heat exchangers shall be designed to meet the full range of CIP cycle duties.

**SD-6.3.4.1.3 Supply Pump**

(a) The CIP skid shall have flow control, either via pump output or by means of flow control valves.

(b) The pump and its associated piping (e.g., partial flow diversion) shall be designed to meet all flow rate and pressure requirements for all CIP circuits.

**SD-6.3.4.1.4 CIP Return**

(a) If CIP fluids are returned to the CIP skid, motive force is required (e.g., pumps, eductors, gravity, or top pressure).

(b) The CIP return sampling system should be designed for two-phase flow (i.e., liquid-gas mixtures) or vacuum conditions where applicable.

**SD-6.3.4.1.5 CIP Return Eductors.** A CIP return eductor is a venturi device that provides motive force (i.e., vacuum) to assist CIP fluid return.

(a) CIP return eductors shall be drainable.

(b) Design factors that should be considered when using CIP return eductors include vapor pressure, return line size, elevation, viscosity, and flow rate.

(c) When CIP return eductors are used, the potential for foaming should be considered.

**SD-6.3.4.1.6 Chemical Delivery.** The CIP skid chemical delivery does not require sanitary design. Acceptable metering methods for chemical delivery include one or more of the following:

(a) weight

(b) flow totalization

(c) duration via metering pump or venturi

(d) conductivity

Typically one method is used for delivery, and a second method is used for confirmation or final control.

**SD-6.3.4.1.7 Compressed Air Supply.** The CIP skid may be provided with a clean compressed air supply to assist the removal of the rinse or wash solution. Compressed air shall meet the quality requirements for the applications (e.g., by installing a point-of-use filter at the CIP skid). The supply pressure and flow rate shall meet the process requirements. Compressed air may be supplied at other locations in the CIP circuit to assist removal of rinse or wash solutions.
SD-6.3.4.1.8 Instrumentation

(a) The CIP supply flowmeter shall be specified and installed to measure the flow rates of CIP liquids.

(b) To address air in the CIP return, final rinse conductivity sensors should be located to ensure proper operation in both liquid and mixed-flow conditions (e.g., by providing a drainable instrumentation cup, compensated through instrument settings).

SD-6.3.4.2 CIP Distribution

(a) General

(1) The use and application of a particular distribution design or combination of designs should be decided by the owner/user.

(2) The use of looped headers, transfer panels, and valve types (e.g., divert, mix-proof, multiport, zero-static, and diaphragm) should be considered in the design of the CIP distribution system.

(b) Looped Headers (see Figure SD-6.3.4.2-1)

(1) The dimension from the looped header to the isolation valve weir or seat should conform to SD-3.1.2.2 (see Figure SD-3.1.2.2-1 for details). The use of short-outlet tees or zero-static valves should be decided by the owner/user.

(2) Future connections (if applicable) on the looped header should use capped short-outlet tees or capped installed zero-static valves.

(3) Loop header connections should be oriented horizontally when used in CIP return applications.

(4) CIP supply header design should provide for adequate velocity in parallel cleaning paths (e.g., line size reduction in loop header).

(5) The entire looped header shall be cleaned during a CIP cycle.

(c) Transfer Panels. Transfer panels shall be designed and fabricated per SD-3.7.1.

(d) Multiport Valves. For this section, a CIP distribution “multiport valve” is defined as a multiple-valve assembly fabricated as a single body to minimize \( \frac{L}{d} \) values and enable drainability [see MC-3.3.2.3(a) for details].

(e) Zero-Static Chains (see Figure SD-6.3.4.2-2). For this section, a CIP distribution “zero-static chain” is defined as a manifold of circuit-specific zero-static valves. Provisions shall be made to flush the manifold in a zero-static chain.

(f) Swing Elbows and Piping Spools (see Figure SD-6.3.4.2-3). Swing elbows or piping spools shall be connected to adequately supported piping to maintain line slope and connection alignment.

(g) Mix-Proof Valves

(1) Mix-proof valves are double-seat valves with a drain path between the seats that allows for simultaneous processes in the two bodies of the valve. Mix-proof valves shall conform to the general design requirements in MC-3.3.2.3(a) and rising stem seal valves requirements in MC-3.3.2.3(c).

(2) If the process requires cleaning across a single seat, the valve shall be provided with individual seat lifts.

(3) Mix-proof valve arrays should be designed to accommodate draining from the leak chamber and sufficient access for maintenance of the valve internals.

(4) The mix-proof valve fitting-bound portion of looped header configurations should be installed level to avoid low points where liquid may accumulate. Pitch of the mix-proof valve array may result in liquid
retention in valve bodies and should be risk assessed (see Figure SD-6.3.4.2-4).

(5) If a mix-proof valve with an exposed sliding stem is used to divert process solutions, it shall allow for cleaning of the stem surfaces prior to contacting the process fluids (e.g., by actuating the valve during CIP).

(h) The distribution piping and components in a recirculated CIP circuit shall be hygienic for design and fabrication as per SD-3.1.2 and SD-2.4.3.

(i) The distribution piping and components in a once-through CIP circuit or path (e.g., not recirculated) shall be hygienic for design and fabrication as per SD-3.1.2 and SD-2.4.3 upstream of the location of cleaning performance verification.

(j) CIP supply piping should be sized to ensure that the fluid flow meets or exceeds the guidelines stated in SD-6.3.5.2.1 and SD-6.3.5.2.2.

(k) The distribution circuits shall be designed such that fluid flow will maintain a positive pressure relative to the process drain, preventing backflow.

(l) CIP return piping shall be designed to maintain hydraulic balance (supply and return flow) of the CIP circuit.

(m) CIP return pumps
(1) CIP return pumps (if required) shall be designed and fabricated per SD-3.3.2. Centrifugal pumps are preferred for CIP return applications. If a gas/liquid mixture is anticipated, then hygienic liquid ring pumps are recommended.
(2) When a vessel is included in the circuit, CIP return pumps should be placed as close as possible to the vessel bottom outlet and at the low point of the circuit.
(3) Provision shall be made to flush through the casing drain of CIP return pumps.
(4) CIP return pumps shall be designed to maintain hydraulic balance (supply and return flow) of the CIP circuit.

SD-6.3.5 Design for Bioburden Control
SD-6.3.5.1 Drainability. [Reserved for future content]

SD-6.3.5.2 Cleaning
SD-6.3.5.2.1 CIP Flow Rates for Process Lines
(a) The CIP system shall be designed to produce turbulent flow through process lines of the CIP client.
(b) For effective cleaning, the CIP flow rate and pressure shall be sufficient to ensure that the cleaning agent and rinsing solutions wet targeted surfaces within the CIP circuit.
(c) Turbulent flow is required to clean targeted surfaces of the CIP client. Table SD-6.3.5.2.1-1 details flow rate guidelines for solution contact in straight horizontal and vertical lines for line sizes up to 2 in. (50 mm)
SD-6.3.4.2 CIP Distribution

A CIP distribution system consists of supply and return piping. The supply distribution piping delivers the CIP fluids from the CIP skid to the CIP clients. The return distribution piping delivers the CIP fluids from the CIP clients to the CIP skid. CIP return motive force should be provided, e.g., by one or more of the following:

- gas overlay pressure in the CIP client
- gravity
- eductor
- pump

Return distribution piping is not required for once-through cleaning or locally recirculated cleaning.

(a) General

(1) The CIP distribution system shall be sized to meet flow rate and pressure requirements of the associated CIP clients (e.g., as defined in SD-6.3.5.2).

(2) The use and application of a particular distribution design or combination of designs is to be decided by the owner/user. The distribution system shall be designed without dead legs under the flow conditions for each CIP circuit.

(3) The use of CIP supply and return distribution should use piping, looped headers, transfer panels, hoses, removable spool pieces, and/or valves types (e.g., divert, mix-proof, cluster, block-body, multiport, zero-static, and diaphragm) should all be considered in the design of the CIP distribution system to route the CIP fluids to or from CIP clients. If rising stem seal valves (e.g., divert valves, mix-proof valves) are used in the CIP distribution system, the risk of contamination or residue retention along the sliding stem should be assessed.

(4) The distribution piping and components, including sample points in a CIP circuit, shall meet design requirements per SD-2 and SD-3.

(5) The CIP distribution system shall be designed to prevent back flow from the drain (e.g., air breaks, check valves, sensor activated valves, pressurization).

(6) The CIP circuit shall be designed to maintain hydraulic balance between supply and return flow to prevent liquid accumulation in the CIP client (e.g., vessel, filter housing).

(7) If the CIP client is cleaned by a once-through process, the piping downstream of a sample point or an instrument for final rinse measurement may be considered a process drain (non-process contact).

(b) Loop Headers (see Figure SD-6.3.4.2-1)

(1) The dimension from the looped header to the isolation valve weir or seat should conform to SD-3.1.2.2 (see Figure SD-3.1.2.2-1 for details). The (e.g., by use of short-outlet tees, mix-proof valves, or zero-static valves) should be decided by the owner/user.

(2) Future spare connections (if applicable) on the looped header should use capped short-outlet tees or capped installed zero-static valves.

(3) A looped header and its connections shall be designed to be drainable. Loop header connections should be oriented horizontally when used in CIP return applications.

(4) CIP supply header design should provide for adequate velocity in parallel cleaning paths to ensure flooding and cleaning of the entire looped header (e.g., line size reduction within the looped header).

(5) The entire looped header shall be cleaned during a CIP cycle.

(c) Transfer Panels. Transfer panels shall be designed and fabricated per SD-3.7.1.

(d) Multiport Valves. Cluster, block-body, and multiport valves should be designed and installed to prevent dead legs, reduce hold up areas, and enable draining. For this section, a CIP distribution “multiport valve” is defined as a multiple valve assembly fabricated as a single body to minimize L/d values and enable drainability [see SG-3.3.2.3(a) for details].
Zero-Static Chains Manifolds. The manifolds shall be designed so any holdup can be flushed and drained during each CIP phase (see Figure SD-6.3.4.2-2). For this section, a CIP distribution “zero-static chain” is defined as a manifold of circuit-specific zero-static valves. Provision shall be made to flush the manifold in a zero-static chain.

Swing Elbows and Piping Spools (see Figure SD-6.3.4.2-3). Swing elbows or piping spools shall be connected to adequately supported piping to maintain line slope and connection alignment.

Mix-proof Valves

(1) Mix-proof valves are double-seat valves with a drain path between the seats that allows for simultaneous processes in the two bodies of the valve. Mix-proof valves shall conform to the general design requirements in MC-3.3.2.3 (a) and rising stem seal valves requirements in MC-3.3.2.3 (c).

(2) If the process requires cleaning across a single seat, the valve shall be provided with individual seat lifts.

(3) Mix-proof valve arrays should be designed to accommodate draining from the leak chamber and provide sufficient access for maintenance of the valve internals.

(4) The mix-proof valve fitting-bound portion of looped header configurations should be installed level to avoid low points where liquid may accumulate. Pitch of the mix-proof valve array may result in liquid retention in valve bodies and should be risk assessed (see Figure SD-6.3.4.2-4).

(5) When mix-proof valves are used in a non-looped manifold (similar to a zero-static manifold), the manifold shall be designed to be flushed and drained during each CIP phase (see Figure SD-6.3.4.2-2).

(6) If a mix-proof valve with exposed sliding stem is used to divert process fluids solutions, it shall allow for cleaning of the stem surfaces prior to contacting the process fluids (e.g., by actuating the valve during CIP).

g The distribution piping and components in a recirculated CIP circuit shall be hygienic for design and fabrication as per SD-3.1.2 and SD-2.4.3.

h The distribution piping and components in a once-through CIP circuit or path (not recirculated) shall be hygienic for design and fabrication as per SD-3.1.2 and SD-2.4.3 upstream of the location of cleaning performance verification.

i CIP supply piping should be sized to ensure that the fluid flow meets or exceeds the guidelines stated in SD-6.3.5.2.1 and SD-6.3.5.2.2.

j The distribution circuits shall be designed such that fluid flow will maintain a positive pressure relative to the process drain, preventing backflow.

k CIP return piping shall be designed to maintain hydraulic balance (supply and return flow) of the CIP circuit.

CIP Return Pumps:

(1) CIP return pumps (if required) shall be designed and fabricated per SD-3.3.2. Centrifugal pumps are preferred for CIP return applications when pumps are required. Self-priming pumps (e.g., liquid ring pumps) should be used where gas/liquid mixtures are anticipated. If a gas/liquid mixture is anticipated, then hygienic liquid ring pumps are recommended.

(2) When a vessel is included in the circuit, the CIP circuit has an air break, the CIP return pumps should be placed as close as possible to the vessel bottom outlet and at the low point of the circuit.

(3) Provision shall be made to flush through the casing drain of CIP return pumps. CIP return pumps shall be drainable.
(4) CIP return pumps shall be designed sized to maintain hydraulic balance between (supply and return flow) of the CIP circuit.

(5) The suction-side piping shall be designed to meet hydraulic requirements for the pump, including liquid ring pumps that may not have published NPSH requirements.

(h) Instrumentation.
For instrumentation in the CIP distribution system, refer to paragraph SD-6.3.4.1.8.
(d) CIP flow rate requirements should be considered in conjunction with other CIP process variables (e.g., temperature, chemical concentration, and time).

(e) Air trapped in branches may inhibit full contact of cleaning agent and rinsing solution to those process contact surfaces. The flow direction, line orientation, line size, and presence and orientation of branches, fittings, and other equipment can have a significant influence on the flow rate required to remove air. Adequate solution contact may be achieved at a flow velocity of 5 ft/sec (1.5 m/s) with 1.5 in. (38 mm) and larger short-outlet tees (see Table DT-4.1.2-5). Smaller-diameter short-outlet tees and tees with longer branches require velocities greater than 5 ft/sec (1.5 m/s) for adequate solution contact. Solution contact in branches can be enhanced in the design by strategic use of zero-static valves.

Table SD-6.3.5.2.1-1: Flow Rates to Achieve 5 ft/sec (1.5 m/s)

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>I.D.</th>
<th>Flow Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2</td>
<td>0.370</td>
<td>9.40</td>
</tr>
<tr>
<td>3/4</td>
<td>0.620</td>
<td>15.75</td>
</tr>
<tr>
<td>1</td>
<td>0.870</td>
<td>22.10</td>
</tr>
<tr>
<td>1 1/2</td>
<td>1.370</td>
<td>34.80</td>
</tr>
<tr>
<td>2</td>
<td>1.870</td>
<td>47.50</td>
</tr>
</tbody>
</table>

Without branches, fittings, and other in-line components. These flow rates correspond to a flow velocity of 5 ft/sec (1.5 m/s), which is well into the turbulent range and typical for CIP solutions.

(d) Dynamic flow conditions during route transitions and air blows may assist wetting.

**SD-6.3.5.2.2 CIP of Process Vessels**

(a) Process vessels shall be designed to consistently enable exposure of the internal surfaces to the CIP liquids by spray device or flooding.

(b) Dished-head vertical vessels should have cleaning solutions delivered with the majority of flow directed toward the upper head and sidewall area at the upper knuckle radius. Cylindrical horizontal vessels should have cleaning solutions delivered with the majority of flow directed toward the upper one-third of the vessel.

(i) If a static spray device is used, gravity provides a solution sheeting over the side wall and bottom head (vertical vessels) or lower surfaces (horizontal vessels).

(ii) If a dynamic spray device is used, the device may directly spray areas through the vessel or rely on sheeting action.

(iii) Figure SD-3.9.2.1-2 details ranges of flow recommendations for static spray devices on vertical process vessels under typical cleaning loads. The recommendations in Figure SD-3.9.2.1-2 ensure sufficient coverage.

(iv) The criteria to ensure sufficient coverage on horizontal process vessels vary with geometry and size.

(c) Spray device design and location shall ensure appurtenances such as manways, baffles, dip tubes, agitator impellers, and nozzles are contacted with cleaning solution. Some appurtenances may require additional provisions for cleaning.

(d) Spray devices only ensure coverage of the exterior of installed appurtenances and equipment. Appurtenances that have interior surfaces not reached by the spray device coverage shall be cleaned by other CIP paths or removed and cleaned out of place.

(e) If a vessel is cleaned with spray devices, the fluid level should be minimized in the process vessel (e.g., dip tubes). Proper hydraulic balance (supply and return flow) of the CIP circuit and sizing of the bottom outlet valve should be considered to minimize fluid level.

(f) A vortex breaker should be installed to prevent vortex formation that may adversely affect the CIP operation.

(g) Vortex breaker surfaces shall be sloped to eliminate pooling during CIP and positioned to not adversely affect the hydraulic balance of the CIP circuit.

(h) For process vessels equipped with an agitator, the impeller should be rotated at an appropriate speed during the CIP cycle.

**SD-6.3.6 Design for Serviceability, Examination, and Operation.** CIP return eductors shall be designed to be removable for examination.

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**SD-6.3.5.3 Chemical Sanitation/Sterilization**

Chemical sterilization is generally not applicable to CIP systems. If liquid chemical sanitization of the CIP skid is required, recirculation should be provided within the skid.

**SD-6.3.5.4 Thermal Sanitation/Sterilization**

Thermal sterilization is generally not applicable to CIP systems. If steam sanitization of the CIP skid is required, the skid shall include provisions for pure steam distribution and condensate removal.

If hot water sanitization of the CIP skid is required, recirculation should be provided within the skid.

(b) Instruments or other devices protruding into the flow path may create additional local turbulence.

(c) Condensate generated during hot washes or hot rinses as part of a CIP cycle may provide some additional rinsing of surfaces.
SD-6.3.7 Testing. During the cleaning of process vessels, sufficient exposure shall be confirmed by coverage testing per SD-7.1 at the site of equipment manufacture or after installation or both.

SD-6.4 Thermal Treatment Systems

SD-6.4.1 General

SD-6.4.1.1 Terminology. The following terms are used in this section:

*average residence time*: the volume of the retention tube divided by the volumetric flow rate. (Average residence time should always be greater than the required residence time.)

*coil heat exchanger*: a coiled tube for process liquid flow, inside a shell or a second tube containing heating/cooling medium.

*cooling equipment*: heat exchangers or a flash cooler used to cool the process liquid after the retention tube.

*energy recovery heat exchange system*: optional equipment that takes heat from the discharge of the retention tube and uses it to preheat the incoming process liquid. These systems may have process fluid on both sides of a heat exchanger.

*heating equipment*: heat exchangers or direct steam injection equipment. Direct steam injection refers to use of a steam injector valve (typical) or a steam infusion chamber.

*high-temperature short time (HTST)*: processing at a combination of temperature and required residence time that is designed to achieve a desired level of bioburden reduction or viral inactivation. Treatment conditions (i.e., exposure temperatures and residence times) for HTST systems range broadly, depending on the performance goal of the system.

*required residence time*: the minimum exposure time required at the specified temperature to achieve desired results.

*retention tube*: a section of tubing used in HTST/UHT systems to retain the process liquid (typically an aqueous solution) at an elevated temperature for a specified time.

*ultra-high temperature (UHT)*: processing at temperatures above 275°F (135°C) with rapid heating and cooling and short exposure times to achieve what is generally accepted as a sterile condition.

Thermal treatment system example configurations are shown in Figures SD-6.4.1.1-1 and SD-6.4.1.1-2.

SD-6.4.1.2 Scope and Purpose. This section addresses thermal treatment systems used in bioprocessing to reduce or eliminate viable microorganisms and viruses in a liquid under continuous flow conditions while minimizing degradation of the product or a product intermediate. Thermal systems may be designed to achieve goals that do not require sterilization of the process liquid, such as inactivation of viruses or a particular bacterial species. Bio-inactivation (waste treatment) systems (SD-4.4.2) and food pasteurization systems are not addressed in the scope of this section.

SD-6.4.2 System Performance Requirements. The following system performance capabilities shall be defined:

(a) treatment temperature range
(b) required residence time at treatment temperature
(c) process liquid flow rate
(d) discharge temperature range
(e) maximum heating surface temperature, heat transfer fluid temperature, or process liquid heating rate (°F/sec, °C/s)

Additional performance requirements may be defined by the owner/user. Additional process parameters required to confirm system capabilities, including specifying the process fluid’s incoming temperature and other properties, should be provided by the owner/user.

SD-6.4.3 Operating Capabilities and System Function

SD-6.4.3.1 Priming. The system shall be capable of a priming operation to fill the piping with liquid, remove air, and establish pressure and flow control. The thermal treatment system should be primed by the process liquid to be treated or a priming liquid (e.g., WFI), or both.

SD-6.4.3.2 Thermal Sanitization. The sanitization conditions (e.g., time and temperature) of the system shall be defined prior to the design or selection. UHT systems shall be designed to enable sanitization. HTST systems shall be designed to enable sanitization when the treated process liquid has the potential to be compromised by the priming activities. The components (e.g., the receiving vessel, cooling exchanger, flash chamber) requiring thermal sanitization to meet functional closure criteria should be identified during design development.
**SD-6.6.5.3 Chemical Sanitization/Sterilization.** All transport systems shall be set in a position (or in motion) such that all process contact surfaces are exposed to the chemical agent used for the decontamination cycle.

**SD-6.6.5.4 Thermal Sanitization/Sterilization.** [Reserved for future content]

**SD-6.6.5.5 Post-Use Storage.** Aseptic isolators should be designed to maintain an ISO class 5 environment under dynamic and static conditions for a period of time specified by the owner/user. A post-use storage time under static conditions should be specified by the owner/user and verified through environmental monitoring.

**SD-6.6.6 Design for Serviceability, Examination, and Operation.** The isolator systems should be designed to enable safe access for inspection and service of components that are subject to wear, and to allow periodic calibration of instruments.

The isolator systems should be designed to provide adequate space for maintenance accessibility of all mechanical components.

**SD-6.6.7 Testing**

**SD-6.6.7.1 Isolator Leak Testing.** Both the pressure decay and pressure hold methods of leak-rate testing are acceptable. When choosing a test method, consideration should be given to the size of the isolator, time required for testing, and external influences that may affect testing (e.g., room temperature changes, room pressure changes).

The maximum leak rate shall be no greater than 1% of the isolator volume per hour with all pass-in/pass-out holes and RTP fittings closed and sealed (ISO 14644-7:2004, ISO 10648-2:1994 class 3). Leak-rate test pressures should be selected at 3 times to 5 times the working pressure as agreed to by owner/user. The temperature during the leak test shall not change more than 0.9°F (0.5°C).

**SD-6.6.7.2 Glove Leak Testing.** System integrity should be confirmed by a glove leak test. A glove port assembly tester is recommended to locate a potential glove leak. It is recommended to test both the installation and the glove sleeve.

Leak testing methods found in ISO 14644-7 are acceptable. Unless otherwise specified by the owner/user, the maximum permissible leak of 0.5% of volume per hour is recommended. The use of a completely automated device that uses pre-assigned test recipes is recommended.

**SD-6.6.7.3 ULPA/HEPA Testing.** The isolator design shall include integral DOP (dispersed oil particulate) or PAO (polyalphaolefin) ports for HEPA filter integrity testing with diocetyl phthalate or other approved testing aerosol challenge. For aseptic isolators, the methods consistent with the certification standards for an ISO class 5 cleanroom should be applied.

**SD-6.6.7.4 Mock-Up.** Unless otherwise agreed to by the owner/user, a mock-up at the factory or user site should be conducted prior to fabrication of aseptic isolators to assess aseptic operations through glove ports and associated ergonomics. When possible, the actual equipment or models of the actual equipment should be in place for the mock-up.

**SD-6.6.7.5 Airflow Verification and Visualization Testing.** The design of airflow in aseptic isolators should be verified to maintain ISO class 5 conditions.

Airflow visualization studies should be conducted under specified conditions (e.g., ISO class 5) to demonstrate that the unidirectional airflow minimizes the risk of contamination during operation. It should demonstrate a sweeping action over and away from the sterilized/decontaminated equipment, product, containers, and closures.

Airflow visualization studies should document the airflow patterns under static conditions, dynamic (operating) conditions, and the airflow during all interventions (e.g., clearing a jammed vial).

**SD-7 DESIGN CONFORMANCE TESTING**

Design conformance testing shall not result in the formation of any surface anomalies or contamination. All design conformance tests and test results documentation shall have the date and time recorded. Each test document shall include a record of personnel who performed and confirmed the test results.

**SD-7.1 Spray Device Coverage Test**

An acceptable spray device coverage test procedure is provided in Nonmandatory Appendix M. The purpose of the spray device coverage test is to demonstrate and document liquid coverage of the process contact surfaces. The test provides information about liquid coverage and the conditions necessary to achieve this coverage as a prerequisite for cleaning of the process equipment. Effective coverage shall be visually determined using a fluorescent solution and an ultraviolet lamp or by other verification methods as agreed to by the owner/user and manufacturer. The minimum acceptable water quantity is 1 gallon (4 L) of pendial purified water (e.g., reverse osmosis or deionized). Acceptance criteria and coverage test protocol should be agreed to by the owner/user and manufacturer.

Spray device coverage tests are not intended to demonstrate system cleanliness. System cleanliness is achieved through the equipment design, the spray design, knowledge of the soils, cleaning agent selection, and cleaning process parameters. Cleanability is verified using a complete CIP per protocol during cleaning validation.

Cleanability should be demonstrated using a complete cleaning cycle.
CHAPTER 5
PROCESS COMPONENTS FOR MULTIUSE

PART DT
DIMENSIONS AND TOLERANCES FOR PROCESS COMPONENTS

DT-1 PURPOSE AND SCOPE

The purpose of this Part is to provide requirements that ensure process component fit-up and compatibility.

This Part specifies dimensions, tolerances, and all supplementary conditions for process components.

(22) DT-2 PRESSURE RATING

Table DT-2-1 shows the maximum allowable working pressure and temperature ratings for metallic fittings manufactured per DT-4.1 and manufactured from materials listed in Tables MM-2.1-1 through MM-2.1-3, with the exception of automatic tube weld caps listed in Table DT-4.1.5-1.

Metallic fittings manufactured to pressure and temperature ratings that exceed those in Table DT-2-1 must be justified by methods accepted by ASME B31.3.

Metallic fittings listed in Table DT-4.1.5-1 (automatic tube weld cap) shall meet or exceed the pressure and temperature ratings shown in Table DT-2-1.

Special angle branch connections per DT-4.3 shall be rated per the manufacturer’s pressure and temperature ratings.

Valves manufactured to this Part shall be rated per the manufacturer’s marked pressure and temperature recommendations.

(22) DT-3 WALL THICKNESS

The nominal wall thickness of the fittings and process components at the point of joining shall be the same as the tube to which they are welded. The thickness of the weld ends shall conform with the tolerances listed in Tables DT-3-1 and DT-3-2.

After fabrication and surface treatment, the wall thickness in any formed part of the fitting or process component, excluding tube, beyond the control portion as defined in DT-7, shall be a minimum of 65% of the nominal wall thickness. For guidelines regarding welds, refer to Part MJ. All welds shall meet the provisions of MJ-8 and Figure MJ-8.4-1.

DT-4 DIMENSIONS

Fittings and process components are designed for use with nominal outside diameter (O.D.) tubing for the sizes listed in Table DT-4-1. The dimensions are accompanied with soft metric conversions from the U.S. Customary units and are listed for reference only (see GR-6). For nominal metric size tubing and fittings, refer to the appropriate international standards.

DT-4.1 Fitting Dimensions

Dimensions for fittings that are governed by this Standard are grouped and categorized into tables.

All sizes shown in these tables are nominal O.D. tube sizes.

All automatic weld end fittings shall have minimum tangent lengths per Table DT-4.1-1. The tangent length, \( T_L \), is defined as the straight length measured from the welding end.

The categorized groups in DT-4.1.1 through DT-4.1.5 designate specific fitting dimensions.

DT-4.1.1 Elbows/Bends. Refer to Tables DT-4.1.1-1 through DT-4.1.1-10.

DT-4.1.2 Tees/Crosses. Refer to Tables DT-4.1.2-1 through DT-4.1.2-13. The branch shall not intersect the longitudinal weld of the run.

DT-4.1.3 Reducers. Refer to Tables DT-4.1.3-1 through DT-4.1.3-3.

DT-4.1.4 Ferrules. Refer to Table DT-4.1.4-1. Metallic hygienic clamp ferrule dimensions are specified in Table DT-7.1-1. Polymeric hygienic clamp ferrule dimensions are specified in Table DT-7.1-2.

DT-4.1.5 Caps. Refer to Tables DT-4.1.5-1 and DT-4.1.5-2.

DT-4.2 Nonstandard Fitting Dimensions

Fittings not specifically described in Tables DT-4.1.1-1 through DT-4.1.5-2 may be constructed using combinations of centerline-to-end dimensions from the tables.
For tees and crosses, use Tables DT-4.1.2-4 and DT-4.1.2-8 for standard clamp leg lengths; Tables DT-4.1.2-2 and DT-4.1.2-7 for short-outlet branch clamp lengths; Table DT-4.1.2-3 for short-outlet run clamp lengths; and Table DT-4.1.2-1 for weld end lengths. Consideration shall be made for clamp clearances when fabricating fittings not depicted in Tables DT-4.1.1-1 through DT-4.1.5-2.

DT-4.3 Special Angle Fittings Dimensions
Special angle fittings can be offered if in accordance with all DT tables, with the exception of “O” (off angle) in Table DT-3-1. Fittings furnished to this Standard shall not be mitered.

(22) DT-4.4 Valve Dimensions
The dimensions of the valve or valve fabrication shall conform to the manufacturer’s standards, or as agreed to by the purchaser and manufacturer.
The categorized group in DT-4.4.1 designates specific valve dimensions.

(22) DT-4.4.1 Two-Way, Weir-Style Diaphragm Valves. Refer to Table DT-4.4.1-1. All sizes shown are nominal O.D. tube sizes.

DT-4.5 Filter Dimensions
Standard dimensions for filter components covered by this Standard are referenced in SD-3.8 and are given in Tables DT-4.5.1-1 and DT-4.5.2-1.

DT-4.5.1 Code 7 Tapered Locking Tab Retainer: Recessed. Refer to Table DT-4.5.1-1.

DT-4.5.2 Code 7 Tapered Locking Tab Retainer: External. Refer to Table DT-4.5.2-1.

(22) DT-4.6 Tube Dimensions
Tube dimensions shall meet the nominal outside diameter (O.D.) tubing sizes and tube wall thicknesses listed in Table DT-4-1.

DT-5 MATERIALS
Materials used in the manufacture of fittings and other process components shall conform to one of the material specifications listed in Part MM.

DT-6 TESTS
Hydrostatic testing of each fitting is not required in this Standard; however, fittings shall be capable of withstanding a hydrostatic test pressure of 1.5 times the pressure rating shown in Table DT-2-1 at 100°F (38°C).

DT-7 TOLERANCES

DT-7.1 Fitting and Process Component Tolerances
Tables DT-3-1, DT-3-2, DT-7.1-1 (metallic), and DT-7.1-2 (polymeric) list the required tolerances for fabricated fittings and process components, excluding tube, depicted by this Standard. Table DT-7.1-1 lists the required tolerances for metallic machined hygienic clamp ferrule profiles. Table DT-7.1-2 lists the required tolerances for polymeric hygienic clamp ferrule profiles. When metallic ferrules are welded to a process component and polished, then the tolerances in Tables DT-3-1 and DT-3-2 shall apply.

These tolerances shall apply after heat and surface treatment. The control portion of the fitting or process components (refer to C in the Table DT-3-1 illustration) is the length from the welding end over which tolerances for wall thickness and O.D. are maintained. The length of the control portion is fixed for all sizes at 0.75 in. (19 mm). For exceptions, see Table DT-4.1.4-1 for ferrule lengths and Table DT-4.1.5-1 for automatic tube weld caps.

DT-7.2 Tubing Tolerances
For tubing tolerances, refer to ASTM A270, including Supplementary Requirement S2. Refer to Table DT-7.2-1 for tubing end square cut tolerances.

Table DT-7.3-1 lists the required tolerances for transfer panel nozzles and jumpers.

DT-8 WELD ENDS

Where austenitic stainless steels listed in Tables MM-2.1-1 and MM-2.1-3 are specified, weld ends of process components that are to be autogenously welded shall conform to the requirements for chemical composition as prescribed in MM-5.2.1.1(a). For nonautomatic weld ends, the chemical composition shall meet the requirements of the applicable ASTM specification.

Automatic weld ends furnished to this Standard shall be furnished with square-cut ends, free from burrs and breaks. All weld end connections for valves shall have a minimum unobstructed weld end length equal to or greater than the minimum control portion as per DT-7.

DT-9 HYGIENIC CLAMP UNIONS

DT-9.1 Typical Hygienic Clamp Unions
Typical hygienic clamp unions are described in MC-2.2.2.
DT-11 MARKING

(22) DT-11.1 Fittings, Valves, and Instrumentation Marking Information

Except as specified in DT-11.1.1, each process component shall be permanently marked to maintain traceability by any suitable method not injurious to the process contact surface to show the following:

(a) a number or unique identifier that provides traceability to the applicable MTR (material test report), surface test report, or other certifications. This number may be a heat number/manufacturer’s code or serial number, marked on each process contact component.

(b) material type.

(c) valve pressure rating.

(d) manufacturer’s name, logo, or trademark.

(e) reference to this Standard (ASME BPE).

(1) ASME BPE Certificate of Authorization holders shall mark the reference to this Standard by applying their ASME Mark with BPE Designator. Refer to Figure CR-1-1.

(2) Non-ASME BPE Certificate of Authorization holders shall only mark “BPE”

(f) process contact surface designation for the appropriate BPE specification [only one surface finish (SF) designation allowed].

NOTE: All marking of a process component should be made outside of the control portion to optimize welding fit-up and identification.

DT-11.1 Exceptions

(a) Where the available marking area does not permit complete marking, the process component shall be marked, at a minimum, with the items identified in Table DT-11.1.1-1.

(b) Where the markings have been removed due to fabrication into another component or system, the heat number or manufacturer’s code and material type shall be re-marked on the fitting or process component.

(c) Polymeric fittings do not require marking per this section (see PM-2.2.2).

DT-11.2 Modified Surfaces

When the surface finish of a process component is modified, the surface finish designation marking shall be changed to match the final surface finish designation according to Table SF-2.4-1-1. Only the final finish designation shall be indicated.

After removal of the original markings, all dimensions and tolerances shall conform to Table DT-3-1 and, as applicable, Table DT-3-2.

DT-12 PACKAGING

All end connections of fittings or process components shall be protected with end caps. Additionally, fittings shall be sealed in transparent bags or shrink wrapped. Additional packaging for process components, other than fittings, shall be as agreed to by the purchaser and manufacturer.

Table DT-2-1

Metallic Fittings: Rated Internal Working Pressure

<table>
<thead>
<tr>
<th>Temperature °F</th>
<th>Temperature °C</th>
<th>&lt;3 in. psig</th>
<th>&lt;3 in. kPa</th>
<th>3 in. psig</th>
<th>3 in. kPa</th>
<th>4 in. psig</th>
<th>4 in. kPa</th>
<th>6 in. psig</th>
<th>6 in. kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>38</td>
<td>200</td>
<td>1379</td>
<td>200</td>
<td>1379</td>
<td>200</td>
<td>1379</td>
<td>150</td>
<td>1034</td>
</tr>
<tr>
<td>200</td>
<td>93</td>
<td>200</td>
<td>1379</td>
<td>200</td>
<td>1379</td>
<td>200</td>
<td>1379</td>
<td>150</td>
<td>1034</td>
</tr>
<tr>
<td>300</td>
<td>149</td>
<td>188</td>
<td>1293</td>
<td>188</td>
<td>1293</td>
<td>188</td>
<td>1293</td>
<td>141</td>
<td>970</td>
</tr>
<tr>
<td>400</td>
<td>204</td>
<td>170</td>
<td>1173</td>
<td>170</td>
<td>1173</td>
<td>128</td>
<td>880</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GENERAL NOTES:

(a) These pressure ratings apply to metallic fittings, including butt welded or hygienic clamp connections.

(b) For installation practices of hygienic clamp connections, refer to Figure DT-9.4-1.

(c) Manufacturers may publish higher pressure ratings; see DT-2.

(a) Manufacturer may publish higher pressure ratings; see paragraph DT-2.

(b) Hygienic clamp connections shall meet criteria in DT-9.
**Table DT-4.1.2-13**  
Automatic Tube Weld:  
Standard Outlet Hygienic Clamp Joint Reducing Tee  

(Cont’d)  

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>Y</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>3.375</td>
</tr>
<tr>
<td>3</td>
<td>2 ½</td>
<td>3.375</td>
</tr>
<tr>
<td>4</td>
<td>½</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>¾</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>1 ½</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>2 ½</td>
<td>4.125</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>4.125</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>5.625</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>5.625</td>
</tr>
</tbody>
</table>

(Insert 6" x 1/2" thru 6" x 2-1/2" sizes)
**Table DT-4.1.4-1**

**Automatic Tube Weld: Ferrule**

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>A (in.)</th>
<th>B (mm)</th>
<th>C (in.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\frac{1}{4}$</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>$\frac{3}{8}$</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>$\frac{1}{2}$</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>$\frac{5}{8}$</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>1</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>$1\frac{1}{2}$</td>
<td>1.750</td>
<td>44.45</td>
<td>1.125</td>
</tr>
<tr>
<td>2</td>
<td>2.250</td>
<td>57.15</td>
<td>1.125</td>
</tr>
<tr>
<td>2$\frac{1}{2}$</td>
<td>2.250</td>
<td>57.15</td>
<td>1.125</td>
</tr>
<tr>
<td>3</td>
<td>2.250</td>
<td>57.15</td>
<td>1.125</td>
</tr>
<tr>
<td>4</td>
<td>2.250</td>
<td>57.15</td>
<td>1.125</td>
</tr>
<tr>
<td>6</td>
<td>3.000</td>
<td>76.20</td>
<td>1.500</td>
</tr>
</tbody>
</table>

**Table DT-4.1.5-1**

**Automatic Tube Weld: Cap**

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>A (in.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\frac{1}{2}$</td>
<td>1.500</td>
</tr>
<tr>
<td>$\frac{3}{8}$</td>
<td>1.500</td>
</tr>
<tr>
<td>1</td>
<td>1.500</td>
</tr>
<tr>
<td>$1\frac{1}{2}$</td>
<td>1.500</td>
</tr>
<tr>
<td>2</td>
<td>1.500</td>
</tr>
<tr>
<td>$2\frac{1}{2}$</td>
<td>1.500</td>
</tr>
<tr>
<td>3</td>
<td>1.750</td>
</tr>
<tr>
<td>4</td>
<td>2.000</td>
</tr>
<tr>
<td>6</td>
<td>2.500</td>
</tr>
</tbody>
</table>

GENERAL NOTE: Minimum I.D. control portion length, $\theta$, is 0.375 in. (9.53 mm) for all sizes.

SEE TABLE DT-4.1.5-1 REPLACEMENT BELOW
### Table DT-4.1.5-1

**Automatic Tube Weld: Cap**

**Type A**

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>Type</th>
<th>O.D. Tangent, A, min.</th>
<th>Inside Knuckle Radius (IKR), R1, min.</th>
<th>Inside Crown Radius (ICR), R2</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>in.</td>
<td>mm</td>
<td>in.</td>
<td>mm</td>
<td>in.</td>
</tr>
<tr>
<td>1/2</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.063</td>
<td>1.60</td>
<td>0.250</td>
</tr>
<tr>
<td>3/4</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.063</td>
<td>1.60</td>
<td>0.375</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.063</td>
<td>1.60</td>
<td>0.500</td>
</tr>
<tr>
<td>1 1/2</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.090</td>
<td>2.29</td>
<td>0.750</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.120</td>
<td>3.05</td>
<td>1.000</td>
</tr>
<tr>
<td>2 1/2</td>
<td>A</td>
<td>1.500</td>
<td>38.10</td>
<td>0.150</td>
<td>3.81</td>
<td>1.250</td>
</tr>
<tr>
<td>3</td>
<td>A</td>
<td>1.750</td>
<td>44.45</td>
<td>0.180</td>
<td>4.57</td>
<td>1.500</td>
</tr>
<tr>
<td>4</td>
<td>A</td>
<td>2.000</td>
<td>50.80</td>
<td>0.240</td>
<td>6.10</td>
<td>2.000</td>
</tr>
<tr>
<td>6</td>
<td>A</td>
<td>2.500</td>
<td>63.50</td>
<td>0.360</td>
<td>9.14</td>
<td>3.000</td>
</tr>
</tbody>
</table>

**GENERAL NOTES:**

(a) Minimum wall thickness in formed areas, C, shall conform to DT-3.
(b) Other shapes permitted as long as the design meets or exceeds the pressure and temperature ratings shown in Table DT-2-1 and dimension minimums A, R1 and R2 are met.
Table DT-4.1.5-1
Automatic Tube Weld: Cap (Cont’d)

<table>
<thead>
<tr>
<th>Nominal Size, in.</th>
<th>Type</th>
<th>O.D. Tangent, A, min.</th>
<th>C, min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>in.</td>
<td>mm</td>
</tr>
<tr>
<td>1/2</td>
<td>B</td>
<td>1.500</td>
<td>38.10</td>
</tr>
<tr>
<td>3/4</td>
<td>B</td>
<td>1.500</td>
<td>38.10</td>
</tr>
<tr>
<td>1</td>
<td>B</td>
<td>1.500</td>
<td>38.10</td>
</tr>
<tr>
<td>1 1/2</td>
<td>B</td>
<td>1.500</td>
<td>38.10</td>
</tr>
<tr>
<td>2</td>
<td>B</td>
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<td>38.10</td>
</tr>
<tr>
<td>2 1/2</td>
<td>B</td>
<td>1.500</td>
<td>38.10</td>
</tr>
<tr>
<td>3</td>
<td>B</td>
<td>1.750</td>
<td>44.45</td>
</tr>
<tr>
<td>4</td>
<td>B</td>
<td>2.000</td>
<td>50.80</td>
</tr>
<tr>
<td>6</td>
<td>B</td>
<td>2.500</td>
<td>63.50</td>
</tr>
</tbody>
</table>

GENERAL NOTES:
(a) Minimum I.D. control portion length, B, is 0.375 in. (9.53 mm) for all sizes.
(b) Other shapes permitted as long as the dimension C minimum is maintained throughout section.
(c) Retaining Ring(s) (Optional). The retaining ring groove and retaining ring shall not contribute to process fluid holdup.

(d) Internal Support Hangers. Each support hanger shall be of a solid piece construction.

(e) Flow Straightener Housing (Optional). In a non-retaining ring design, the flow straightener housing shall be designed to keep the turbine flowmeter internals in place.

**PI-4.2.2** Non-process Contact Components. The pickoff shall not contact the process.

**PI-4.2.3** Installation. The flowmeter shall be installed with a minimum straight run of 10 pipe diameters upstream of the inlet and 5 pipe diameters downstream of the outlet.

**PI-4.2.3.1** Orientation. Turbine flowmeters shall be oriented to ensure that the meter is completely filled with the process fluid during operation.

The manufacturer’s recommendations for the orientation and the structural support of turbine flowmeters shall be followed.

**PI-4.2.4** Performance. Turbine flowmeter performance details are provided in ASME MFC-22.

**PI-4.2.4.1** Accuracy. Turbine flowmeter accuracy details are provided in ASME MFC-22.

**PI-4.2.4.2** Process Influences. Entrained gas shall be eliminated by having sufficient back pressure downstream of the flowmeter to prevent cavitation, or by the use of a vapor eliminator upstream of the meter.

The owner/user should consult the manufacturer for recommendations on the minimum operational pressure, as the meter outlet pressure is dependent upon the process fluid conditions, specific gravity, and viscosity.

For process liquids where abrasives or other entrained particles may exist, hygienic filters, strainers, or other devices shall be installed upstream of the flowmeter to prevent damage.

**PI-4.2.4.3** Ambient Influences. External environmental conditions do not affect the performance of the turbine flowmeter when the flowmeter is operated within the manufacturer’s specifications.

**PI-4.2.5** Selection. Maximum process fluid velocity should be taken into consideration during air purge or clean steam sanitization to prevent over ranging of the bearings and damaging the rotor assembly. Turbine flowmeter selection details are provided in ASME MFC-22.

**PI-5 LEVEL INSTRUMENTS**

**PI-5.1** Radar Level Instruments

**PI-5.1.1** General. Radar level instruments are also referred to as noncontact radar, free space radar, and through-air radar level instruments.

These instruments use high-frequency electromagnetic signals to measure the distance between the instrument and the upper surface of the targeted process fluid directly below the instrument.

These instruments should be configured for the specific combination of vessel and process fluid to ensure measurement performance.

**PI-5.1.2** Essential Components. A radar level instrument is comprised of an antenna, a process connection, and supporting electronics.

The process contact components of a radar level instrument shall meet the surface requirements as specified in Part 5F and material of construction requirements as specified in Part 5M or Part 5R. Requirements of process contact welds are specified in Part 5M.

**PI-5.1.2.1** Antenna. The antenna of a radar level instrument is available in bulb horn, or rod construction (see Figure PI-5.1.2.1-1). The antenna is either isolated by or encapsulated in polymers or other nonmetallic material.

**PI-5.1.2.2** Process Connection. The radar level instruments and isolating seals shall use hygienic connections as per Parts 5D, DT, and 5C.

**PI-5.1.3** Installation. The mounting location and orientation of the antenna should be in accordance with the manufacturer’s recommendations. This is important in order to achieve the specified performance, as well as to ensure cleanliness.

**PI-5.1.3.1** Drainability. To prevent any liquid holdup on the sensor’s process contact surfaces, the radar level instrument should be mounted perpendicular to the surface of the process fluid.

**PI-5.1.3.2** Cleanability. Cleanability is determined by the combination of antenna design and geometry and the location of the process connection. For effective cleanability, shadowing effects, recessed areas, and annular spaces created by the installed antenna should be taken into consideration.

**PI-5.1.3.3** Mounting Location. The process connection should be located on top of the vessel. For the most accurate results, the mounting location should be selected to minimize or avoid obstructions within the space below the antenna.
To ensure a reliable level measurement, the mounting location should be $\frac{1}{3}$ to $\frac{2}{3}$ of the vessel radius, as measured from the vessel centerline (see Figure PI-5.1.3.3-1).

The minimum detectable vessel level is given by the mounting location. To determine if the vessel is completely empty, the sensor should be pointed to the lowest section of the vessel.

**PI-5.1.3.4 Orientation.** The sensor should be mounted perpendicular to the surface of the process fluid.

**PI-5.1.3.5 Insertion Length/Depth.** A vessel’s maximum working level shall be below the insertion depth of the radar level instrument.

**PI-5.1.3.6 Special Considerations.** Each instrument has a specific minimum measuring distance (also referred to as blocking distance or dead band) (see Figure PI-5.1.3.3-1) immediately in front of the antenna, in which measurements are not possible.

When radar level instruments are installed in nonmetallic vessels, the signal may detect objects outside the vessel. The owner/user should consult with the manufacturer for additional requirements.

The owner/user should consult the manufacturer regarding energy emitted by the radar level instrument to evaluate potential impact on the process fluid.

**PI-5.1.4 Performance.** Performance is determined primarily by the reflective properties of the process fluid, mounting location, and orientation within the vessel.

**PI-5.1.4.1 Accuracy.** The accuracy shall include the combined effects of linearity, repeatability, and hysteresis.

**PI-5.1.4.2 Process Influences.** The following process conditions may reduce the radar signal strength returned to the antenna, which may impact on the measuring performance:
- (a) a wavy or rippled surface
- (b) vortices in the process fluid
- (c) large changes of the reflective properties of the process fluid
- (d) foam, steam, or mist on top of the process fluid
- (e) buildup on the antenna

**PI-5.1.4.3 Ambient Influences.** Ambient influences do not affect the measuring performance if they are within the manufacturer’s specifications.

**PI-5.1.5 Selection.** The main consideration when selecting a radar level instrument is the required performance for the specific application as described in PI-5.1.4.

**PI-6 PRESSURE INSTRUMENTS**

**PI-6.1 Pressure Sensors**

**PI-6.1.1 General.** Pressure sensors used in bioprocessing applications shall be isolated from the process by means of an integral diaphragm. The pressure may be transmitted between the isolation diaphragm and the sensing element using a fill fluid.

**PI-6.1.2 Installation.** Pressure sensor installation methods include flush tee, in-line instrument tee, and short-outlet tee. See Figure PI-6.1.2-1. To minimize branch legs, flush tee or in-line installations are preferred. See Figure PI-6.1.2-1, illustrations (a) through (d).

**PI-6.1.2.1 Mounting Location.** Pressure sensors should be mounted away from flow restrictions to reduce the impact of pressure fluctuations on the measurement.

**PI-6.1.2.2 Special Considerations.** Diaphragms shall be protected and handled in accordance with the manufacturer’s guidelines to prevent damage.
PI-5.1 Free-Space Radar Level Instruments

PI-5.1.1 General
This section provides device specific requirements related to free-space radar level instruments. See PI-2.1 for information on general requirements. Free-space radar level instruments are also referred to as noncontact radar and through-air radar level instruments.

PI-5.1.3.1 Mounting Location
The process connection shall be located on top of the vessel. The mounting location should be selected to avoid or minimize obstructions below the antenna. The mounting location should be 1/3 to 2/3 of the vessel radius, as measured from the vessel centerline (see Fig. PI-5.1.3.1-1).

PI-5.1.3.2 Orientation
The free-space radar antenna should be mounted perpendicular to the surface of the process fluid.

PI-5.1.3.3 Immersion Length/Depth
A vessel's maximum working level shall be below the insertion depth of the free-space radar antenna.

PI-5.1.3.4 Special Installation Considerations
(a) Each instrument has a specific minimum measuring distance (also referred to as blocking distance or dead band) (see Fig. PI-5.1.3.1-1) immediately below the antenna, in which measurements are not possible.
(b) Considerations should be made for free-space radar level instruments installed in nonmetallic vessels. Radar level instruments installed in nonmetallic vessels can detect objects outside the vessel.
(c) For effective cleanability, shadowing effects, recessed areas, and annular spaces created by the installed antenna should be evaluated.
PI-5.1.4 Performance

PI-5.1.4.1 Accuracy
No requirements or recommendations apply.

PI-5.1.4.2 Response Time
No requirements or recommendations apply.

PI-5.1.4.3 Process Influences
The following process conditions may reduce the radar signal strength returned to the antenna, which may impact the measuring performance:
(a) a wavy or rippled surface
(b) vortices in the process fluid
(c) large changes of the reflective properties of the process fluid
(d) foam, steam, or mist on top of the process fluid
(e) buildup on the antenna

PI-5.1.4.4 Ambient Influences
Mounting of the free-space radar level instrument in areas of high electromagnetic interference should be avoided.

PI-5.1.4.5 Special Performance Considerations
No requirements or recommendations apply.

PI-5.1.5 Selection
Antenna construction type (see figure PI-5.1.2-1) and its material of construction shall be compatible with the stated process conditions, cleaning solutions, and sanitization conditions.
PI-8.4 Total Organic Carbon (TOC) Instruments

PI-8.4.1 General
This section provides device-specific requirements related to TOC instruments. See PI-2.1 for information on general requirements.
TOC measurement is used to quantify the presence of organic carbon in aqueous media. On-line monitoring of TOC is an integral component of compendial water as defined by the Global Pharmacopeias (e.g., USP <643>, JP 2.59, EP 2.2.44).

PI-8.4.2 Components
TOC measurement is achieved via oxidation by ultraviolet (UV) radiation measured by differential conductivity. TOC measurement utilizes conductivity sensors in two ways:

a) with internal reactor for batch measurement
b) with internal reactor for continuous measurement

The TOC measurement method should be selected based on the application.

PI-8.4.2.1 Process Contact Components
A TOC analyzer shall include a sample valve of hygienic design.

PI-8.4.2.2 Non-Process Contact Components
TOC analyzer sampling systems should include but are not limited to, sample tubing, drain valve(s), flow control, and sample coolers. The sampling system shall not contribute to the contamination of the compendial water system. The slipstream flow to the TOC analyzer shall be continuous while the sample valve is open to avoid stagnant conditions.

PI-8.4.3 Installation
Installation shall be performed in accordance with figure PI-8.4-1.

PI-8.4.3.1 Mounting Location
TOC sensors shall be mounted at an elevation below the sample valve of the compendial water system.
PI-8.4.3.2 Orientation
No requirements or recommendations apply.

PI-8.4.3.3 Immersion Length/Depth
No requirements or recommendations apply.

PI-8.4.3.4 Special Installation Considerations
The TOC sample valve shall be closed during CIP or SIP to prevent damage to the sensor. TOC instruments are not designed for CIP or SIP operations.

Fig. PI-8.4-1 Accepted Installation for a TOC instrument
PART MC
COMPONENTS FOR MULTIUSE

MC-1 PURPOSE AND SCOPE

The purpose of this Part is to provide the requirements for the sealing components of seals, valves, and fittings. Polymeric ferrules and clamps should be designed and manufactured to ensure proper fit-up and avoid leakage. Material of construction and the molding process impact the tolerances of polymeric ferrules; consequently, tolerances are not the same as they are for metallic ferrules. Polymeric ferrules shall meet the nominal dimensions and tolerances of Table DT-7.1-2 and shall achieve clearance as per DT-9.4(e).

Polymeric ferrules and clamps should be designed and manufactured to ensure proper fit-up and avoid leakage. Material of construction and the molding process impact the tolerances of polymeric ferrules; consequently, tolerances are not the same as they are for metallic ferrules. Polymeric ferrules shall meet the nominal dimensions and tolerances of Table DT-7.1-2 and shall achieve clearance as per DT-9.4(e).

The process integrity is maintained. They include seals between two ferrules.

The geometry of the most common hygienic union is governed by Table DT-7.1-1 and is shown in Figures MC-2.2.1-1 and MC-2.2.2.2. Other geometries for the opposing ferrules are also used in the industry and are controlled by relevant industry standards [e.g., ISO 2852, DIN 11864 (-1, -2, -3, O-rings)]. (See Figures MC-2.2.2-3 and MC-2.2.2-4.)

Other hygienic unions and cross-sectional geometries shall meet all of the requirements of this Standard, except for the ferrule dimensions.

Nonhygienic connections shown in Figure MC-2.2.2-5 are not recommended (e.g., threaded fittings exposed to process fluid).

MC-2 SEALING COMPONENT TYPES

MC-2.1 General

When using polymeric hygienic unions, several application variables should be considered to ensure optimum performance. Some variables include fluid type, process temperature, system pressure, vibration, materials of construction, sterilization method (where appropriate), cleaning methods (where appropriate), and duration of use. Pressure and temperature ratings of polymeric hygienic unions shall be provided by the manufacturer.

MC-2.2 Static Seals

MC-2.2.1 General. A static seal is characterized by the absence of relative motion between sealing surfaces, or between the sealing surface and a mating surface, after initial installation. Small amounts of movement that might be caused by thermal expansion, vibration, bolt stretch, or seal response to fluid pressure do not alter the static definition.

MC-2.2.2 Hygienic Unions. Hygienic unions provide connections between process components (e.g., pipe fittings, tank fittings, instruments, and hoses) to ensure the process integrity is maintained. They include seals between two ferrules.

Other ring seal geometries of varying cross sections (e.g., manway gaskets) may be used in hygienic applications. However, significant differences may exist in their performance (e.g., pressure and cleanability), and they should be evaluated accordingly.


For use in bioprocessing applications, O-rings and their mating surfaces shall meet the requirements of this Standard.

MC-2.2.4 Other Static Seals. Other static seals used in bioprocessing applications shall meet the requirements of this Standard (e.g., flat gaskets, L-cups, U-cups, stoppers, septums, and bioseals).
(22) Figure MC-2.2.2-1
Hygienic Union per Table DT-7.1-1

(a) Typical Hygienic Clamp Union — 1 in. and Smaller (Type A) per Table DT-7.1-1 (Accepted)

(b) Typical Hygienic Clamp Union — 1 in. (Type B) per Table DT-7.1-1 (Accepted)

(c) Typical Hygienic Clamp Union — 1.5 in. and Larger (Type B) per Table DT-7.1-1 (Accepted)

See Figure MC-4.2-1 intrusion/recess

Figure MC-2.2.2-2
Hygienic Clamp Union per Table DT-7.1-1

Symmetric ferrules

(Accepted)
Figure MC-2.3.1.9-1
Pressure Relief and Check Valves

(a) Spring-Type Check Valve

(b) Poppet-Type Check Valve (Vertical Configuration) [Note (1)]

(c) Poppet-Type Check Valve (Horizontal Configuration) [Note (1)]

NOTE: (1) Gray color represents backflow blocked by the poppet.

Current Figure MC-2.3.1.9-1 has been completely revised. See updated version attached.
Figure MC-2.3.1-9-1 Check Valves

(a) Spring-Type Check Valve [Note (1)]

(b) Poppet-Type Check Valve (Vertical Configuration) [Note (1)]

(c) Poppet-Type Check Valve (Horizontal Configuration) [Note (1)]
(6) Buffer fluid shall be at an appropriate flow, pressure, and temperature and should be based on the recommendation of the equipment manufacturer.

(7) A typical dual mechanical seal–unpressurized is illustrated in Figure MC-2.3.2.3-3.

**MC-2.3.2.4 Flush Plans.** A flush plan describes how the end face mechanical seal is lubricated and cooled. The flush plan numbers directly reflect plans that were developed by the American Petroleum Institute (API 682), were subsequently approved by the American National Standards Institute (ASME B73 series), and are global standard shorthand for seal support systems. If properly implemented to the requirements of this Standard, all of the following flush plans are acceptable for use in the bioprocessing industry. The numbering system used below is also recognized and used by the Fluid Sealing Association (FSA) and the European Sealing Association (ESA), as a group associated with FSA. ISO 21049, API 682, and ISO 13709 also contain important information about support systems for mechanical seals.

(a) **Flush Plan 01.** Internal seal chamber circulation for single seal from pump discharge. A high-pressure discharge of the process fluid flows to the low-pressure seal chamber. The flow of process fluid cools and lubricates the seal faces. See Figure MC-2.3.2.4-1.

(b) **Flush Plan 02.** Dead-ended seal chamber with no other sources of flush for single seal. The ambient conditions of the seal chamber are satisfactory for the process fluid to remain a coolant and lubricant for the seal faces. See Figure MC-2.3.2.4-2.

(c) **Flush Plan 03.** Dead-ended seal chamber with circulation between the seal chamber and the pump created by the design of the sealing chamber. The flow of process fluid cools and lubricates the seal faces and may prevent the accumulation of solids in the seal chamber. See Figure MC-2.3.2.4-3.

(d) **Flush Plan 11.** Seal flush from pump discharge for single seal. Often uses an orifice, but the flush line itself may be considered an orifice. A high-pressure discharge of the process fluid flows to the low-pressure seal chamber.
The flow of process fluid cools and lubricates the seal faces. See Figure MC-2.3.2.4-4.

(e) **Flush Plan 32.** Seal flush from external source. This plan is used for single seals. A fluid that is compatible with the process is injected into the seal cavity to cool and lubricate the seal. Plan 32 flush fluid will go into the process. See Figure MC-2.3.2.4-5.

(f) **Flush Plan 52.** This plan is for dual seals—unpressurized only. Unpressurized buffer fluid circulates through a reservoir. The buffer fluid is at a pressure less than the process side of the inboard seal. This plan offers protection from product entering the atmosphere and, when used under vacuum conditions, from the atmosphere entering the seal chamber. See Figures MC-2.3.2.4-6 and MC-2.3.2.4-7.

(g) **Flush Plan BPE52.** Flow and pressure are taken from the pump discharge and injected between the dual seals. The seal cavity is vented to a low-pressure point. This flush plan is used exclusively for dual seals—unpressurized. See Figure MC-2.3.2.4-8.

(h) **Flush Plan 53.** This plan is for dual seals—pressurized only. Pressurized barrier fluid is circulated through a reservoir where the barrier fluid is cooled then returned to the seal cavity. Circulation must be provided by a pumping mechanism located in the dual-seal design or externally. Adequate flow shall be provided to cool the seal. This plan offers protection from cross-contamination between the atmosphere and process fluid under normal operating conditions. See Figures MC-2.3.2.4-98 and MC-2.3.2.4-99.

(i) **Flush Plan 54.** This plan is for dual seals—pressurized only. Pressurized barrier fluid is circulated through the dual-seal cavity from an external source. The source of flow and pressure is undefined in this flush plan. The barrier fluid pressure between the inboard and outboard seals shall be higher than the process pressure acting on the inboard seal. The barrier fluid shall be compatible with the process fluid. See Figures MC-2.3.2.4-110 and MC-2.3.2.4-111.

(j) **Flush Plan 55.** This plan is for dual seals—unpressurized only. Unpressurized buffer fluid is circulated through the dual-seal cavity from an external source. The source of flow and pressure is undefined in this flush plan. The buffer fluid is at a pressure less than the process side of the inboard seal. This plan offers protection from the process fluid entering the atmosphere and, when used under vacuum conditions, from the atmosphere entering the seal chamber. See Figures MC-2.3.2.4-12, MC-2.3.2.4-13 and MC-2.3.2.4-14.

(k) **Flush Plan 74.** This plan is only for dual gas mechanical seals—pressurized. The barrier fluid pressure between the inboard and outboard seals shall be higher than the process pressure acting on the inboard seal. The barrier fluid shall be compatible with the process fluid. See Figures MC-2.3.2.4-15 and MC-2.3.2.4-16.

Figure MC-2.3.2.4-13 shows an example of Plan 55 where flow and pressure are taken from the pump discharge and injected between the dual seals. The seal cavity is vented to a low-pressure point.
**MC-2.3.3 Other Dynamic Seals**

**MC-2.3.3.1 Reciprocating Seals.** Reciprocating seals have axial movement between the inner and outer elements, as in a plunger or a piston and a cylinder. The seal, usually an O-ring, slides along the sealing surface.

**MC-2.3.3.2 Oscillating Seals.** Oscillating seals have angular movement around an arc, as in a valve handle. The seal, usually an O-ring, slides between the inner and outer elements and has limited or no longitudinal movement.
Figure MC-2.3.2.4-7
Flush Plan 52 for Top-Entry Agitator

Figure MC-2.3.2.4-98
Flush Plan 53 for Pump

Figure MC-2.3.2.4-813
Flush Plan 55_BPE52 for Pump

Figure MC-2.3.2.4-109
Flush Plan 53 for Top-Entry Agitator

Move this figure to with the changes shown to the next page
Figure MC-2.3.2.4-110
Flush Plan 54 for Pump

Figure MC-2.3.2.4-111
Flush Plan 54 for Top-Entry Agitator

Figure MC-2.3.2.4-112
Flush Plan 55 for Pump

Figure MC-2.3.2.4-114
Flush Plan 55 for Top-Entry Agitator

Move Figure MC-2.3.2.4-13 from previous page here
reactivity (see Part PM for additional details). Examples of seals coming in direct contact with a process stream include gaskets, O-rings, diaphragms, pinch tubes, and valve stem seals.

**MC-3.4.2 Certificate of Conformance.** See PM-2.2.1.

**MC-3.4.3 Test Requirements.** Conformance testing is done on initial qualification of the hygienic union. Testing is intended to show design conformance and is not required on every seal. Testing shall be repeated for significant changes in raw materials or processes used to fabricate seals. The seal manufacturer shall provide a certificate of design conformance that the sealed union meets the intrusion requirements of MC-4.2. The intrusion value is defined as the measured quantity that provides the maximum radial distance from the fitting I.D. to the point of maximum intrusion under the manufacturer's specified conditions (e.g., torque, fitting design, clamp design). The point of maximum intrusion/recess shall be measured using a method that does not cause deformation of the components being measured.

**MC-3.4.4 Additional Requirements.** [Reserved for future content]

**MC-3.5 Seal Identification**

Marking on the seal package should include all items listed in MC-3.4.2.

Manufacturer's name and lot number shall be marked on either the seal itself or the seal package containing the seal. The lot number should enable the manufacturer to identify the raw material and processing conditions used to fabricate the article. Manufacturers are encouraged to mark the seal itself to avoid potential loss of traceability and to aid in positive identification of seals after removal from a process stream. When marking diaphragms, any marking shall be done on those portions of the diaphragm that are not exposed beyond the sealing portion of the housing.

**MC-3.6 Other Seal Requirements**

[Reserved for future content]

**MC-4 SEAL PERFORMANCE REQUIREMENTS**

**MC-4.1 General Requirements**

Seals form an integral part of process systems and maintain static and/or dynamic system boundaries while being exposed to chemical, thermal, and mechanical (hydraulic and pneumatic) conditions in both cyclic and continuous modes of operation. On exposure to operating conditions, the seal shall not swell, shed, crack, erode, or otherwise deteriorate to an extent that it impacts the product or process during its expected lifetime. The seal shall not add to nor remove from the process or product to which it is exposed beyond an acceptable level (see PM-3). Following exposure to the process conditions, the seal shall be capable of being inspected, serviced, and/or replaced. Specific seal performance criteria should be established by the owner/user. Form S-1, Application Data Sheet, may be used to communicate expected process conditions.

Any given seal is not designed to perform in all possible operating conditions.

Parameters for evaluating the performance of a seal include leak rate, sealing location, dimensional stability, material stability (including shedding), and serviceability. The requirements for each of the parameters depend on the seal type and application. To predict how a seal will perform in service it shall be performance). Standardized test methods permit a consistent approach to gathering data used to evaluate seal performance. When evaluating performance test data, the owner/user should consider if the test parameters are relevant to the conditions expected in the application. Performance data should be considered when determining the appropriate service interval for the desired application.

**MC-4.2 Static Seal Performance**

Static seals shall meet the general performance requirements of MC-4.1.

On initial installation, a hygienic static seal shall provide a substantially flush interface with the hygienic clamp ferrules. Hygienic seals shall meet and be designated by one of the following intrusion categories when tested by the seal manufacturers:

(a) **Intrusion Category I.** Seals having a maximum intrusion/recess of 0.025 in. (0.6 mm).

(b) **Intrusion Category II.** Seals having a maximum intrusion/recess of 0.008 in. (0.2 mm).

The purpose of a flush interface is to minimize the entrapment of material in a dead space that can lead to microbial growth and contamination (see Figure MC-4.2-1). Excessive intrusion into the process stream may lead to erosion of elastomeric seals, thereby contaminating the process stream. The amount of intrusion depends on the dimensional control of the seal, the hygienic clamp ferrule dimensions [see Table DT-7.1-1 and Figure MC-2.2.2-1, illustrations (a) through (c)], the amount of torque applied to the flange, the material properties of the seal, the application of steam, and the surface of the seal (wet or dry) during installation.

Testing parameters used to identify the desired performance should be based on the intended operating conditions. Nonmandatory Appendix K identifies standard process test conditions (SPTC) and a method for performing testing to gather data used to evaluate the appropriate level (e.g., 10, 100, or 500) of the seal for the given service life. Performance data are collected
might be evaluated for performance. The four key points are manufacturing, installation, assembly, and use.

(a) Point of Manufacture. Mechanical seal manufacturers have performance requirements for new seals. The manufacturer’s tests should be accepted. If special performance requirements are necessary, those special requirements shall be specified.

If the mechanical seal manufacturer alters the design, material, or manufacturing technique of a mechanical seal in service, it is the responsibility of the mechanical seal manufacturer to inform all relevant parties that changes have occurred. Specific information may be requested from the seal manufacturer to support the premise that seal performance has not been altered.

(b) Point of Seal Installation. The mechanical seal will be installed in a piece of equipment. An original equipment manufacturer (OEM) will typically have its own test to verify the performance of the mechanical seal. The test of the OEM should be accepted. A review of the OEM test procedure may be requested. The OEM should consult with its seal supplier/manufacturer for seal performance issues and questions.

Contractors may install a new seal in a piece of equipment. The seal performance test may be reviewed with the installation contractor.

If unique conditions exist where special performance requirements are necessary, it is the customer’s responsibility to specify the additional requirements. An acceptable performance test may be developed.

If the OEM alters the design, material, or manufacturing technique of a mechanical seal in service, or is informed by the seal manufacturer that the design, material, or manufacturing technique has been altered, it is the responsibility of the OEM to inform all relevant parties that changes have occurred.

(c) Point of Systems Assembly. The equipment that contains the seal is installed in a system. The system’s supplier/manufacturer will have standard test procedures for testing the system integrity. The test procedures of the system’s supplier/manufacturer should be accepted. A review of the test procedure may be requested. The system assembler should consult with the OEM/supplier for seal performance issues and questions.

If the system assembler alters the design, material, or manufacturing technique of a mechanical seal in service, or is informed by the OEM that the design, material, or manufacturing technique has been altered, it is the responsibility of the system assembler to inform all relevant parties that changes have occurred.

(d) Point of Use. It is the owner/user’s responsibility to determine if the mechanical seals meet performance requirements.

MC-4.3.2.2 Installed Seals. Original point-of-use performance requirements shall be used to determine if the seal is suitable for continued use. Refurbished seals shall be held to the original point-of-use performance requirements. It is the owner/user’s responsibility to monitor equipment for failure.

MC-5 SEAL APPLICATIONS

MC-5.1 General Considerations

This section provides guidance for selecting sealing components for common applications. Each component is recommended for its suitability for the particular application, and the selection reflects current common industry practice.

Every component has its own limited process capabilities and service life for each application in which it is used. Application characteristics such as size, speed, pressure, temperature, cycles, and cycle time help define an application envelope and will determine the suitability of a particular component. Appropriate component selection requires understanding of the application requirements and component capabilities.

In order to use the component selection guidance in this section

(a) The owner/user shall collect the required application data (e.g., Form 5-1, Application Data Sheet).

(b) If the owner/user’s application data fall inside the component’s application envelope, then the guidance provided is valid.

(c) If the owner/user’s application data fall outside the component’s application envelope, then the owner/user should consult with the vendor to find the appropriate component.

Sections describing each seal type may list additional characteristics of the system and equipment necessary to ensure proper application of that component.

Seals shall be accessible for maintenance.

MC-5.1.1 Static Seals. Static seals used in all applications shall (22)

(a) meet the specific design requirements of MC-3.3.2.2.

(b) meet the operational requirements of the application envelope as defined in the relevant section of MC-5. Static seal performance (chemical resistance, physical properties, and maintenance considerations) varies significantly with both material class (e.g., EPDM, FKM, PTFE) and each supplier’s formulation and manufacturing choices.

Application-specific static seals selection guidance is provided in Nonmandatory Appendix AA.

Hygienic union fitting details (e.g., torque settings, choice of clamping mechanism, and alignment) significantly affect the performance and longevity of static sealing components and should be considered (see also ASME B31.3). For example, overtightening of these clamps may damage seals or cause excessive intrusion (see MC-4.2).
MC-5.2 Process Systems
[Reserved for future content]

MC-5.3 Compendial Ambient/Hot-Water Distribution Systems

The application and selection of sealing components are based on compeadial water at temperatures between 68°F and 185°F (20°C and 85°C) and pressures greater than 0 psig (0 barg) up to 87 psig (6 barg). Systems may be exposed to hot-water sanitization and/or intermittent steam at up to 266°F (130°C).

These systems are typically constructed of metallic materials.

Sealing components used in compeadial water systems should be selected based on requirements for long-term seal reliability in a continuous-duty cycle.

(a) Most compeadial water systems are sanitized with hot-water (self-sanitizing). When systems are steam-sanitized, the owner/user should select appropriate materials/fittings based on operational requirements.

(b) Seals used in systems that are periodically heated for sanitization should be selected to accommodate thermal cycling.

MC-5.3.1 Valves for Compeadial Water

MC-5.3.1.1 Seals for Compeadial Water. A polymer seal material is acceptable provided that the manufacturer rates the seal material for the pressure and temperature limits and the material is compatible with the service stated in MC-5.3.

MC-5.3.1.2 Valve Types for Compeadial Water

(a) Valves shall meet the general design requirements of MC-3.3.2.3(a).

(b) Diaphragm valves, which have nonsliding seals, as designated in MC-2.3.1.2(a) through MC-2.3.1.2(c), are preferred.

(c) Other valve types with nonsliding seals are acceptable (e.g., pinch valves designated in MC-2.3.1.8; bellows seals like those shown in Figure MC-2.3.1.2-2, illustration (c); membrane or diaphragm seals like those shown in Figure MC-2.3.1.2-4, illustrations (b) and (c), Figure MC-2.3.1.2-5, or Figure MC-2.3.1.4-1, illustration (a)).

(d) Valves with sliding seals in process contact are not acceptable (e.g., ball, butterfly, or plug valves) unless the design enables maintaining both sides of the sliding seal in a clean and sanitized condition or the valves are used in a continuously self-sanitizing system.

(e) Valves with nonsliding and sliding seals are acceptable if only the nonsliding seal is in process contact (e.g., needle, control, or rising stem valves with 0-ring seals).

MC-5.3.2 Single Mechanical Seals for Compeadial Water per MC-3.3.2.4(a) and MC-3.3.2.4(b)

MC-5.3.2.1 Additional Application Conditions Relevant to Mechanical Seals. The fluid in contact with the mechanical seal is process compeadial water during operation. The corrosive component is compeadial water.

MC-5.3.2.2 Additional Equipment Characteristics Relevant to Mechanical Seals. The selections shown in MC-5.3.2.3 and MC-5.3.2.4 apply only for equipment with:

(a) shaft sizes: ≤2 in. (50 mm)
(b) shaft speed: 0 RPM to 3,600 RPM
(c) radial runout: <0.002 in. (0.05 mm) total indicator reading (TIR)
(d) perpendicularity or mounting flange: <0.002 in. (0.05 mm) TIR to shaft
(e) axial movement: <0.005 in. (0.13 mm)

MC-5.3.2.3 Materials of Construction. Materials of construction shall conform to Part MM and/or Part PM, as appropriate.

There are two sets of conditions that should be considered for material selection in compeadial water due to the tribological characteristics of the seal face pair:

(a) operating 68°F to 160°F (20°C to 71°C), steam at 266°F (130°C) and 0 RPM, and 0 psig to 87 psig (0 barg to 6 barg)

(b) operating 68°F to 185°F (20°C to 85°C), steam at 266°F (130°C) and 0 RPM, and 0 psig to 87 psig (0 barg to 6 barg)

MC-5.3.2.4 Flush Plans. Flush Plan numbers 01, 02, 03, and 11, as defined in MC-2.3.2.4, are recommended. Compeadial water is the seal face lubricant.

MC-5.4 Pure Steam Distribution Systems

The application and selection of sealing components is based on pure steam with pressures to 45 psig (3.1 bar), at 292°F (145°C) (saturated steam) in high-pressure distribution areas, and 25 psig (1.7 bar), at 267°F (130°C) (saturated steam) in low-pressure distribution areas.

Seals used in service conditions beyond these limits require special consideration.

Sealing components used in pure steam distribution systems should be selected based on requirements for long-term seal reliability in a continuous-duty cycle.

Pure steam systems should be designed to provide access for examination and replacement of sealing components as many seal types used with pure steam lines may leak after thermal cycling.

MC-5.4.1 Static Seal Recommendations for Pure Steam Distribution Systems. Static seals used for pure steam applications should be selected (see Nonmandatory Appendix AA) for their ability to

(a) resist pure steam
(b) withstand continuous high temperatures
(c) minimize retightening

Hardware for use with static seals in pure steam systems should be selected to accommodate creep (cold flow) when plastic seals (e.g., PTFE or PTFE composites) are used.

**MC-5.4.2 Valves for Pure Steam Distribution Systems**

**MC-5.4.2.1 Valve Seals.** A polymeric seal material is acceptable provided that the manufacturer rates the seal material for the pressure and temperature limits and the service conditions stated in **MC-5.4**.

**MC-5.4.2.2 Valve Types**

(a) Valves shall meet the general design requirements of **MC-3.3.2.3(a)** and **SD-4.2.3**. Valve design and materials of construction shall be rated for the pressure and temperature ranges of the service stated in **MC-5.4**.

(b) Valve types with nonsliding or sliding seals are acceptable (e.g., diaphragm, ball, rising stem, steam trap, pressure control, check, pressure relief, and plug valves).

**MC-5.5 CIP**

[Reserved for future content]
MC-5 Hose Assemblies

MC-5.1 General. Hose assemblies are defined here as a length of a flexible polymeric element with at least one end connection securely affixed and capable of containing fluids under specified conditions (e.g., pressure and temperature).

MC-5.2 Hose Construction

MC-5.2.1 Flexible Elements. Elements may be constructed from a single, homogeneous material or multiple layers. Multilayer elements may consist of an inner contact layer surrounded by one or more additional reinforcement layers and an outer cover. Reinforcement layers may include fabric braiding, metal wire braiding, and various elastomeric materials. The liner design shall allow for drainability and cleanliness as required by the end-user.

MC-5.2.2 Mechanically Affixed and Reusable End Connections. Metallic and nonmetallic end connections are attached to the flexible element by mechanical compression. The design shall ensure a seal is maintained at the end of the barb [see Figure SD-3.2.1-1, illustration (d)]. Band-style hose clamps are not recommended [see Figure SD-3.2.1-1, illustration (c)]. The fitting should be designed to minimize entrainment of liquid in the hose assembly. Dimensions and tolerances of the process connection shall be consistent with Table DT-7.1-1 or Table DT-7.1-2.

MC-5.2.3 Flare-Through End Connections. Flarethrough end connections are connections in which the inner contact layer of the flexible element extends through the fitting and is formed into the end connector. Flarethrough end connections may have integral gaskets or provisions for standard gaskets.

MC-5.2.4 Molded-in-Place End Connections. Molded-in-place end connections are secured to the flexible element by a thermal or chemical bond. Molded-in-place end connections using nonrigid materials may require additional stiffening reinforcement to achieve an adequate process connection seal. Molded-in-place end connections may include an integral gasket.

MC-5.2.5 Hose Materials. Hose assembly materials shall conform to applicable sections of SD-2.4.1.2 and PM-2.1:

(a) Biocompatibility. The biocompatibility and proper material selection shall be the responsibility of the enduser. Biocompatibility testing of candidate hose assemblies for qualification requires USP <87> (or ISO 10993-5) and USP <88> Class VI (or ISO 10993-6, -10, and -11) tests on all polymeric process contact materials. End-users may request similar testing on noncontact layers that may come in contact with the process fluid if the inner liner fails. Hose assembly suppliers shall provide, on customer request, documentation of the biocompatibility testing on final manufactured hose assembly materials. Failure of either test indicates unacceptable biocompatibility of the candidate hose assembly.

(b) Surface Finish. Surface finish of metallic end fittings shall conform to the requirements of Part SF.

(c) Particle Generation. Hose assembly designs should minimize wear that generates particles that could enter the process.

(d) Extractables. Hose assembly materials shall conform to the requirements of PM-3.2.

MC-5.3 Hose Assembly Performance. The equipment supplier should be informed of all the conditions under which the hose assembly may be expected to operate. This should include the methods, frequency, and length of cleaning and sterilization procedures. In addition to the service temperature and pressure, any parameters that may affect the hose assembly performance should be provided. The equipment supplier should inform the end-user of the life cycle expectancy and the methods that will ensure that the hose assembly operates within its design specification (e.g., routine maintenance).

MC-5.3.1 Service Temperatures and Pressures. Hose assemblies shall be capable of withstanding thermal and pressure cycling between the rated upper and lower temperature and pressure limits.

MC-5.3.2 Nonroutine Events. The complete procedure for nonroutine events such as passivation, deroking, and postconstruction cleaning shall be supplied by the end-user. The supplier should inform the end-user whether the hose assembly will perform as specified during these events. The end-user should perform a risk assessment to determine if a new hose assembly is required after nonroutine events.

MC-5.3.3 Cleaning Systems. Hose assembly requirements shall be based on the sterilization method used. All process contact surfaces should be designed to minimize crevices. When crevices cannot be avoided, sterilization testing shall be performed to validate sterility within the system boundaries. All hose assemblies and hose assembly process contact surfaces shall be designed to allow effective removal of cleaning agents from external surfaces.

MC-5.3.4 Sterilizing Systems. Hose assembly requirements shall be based on the sterilization method used. All process contact surfaces should be designed to minimize crevices. When crevices cannot be avoided, sterilization testing shall be performed to validate sterility within the system boundaries. All hose assemblies and hose assembly process contact surfaces shall be designed to allow effective removal of cleaning agents from external surfaces.

MC-5.4 Hose Assembly Installation. Hose assemblies shall be installed per SD-3.2 and used in accordance with the supplier's guidelines (e.g., bend radius). Change in hose assembly length due to pressure and temperature cycling and the potential effect on drainability should be considered by the end-user.

MC-5.5 Conformance Requirements for Hose Assemblies

MC-5.5.1 Certificate of Conformance. A Certificate of Conformance shall be issued by the hose assembly supplier containing the following information:

(a) manufacturer's name
(b) part number
(c) unique identifier of the hose assembly
(d) material of construction of process contact items
(e) compliance to USP <87> (or ISO 10993-5) and USP <88> Class VI (or ISO 10993-6, -10, and -11)
(f) packaging and storage recommendations (this may be in another document)

The supplier's name and unique identifier shall be marked on either the hose assembly itself or the package containing the hose assembly. The unique identifier shall enable the supplier to identify the raw material and processing conditions used to fabricate the article. Suppliers shall mark the hose assembly itself to avoid potential loss of traceability and to aid in positive identification of hose assemblies.

MC-5.5.2 Test Requirements. Conformance testing is done on initial qualification of the hose assembly. Testing is intended to show design conformance and is not required on every hose assembly. Testing shall be repeated for significant changes in raw materials or processes used to fabricate hose assemblies.
**MJ-2.2 Nickel Alloys.** When filler metals are used, the matching filler metals listed in Table MM-5.3-4 shall be used, except that higher alloy filler metals may be used when specified by the owner/user. Nickel alloys may be welded with or without filler metals. Postweld solution heat treatment is not required. See MM-5.3 for further instructions.

**MJ-2.3 Copper Alloys.** Brazing joint filler metals shall conform to Table MM-5.3.4-1. Copper-to-copper joints shall be brazed using copper-phosphorus or copper-phosphorus-silver brazing filler metal (BCuP series) without flux.

**MJ-2.3 Nonmetallics**

Joining of polymeric materials shall be performed in accordance with MJ-9. Joining of other nonmetallic materials shall be in accordance with procedures and processes recommended by the material manufacturer, and approved by the owner/user, using materials or compounds that are inert to the intended service.

**MJ-3 JOINT DESIGN AND PREPARATION**

**MJ-3.1 General**

All joints shall have complete fusion on process contact surfaces. All weld joints shall have the process contact surfaces properly purged or protected for the prevention of discoloration or contamination. External attachments (e.g., lift lugs, dimple jackets, or ladder clips) shall have any discoloration or contamination. External attachments of discoloration or contamination. External attachments (e.g., lift lugs, dimple jackets, or ladder clips) shall have any discoloration or contamination.

Welds attaching any connection that passes through the wall of a tank or vessel, or a branch connection on a pipe or tube system, in which one or both sides of the weld joint is a process contact surface, shall either be joined with a full penetration groove weld with a reinforcing fillet weld [similar to Figure SD-3.4.2-2, illustration (a)], or have at least one vent hole provided if double fillet welded only [similar to Figure SD-3.4.2-2, illustration (b)]. A vent hole is required on all lap, tee, corner, or edge (parallel) joints that have one weld as a process contact surface and are not attached by full penetration welds. The vent hole shall provide a path for process fluid or test media flow if the inner weld containment fails. Vent holes are not required when all welds are on process contact surfaces [e.g., Figure SD-3.4.3-2, illustration (c) detail or similar]. The vent hole shall be no larger than 1∕2 in. (13 mm) and may be tapped for a preliminary compressed air and soapuds test for tightness of inside welds. These vent holes may be plugged when the vessel is in service. The plugging material used shall not be capable of sustaining pressure between the lapped surfaces.

Socket welding is not permitted in process stream systems or where CIP or SIP requirements are defined.

**MJ-3.2 Pressure Vessels and Tanks**

Intermittent welds shall not be used on process contact surfaces on vessels and tanks. Head and shell welds leaving an unwelded process contact joint shall not be used.

See Figures MJ-3.2-1 and MJ-3.2-2 for examples of unacceptable and acceptable head-to-shell weld joints.

**MJ-3.2.1 Pressure Vessels.** Weld joint designs shall be those permitted by ASME BPVC, Section VIII and shall conform to MJ-3.1.

**MJ-3.2.2 Tanks.** Weld joint designs shall be those permitted by the code or standard of construction for the tank and shall conform to MJ-3.1.

**MJ-3.3 Piping**

Weld joint designs shall be those permitted by ASME B31.3 and shall conform to MJ-3.1.

**MJ-3.4 Tubing**

Weld joint designs for hygienic tubing and fittings shall be square butt joints. The tubing and fittings shall have ends prepared by machining or facing to provide a square end that meets the requirements of Tables DT-3-1 and DT-3-2. The butt weld joints shall be properly cleaned within 1∕2 in. (13 mm) of the joint area on the inside and outside surfaces prior to welding. Welding on tubing shall be done using automatic welding techniques (such as orbital tube welding or lathe welding), except where the permit. In that case, manual welding is acceptable and acceptable head-to-shell weld joints.

**MJ-3.5 Tube-Attachment Welds**

(a) Tube-attachment welds are those that

(1) make branch connections other than those used to fabricate the fittings described in Part DT

(2) attach tubes to other product forms

(3) attach nozzles to transfer panels

(4) attach channels to transfer panels

When vent holes are installed in a component with a published rating, e.g. ASME B16.5 slip on flanges (see Figure MJ-3.1-1), the published pressure rating may no longer be valid. The pressure rating of the component shall be evaluated considering the addition of the vent hole. The marking on the component shall be changed to reflect that it is no longer in conformance with the original standard.
Note to Editor: Insert new Figure MJ-3.1-1 Vent Hole Examples before Figure MJ-3.2-1. File to be provided.
GENERAL NOTE: This figure does not provide design criteria for weld joints. It only depicts examples of unacceptable weld configurations.
within \( \frac{1}{2} \) in. (13 mm) on the inside and outside surfaces, where accessible, prior to welding. Fillet welds, groove welds, or a combination of both may be used.

**MJ-3.6 Brazed Joints**

Joint design shall conform to the latest edition of NFPA 99.

**MJ-4 JOINING PROCESSES AND PROCEDURES**

**MJ-4.1 Introduction**

All welds, including tack welds, shall be made in accordance with a welding procedure qualified in accordance with MJ-5. All welders and welding operators, including those who make tack welds, shall be qualified per MJ-6.

**MJ-4.2 Welds Finished After Welding**

For pressure vessels, tanks, and piping and tubing systems where the process contact surface of the weld is to be finished after welding, the welding processes used shall be limited to the arc or high-energy beam (electron beam and laser beam) processes as defined in AWS A3.0. The owner/user and contractor shall agree that the welding process selected will provide the desired results.

**MJ-4.3 Welds Used in the As-Welded Condition**

For pressure vessels, tanks, and piping and tubing systems where the process contact surface of the weld is to be used as is, welding processes shall be limited to the inert-gas arc processes (such as gas tungsten-arc welding and plasma arc welding) or the high-energy beam processes (such as electron beam or laser beam welding), as defined in AWS A3.0. Every effort shall be made to use an automatic or machine welding process. Autogenous welds, welds with filler wire, or welds with consumable inserts are acceptable provided they meet the requirements for all applicable codes. The owner/user and contractor shall agree that the welding process selected will provide the desired results.

**MJ-4.4 Brazing**

Joining of copper and copper alloy materials by brazing shall be in accordance with NFPA 99. All brazing procedures shall be qualified per MJ-5. All brazers shall be qualified per MJ-6.

**MJ-5 PROCEDURE QUALIFICATIONS**

**MJ-5.1 Pressure Vessels and Tanks**

Welding procedures for pressure vessels and tanks shall be qualified in accordance with ASME BPVC, Section VIII.

**MJ-5.2 Piping**

Welding procedures for piping systems shall be qualified in accordance with ASME B31.3.

**MJ-5.3 Tubing**

Welding procedures for hygienic tubing systems shall be qualified in accordance with ASME B31.3, with the following additions:

(a) A change in the type or nominal composition of the backing (purge) gas shall require requalification.

(b) If filler metal is used, a change from one AWS classification of filler metal to another, or to a proprietary filler metal, shall require requalification.

This includes qualification of procedures for welding of components to Part DT but does not apply to longitudinal welds on tubes made in accordance with a recognized standard.

**MJ-5.4 Duplex Stainless Steels**

In addition to the welding procedure specification test requirements of ASME BPVC, Section IX, the weld metal and heat-affected zones from qualification test coupons of duplex stainless steels shall meet the requirements of ASTM A923 Methods A and/or C.

**MJ-5.5 Brazing**

Brazing procedures for piping systems in accordance with NFPA 99.

**MJ-6 PERFORMANCE QUALIFICATIONS**

**MJ-6.1 Pressure Vessels and Tanks**

Welder and welding operator performance qualifications for pressure vessels and tanks shall be in accordance with ASME BPVC, Section VIII.

**MJ-6.2 Piping**

Welder and welding operator performance qualifications for piping systems shall be in accordance with ASME B31.3. When the piping is to be used for hygienic systems, the essential variables for welding operators in MJ-6.3 shall also apply.

**MJ-6.3 Tubing**

Welder and welding operator performance qualifications for hygienic tubing systems shall be in accordance with ASME B31.3. This includes qualification of welders and welding operators who fabricate components in accordance with Part DT but not those who manufacture tubes in accordance with a recognized standard.

For the qualification of welding operators, the following essential variables also apply:
Figure MJ-8.4-4
Acceptable and Unacceptable Metallic Weld Bead Width and Meander on Non-Process Contact Surfaces of Groove Welds on Tube-to-Tube Butt Joints

(a) Acceptable Weld Bead

(b) Acceptable and Unacceptable Weld Bead Width Variation

(c) Acceptable and Unacceptable Weld Bead Meander

GENERAL NOTE: Applies only to non-process contact surfaces and only if weld on process contact surface cannot be examined.

examined (blind weld).
ON SURFACE FINISH

G. Kroenert, Neumo
M. Lovelace, Steel and O'Brien Manufacturing, Inc.
N. Marcum, A-T Controls, Inc.
R. McGonigle, Consultant
A. Navabi, Massachusetts Division of L. J. Star of Ohio
L. J. Peterman, United Industries, Inc.
P. A. Pettillo, Millenium Facilities Resources, Inc.
J. Rau, Dockweiler AG
J. Schaefer, Astropak Corp.
P. D. Sedivy, RathGibson
C. A. Trumbull, Paul Mueller Co.
T. J. Winter, Elkhorn Electropolish
R. E. Avery, Contributing Member, Nickel Institute
M. M. Gonzalez, Contributing Member, Consultant
B. D. Henon, Contributing Member, Consultant
J. J. Manning, Contributing Member, VNE Corp.
R. K. Raney, Contributing Member, UltraClean Electropolish, Inc.

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J. Carter, Cytiva
K. R. Davis, Nordson Medical
P. G. Galvin, GF Piping Systems, LLC
S. Hanstke, Genentech
J. R. Harp, Avantor
R. Hayes, BioMarin Pharmaceutical, Inc.
L. T. Hutton, Plasticwelding, LLC
M. W. Johnson, Entegris
T. Larkin, Jr., Mass Biologics
J. T. Mahar, 3M Purification
A. Palovcak, Arkema, Inc.
J. Pouliot, Amgen
P. Priebe, Qosina
T. Seelert, MMR Consulting
D. A. Seiler, Arkema, Inc.
H. Sinkovich, Meissner
R. A. Snow, Sanofi Global
A. Palovcak, Arkema, Inc.
A. Witmer, Regeneron

SUBCOMITTEE ON METALLIC MATERIALS

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J. Hammer, Secretary, Procter & Gamble
N. Alms, RathGibson
P. Anderson, Samuel Pressure Vessel Group
R. D. Campbell, Bechtel
J. W. Franks, Electrol Specialties Co.
J. D. Fritz, JDF Metal Consulting
S. T. Harrison, Harrison Electropolishing, LP
W. M. Huit, W. M. Huit Co.
C. Ketterman, United Industries
T. Kobayashi, JGC Corp.
K. J. Matheis, Sr., Complete Automation, Inc.
D. P. McCune, Allegheny Bradford Corp.
T. M. O'Connor, Central States Industrial Equipment
D. L. Roll, Astro Pak Corp.
W. L. Roth, Welding Engineering Consultants
N. A. Schmidt, Boccard Life Sciences
P. Sturgill, Sturgill Welding and Code Consulting
R. E. Avery, Contributing Member, Nickel Institute
Electropolished surfaces may have variances in luster that are acceptable, if the surface roughness values meet the requirements in Table SF-2.4.1-1. Mechanical buffing as a final polishing finish is unacceptable. All surfaces shall be clean. Cleanliness applies to finished components/equipment as produced and packaged by the manufacturer. Subsequent shipping, storage, handling, and installation may affect the cleanliness.

**SF-2.5 Electropolishing Procedure Qualification**

Electropolishing service providers shall maintain and implement a quality assurance/control program for their electropolishing procedures. They shall also qualify their electropolishing method(s) in accordance with a written procedure. This procedure shall specify the acceptable ranges of the electropolishing essential variables.

Nonmandatory Appendix H has been provided as a guide.

Flash electropolishing shall not be acceptable. Spot electropolishing shall be acceptable if it meets the requirements in this section.

**SF-2.6 Passivation Procedure**

Passivation for this Part shall be limited to newly installed or newly modified sections of systems and components. Flushing for construction debris or particulates should reference SD-2. Passivation shall be performed in accordance with an approved quality assurance/control program. The passivation method(s) including procedures for chemical cleaning and degreasing, passivation, and final rinse(s) shall be qualified in accordance with a written procedure and documentation package. This procedure shall specify the acceptable ranges of the passivation essential variables.

Nonmandatory Appendix E has been provided as a guide to passivation practices and evaluation of passivated surfaces. Spot passivation is permitted. The pickling process shall not be accepted as a substitute for passivation. There is no universally accepted nondestructive test for the presence of a passive layer.

For passivated process contact surfaces, the acceptance criteria in Table SF-2.6-1 apply in addition to Tables SF-2.2-1 and SF-2.2-2, as applicable. Tests to ensure the presence of a passive layer shall be specified by the owner/user.

**SF-2.7 Normative References**

The following standards contain provisions that, through reference, specify terms, definitions, and parameters for the determination of surface texture (roughness, waviness, and primary profile) by profiling methods.

- **ASME B46.1**, Surface Texture (Surface Roughness, Waviness, and Lay)
  - Publisher: The American Society of Mechanical Engineers (ASME), Two Park Avenue, New York, NY 10016-5990 (www.asme.org)
- **ISO 3274**, Geometrical Product Specifications (GPS) — Surface texture: Profile method — Nominal characteristics of contact (stylus) instruments
- **ISO 4287**, Geometrical Product Specifications (GPS) — Surface texture: Profile method — Terms, definitions and surface texture parameters
- **ISO 4288**, Geometrical Product Specifications (GPS) — Surface texture: Profile method — Rules and procedures for the assessment of surface texture
- **ISO 11562**, Geometrical Product Specifications (GPS) — Surface texture: Profile method — Metrological characteristics of phase correct filters
  - Publisher: International Organization for Standardization (ISO), Central Secretariat, Chemin de Blandonnet 8, Case Postale 401, 1214 Vernier, Geneva, Switzerland (www.iso.org)

**SF-2.8 Rouge and Stainless Steel**

Rouge is a naturally occurring phenomenon in existing stainless steel high-purity process systems (including water or pure steam). The degree to which it forms depends on

(a) the stainless steel material used for each component within the system

(b) how the system was fabricated (e.g., welding, surface finish, passivation treatment)
CHAPTER 7
DESIGN FOR SINGLE-USE

PART SU
SYSTEMS DESIGN FOR SINGLE-USE

SU-1 GENERAL
The purpose of this Part is to define the requirements that are applicable and unique to the use and manufacturing of single-use components and assemblies.

SU-2 GENERAL GUIDELINES
Single-use components and assemblies are intended for one-time use and may be referred to as disposables. Single-use components and assemblies are different from multiuse components and assemblies as they are not intended for SIP and CIP cycles. In this Part, “component” is defined as an individual unit, and “assembly” is defined as the combination of two or more individual components. This Part addresses the methods for identifying, inspecting, packaging, joining, biocompatibility, and sterilization applicable to single-use components and assemblies.

SU-3 INTEGRITY
Integrity of single-use components and assemblies shall be maintained throughout the life cycle of the product (i.e., packaging, shipping, setup, assembly, and use). Compromise in the integrity of single-use components and assemblies that may result in loss of material, microbial ingress, or impact to operator safety should be mitigated.

SU-3.1 Maintenance of Integrity
Maintenance of system integrity is paramount to both bioburden control and maintaining a sterile envelope. Qualification of design, manufacturing, testing, and distribution should be conducted by the suppliers of single-use components and assemblies. Leak-detection tests should be conducted, commensurate with the level of risk for the intended use of the single-use component or assembly. Monitoring throughout the product life cycle should be performed to deliver reliability of performance. The owner/user shall ensure that single-use component or assembly system integrity is appropriately considered during design and maintained during installation and use.

SU-3.2 Common Leak Test Methods
The decision to implement a leak test should be based on an overall risk mitigation strategy. Nonmandatory Appendix FF describes common leak test methods used for single-use components and assemblies. The specific test methods used during the life cycle shall be selected based on sensitivity, suitability, and practicality of the method.

SU-4 BIOMICABIILITY
The biocompatibility of single-use components and assemblies shall be considered carefully due to the potential for large product contact areas and long contact times. Many of these components and assemblies are composed of multiple materials or multilayer structures, and the primary concern is how the process interacts with the contact surfaces. The design of the component and assembly shall not compromise the integrity, safety, or efficacy of the process fluid. The focus of evaluations should be on the material of construction of the process contact surface, but it is preferred to evaluate the complete component and assembly. At a minimum, the process contact surface shall conform to the following tests:
   (a) biological reactivity, in vitro (cytotoxicity, i.e., USP <87>)
   (b) biological reactivity, in vivo (i.e., USP <88>) or equivalent per recognized compendia

Additionally, the user should consider protein adsorption, preservative absorption, leaching of low-molecular-weight compounds, endotoxins, and the presence of animal-derived ingredients in single-use components and assemblies.

SU-5 EXTRACTABLES AND LEACHABLES
SU-5.1 General
Testing of process equipment/components made of polymeric materials for extractables and leachables should be done to identify chemical substances that
SU-3 INTEGRITY

Integrity of single-use components and assemblies shall be maintained throughout the life cycle of the product (e.g., packaging, shipping, unboxing, storage, unpacking, set up, assembly and use) as a joint responsibility between single-use suppliers and owner/users. Integrity in this context is the ability of the entire single-use system to maintain its intended barrier properties. A compromise in the integrity of single-use systems may result in loss of process material, microbial ingress, or impact to operator safety, and should be mitigated.

SU-3.1 Maintenance of Integrity

Maintenance of system integrity is paramount to both bioburden control and maintaining a sterile envelope. Qualification of design, validation of manufacturing processes and, depending on the criticality of the process the single-use system is used for, appropriate levels of leak or integrity testing shall be implemented by the single-use system supplier to prove inherent integrity of the single-use system before shipment. Packaging and shipping validation according to relevant ASTM or ISTA standards (e.g., ASTM D4169 or ISTA 3 as referenced in Table X1-2 Functional Testing References used to Characterize Single-use Bags) shall be conducted by the suppliers of single-use systems to ensure maintenance of integrity during the transportation to the owner/user sites. At the owner/user site, visual inspection and leak tests should be conducted, commensurate with the level of risk for the intended use. Operator training and appropriate procedures shall be implemented to reduce the risk of compromising the integrity during installation and use. Monitoring of integrity throughout the product lifecycle, from manufacturing to disposal, should be performed to deliver reliability of performance.

SU-3.2 Integrity vs. Leak Testing and Correlation to Maximum Allowable Leakage Limit (MALL)

When implementation of a test is required, physical test methods such as helium or pressure decay testing are nondestructive test methods that can be applied on single-use systems throughout their lifecycle to allow further use. To ensure that such a test can fully cover the integrity of the single-use system, its detection limit shall be correlated to the maximum allowable leakage limit, called MALL (see GR-8 and Nonmandatory Appendix FF).

The manufacturer shall disclose if the physical test used is an “integrity test” or a “leak test”. If the physical test method can robustly detect a defect size at the MALL level and can confirm the barrier properties of the single-use system, it is called an “integrity test”. If the test is less sensitive and cannot confirm the barrier properties of the single-use system, it is called a “leak test”. Direct correlation methods can be used in lieu of the indirect correlation method based on leak size.

SU-3.3 Common Leak and Integrity Test Methods

The decision to implement a leak or integrity test should be based on an overall risk mitigation strategy. Nonmandatory Appendix FF, Table FF-1 describes common physical nondestructive leak and integrity test methods utilized for single-use systems. Nonmandatory Appendix FF, Table FF-2 describes common destructive leak and integrity test methods, including microbial challenge test methods that can be used to determine the MALL for microbial integrity. The specific test methods used during the life cycle shall be selected based on sensitivity, suitability, and practicality of the method.
could migrate into the process fluid, potentially affecting the process or altering the final product. Some examples of chemical substances identified in this testing include oligomers, monomers, curing (cross-linking) agents, catalysts, antioxidants, initiators, dyes, pigments, plasticizers, and mold release agents. The data generated may be used to make risk-based decisions of the potential impact that any identified substances may have on the final drug product and may aid in the selection of equipment/components. PM-3.2 provides information on extractables and leachables from polymeric materials. Nonmandatory Appendix P, P-4 provides an overview of bioprocessing equipment/component evaluation related to extractables and leachables characterizations.

SU-6 IDENTIFICATION

Single-use components and assemblies shall be designed and packaged to provide lot traceability. The traceability shall enable the owner/user to identify raw materials, processing conditions critical to support the manufacturer’s specifications, and the date of manufacture.

SU-6.1 Labeling

The primary packaging of single-use components and assemblies shall be labeled with the following information:
(a) manufacturer
(b) part identifier
(c) lot identifier
Additional information for the label may be requested by the owner/user.

SU-7 CERTIFICATE OF CONFORMANCE

The single-use component or assembly manufacturer shall issue a Certificate of Conformance that contains the following information:
(a) manufacturer
(b) part identifier
(c) lot identifier
(d) date of manufacture and/or expiration date
(e) conformance information
Additional information for the Certificate of Conformance may be requested by the owner/user.

SU-8 INSPECTION AND PACKAGING

The packaging of single-use components and assemblies shall mitigate the risk of bioburden, particulates or other contaminants (see SU-10 and Nonmandatory Appendix P, P-2). Inspection shall be performed to confirm the quality of the packaging and that the contents meet the specified criteria.

SU-8.1 Inspection

Single-use components and assemblies shall be inspected for the presence of particulates or other contaminants before primary packaging. This inspection shall take place in a controlled environment in accordance with the intended use of the final component or assembly.

SU-8.2 Packaging

The purpose of packaging of single-use components and assemblies is to control the potential introduction of bioburden, particulates, or other contaminants. The packaging shall not adulterate the component and assembly. Primary packaging shall take place in a controlled environment at a level suitable for the final use of the component or assembly. The packaging of single-use components and assemblies shall be labeled according to SU-6.1.

SU-9 STERILIZATION (BIOBURDEN CONTROL)

Single-use assemblies and components shall be compatible with the intended sterilization method. Common sterilization methods include autoclaving and gamma irradiation. Autoclaving is generally performed by the owner/user. Gamma irradiation is generally contracted to a third party by the manufacturer. The owner/user shall determine the appropriate method and level of documentation required for the given application.

SU-9.1 Gamma Irradiation

Single-use assemblies that will be gamma irradiated shall be manufactured in a controlled environment. The maximum recommended gamma irradiation dose should be specified by the manufacturer of the single-use assembly or component. When establishing a maximum dose, the manufacturer should consider the effects on physical and mechanical properties (e.g., appearance, tensile strength, and chemical characteristics of the materials used (e.g., leachable/extractable effects). The supplier shall provide lot-specific certification of processing to the owner/user. The degrees of validation are the following:
(a) validated sterility assurance level per a recognized standard (e.g., ISO 11137).
(b) gamma irradiated to the specified dose range. No validation of the effectiveness is conducted.

SU-10 SHELF LIFE, STORAGE, AND EXPIRATION DATE

The shelf life of a single-use component or assembly is the duration under specified storage conditions from the date of manufacture to the last date the product can be placed in service and remain suitable for its intended use. The expiration date is the date after which the shelf life has been exceeded. The manufacturer shall, on request, Replace with INSERT #6 – Next page

AND REDUCTION

REPLACE WITH
INSERT #6 – Next page
The materials shall be compatible with the intended bioburden reduction method. The effects on physical and mechanical properties (e.g., appearance, tensile strength) and chemical characteristics of the materials used (e.g., leachable/extractable effects) shall be addressed (refer to PM-3). Lot-specific certification of processing shall be provided to the owner/user.

Bioburden reduction of single-use components and assemblies occurs prior to process contact. Bioburden reduction is typically accomplished by but not limited to:

(a) Ionizing Radiation
   (1) Gamma irradiation
   (2) X-ray irradiation
   (3) Electron beam (E-beam)
(b) Steam sterilization
   (1) Autoclaving
   (2) Steam-in-place (SIP)
(c) Chemical sterilization
   (1) Ethylene oxide (ETO)

The owner/user shall determine the appropriate level of documentation required for the given application.

When a bioburden reduction methodology is applied to a single-use component or assembly, the supplier-issued certificate of conformance shall indicate the methodology to which the component or assembly was subjected.

**SU-9.1 Ionizing Radiation**

Single-use assemblies that will be subjected to ionizing radiation shall be manufactured in a controlled environment. The maximum recommended ionizing radiation dose shall be specified by the manufacturer of the single-use assembly or component.

The degrees of validation are the following:

(a) validated sterility assurance level of $10^{-6}$ per a recognized standard (e.g., ISO 11137).
(b) irradiated to the specified dose range. No validation of the effectiveness is conducted. The supplier is not certifying a sterility assurance level per a recognized standard (e.g., ISO 11137). This is often referred to as bioburden or microbial control.
Changes to SU-9

SU-9.2 Steam Sterilization

(a) Single-use assemblies that will be autoclaved shall be manufactured in a controlled environment. Refer to section SD-6.2.4 for autoclave material requirements of single-use components and assemblies.

(b) Single-use assemblies used to connect single-use systems to multiuse (metallic) systems that are subjected to Steam-in-place (SIP) shall meet the requirements in section SC-1(e).

SU-9.3 Chemical Sterilization

Single-use assemblies that will be subjected to ethylene oxide shall be manufactured in a controlled environment. The allowable limits for residual ethylene oxide shall be considered when establishing the ETO cycle.

The degrees of validation are the following:

(a) validated sterility assurance level of $10^{-6}$ per a recognized standard (e.g., ISO 11135)

(b) ethylene oxide exposure to the specified operational range. No validation of the effectiveness is conducted. The supplier is not certifying a sterility assurance level per a recognized standard (e.g., ISO 11135). This is often referred to as bioburden or microbial control.
(c) Nonsterile Components Marketed for Use in Sterilized Assemblies. The component manufacturer should provide one of the following:

1. Expiration date or shelf life independent of sterilization date,
2. Shelf life plus post-sterilization shelf life.

The shelf life of any assembly shall not be longer than the shelf life of any component in the assembly.
**SU-12 Design Conformance**

Design conformance testing shall be specified, performed and documented by the component or assembly manufacturer. Verified design aspects should include, but are not limited to, those listed in Table SU-12-1. Manufacturers shall specify/indicate testing frequency. Manufacturers shall provide a certificate of conformance to substantiate that the design aspects relevant to the component or assembly have been verified. Pertinent test data should be available for review upon request.

The owner/user should assess design conformance to ensure the components and assemblies meet the user requirements. This may be performed through design review, design qualification, or another method established by the owner/user.

**Table SU-12-1**

<table>
<thead>
<tr>
<th>Design Aspect</th>
<th>Applicable ASME BPE Guidance Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical and Mechanical Properties of Thermoplastic Polymers</td>
<td>PM-3.3</td>
</tr>
<tr>
<td>Chemical Compatibility of Thermoplastic Polymers</td>
<td>PM-3.4</td>
</tr>
<tr>
<td>Animal-Derived Ingredients</td>
<td>SD-2.6</td>
</tr>
<tr>
<td>Integrity</td>
<td>SU-3</td>
</tr>
<tr>
<td>Biocompatibility</td>
<td>SU-4</td>
</tr>
<tr>
<td>Extractables and Leachables</td>
<td>SU-5</td>
</tr>
<tr>
<td>Identification</td>
<td>SU-6</td>
</tr>
<tr>
<td>Sterilization (Bioburden Control)</td>
<td>SU-9</td>
</tr>
<tr>
<td>Shelf Life, Storage and Expiration Date</td>
<td>SU-10</td>
</tr>
<tr>
<td>Particulates</td>
<td>SU-11</td>
</tr>
<tr>
<td>Microbial Ingress</td>
<td>SC-2.1</td>
</tr>
</tbody>
</table>
**SC-3.2 Qualifications**

The manufacturer shall provide the operating temperature and pressure limits of the single-use bag. The manufacturer shall specify appropriate sterilization methods, including range of exposure, post-sterilization shelf life, and other limitations. The manufacturer should provide handling and safe use procedures, including hanging restrictions, filling limitations, and secondary containment recommendations.

**SC-4 POLYMERIC HYGIENIC UNIONS**

See PH-14.

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**INSERT: SC-3.1.1 Material Attributes and Characterization**

The single-use bag manufacturer shall provide the physical and functional characterization of single-use bags (for examples, refer to non-mandatory appendix X1).

**INSERT #9: SC-3.2.1 Physical Qualifications**

The single-use bag manufacturer shall provide single-use bag dimensions such as overall size, accessories sizes and locations (e.g., inlets, outlets, impellers, sensors, handles).

The single-use bag manufacturer shall provide the nominal and maximum operating volume of the single-use bag. The single-use bag manufacturer should provide minimum functional volumes where relevant for the purposes of the operation (e.g., storage, mixing).

The single-use bag manufacturer shall provide application specific dimensions required for assessing fluid contact area.

**SC-3.2.2 Temperature and Pressure Qualifications**

The single-use bag manufacturer should provide maximum operating pressure conditions. Unless specifically stated, single-use bags are generally not intended for use with atmospheric pressures exceeding 0.2 psig (13.8 mbarg) at the top of the fluid.

Where applicable (e.g., 3D bags, applications under pressure), the single-use bag manufacturer shall provide specifications for a rigid outer container, ventilation, pre-use inflation and port locations.

Single-use bag operating temperature ranges shall be specified by the single-use bag manufacturer, substantiating performance via an established testing program.
SC-5 Valves

SC-5.1 General

(a) For the purpose of this section, valves intended for single-use applications are defined as valves that allow for the replacement of the single-use process contact components after each use.

(b) Process contact surfaces of valves requiring sterilization shall conform to SU-9.

(c) The internal geometry of valves should be designed to minimize holdup volume.

(d) Valves shall be compatible with chemical and thermal sanitization conditions where required, and capable of operating as required during those processes.

(e) Pneumatically controlled valves shall be designed to prevent air transfer from the actuator to the process.

(f) The valve supplier/manufacturer should provide performance data for the intended single-use process contact polymeric material type (e.g., platinum cured silicone, thermoplastic elastomer).

(g) For valve assemblies, the manufacturer shall specify an enclosure rating (e.g., ingress protection rating, washdown duty) when required.

(h) Installation of valves shall be as per the manufacturer’s recommendations to ensure valve performance, and to minimize holdup volume when applicable (e.g., orientation of a diaphragm valve).

SC-5.2 Pinch Clamps

(a) For the purpose of this section, pinch clamps (see Figure SC-5.2-1) are manually operated, self-supporting, lightweight components used in conjunction with tubing to create an internal sealing surface.

(b) Consideration should be given to the maximum number of actuations when using multiple cycles to assess fatigue caused by operation.

(c) The supplier/manufacturer shall provide tubing material types and sizes that can be utilized per clamp model to ensure sealing performance.

(d) As pinch clamps are not designed to be fixed in place, consideration should be given to the pinch clamp configuration and weight to avoid unintentional restriction of flow.

(e) Pinch clamps intended for sterilization shall conform to SU-9.
SC-5.3 Pinch Valves

(a) For the purpose of this section, pinch valves (see Figure SC-5.3-1) are used to control flow or pressure, or create a seal within elastomeric tubing.
(b) The pinch valve assembly used shall be suitable for the intended tubing, as recommended by the pinch valve assembly supplier/manufacturer, as pinch valve compression and cycling affects tubing performance.
(c) A mechanism shall be included to ensure the sealing pinch point is protected from operator interaction.
(d) The tubing size range shall be specified to allow complete compression to form an internal seal. The amount of compression is dependent on the tubing material selected. The tubing size range is determined by the inner diameter and tubing wall thickness.
(e) The supplier/manufacturer shall specify the mounting options for assembly to equipment to ensure intended operation.
Figure SC-5.3-1 Typical Pinch Valves

(a) Actuated type  (b) Manual type

SC-5.4 Diaphragm Valves.

(a) Diaphragm valves (see Figure SC-5.4-1) intended for single-use, utilize a disposable body and diaphragm set, and are generally used for flow, pressure or proportional control.

(b) Weir diaphragm valves, where required, shall be installed at the optimum position and orientation to minimize internal holdup volume.

(c) Diaphragm valves shall be manufactured with appropriate mating connections for single-use components (e.g., hose barb, hygienic clamp union).

(d) The valve design should enable immediate leak detection between the process side and the environment.

(e) The valve actuator should be fitted with a leak detection port to indicate primary seal leakage.

(f) The single-use portion of a diaphragm valve assembly shall conform to SU-9.

(g) Once installed, the diaphragm and valve body should form a closed system to prevent product leakage.
**SC-5.5 Material Requirements**

**SC-5.5.1 Process Contact**
(a) Process contact materials shall conform with PM-2.2, PM-3.1, PM-3.2, SU-4, and SU5.
(b) Materials shall conform to SU-9.

**SC-5.5.2 Non-Process Contact**
(a) Non-process contact materials should be compatible with the conditions to which the materials will be exposed.
(b) Materials exposed to external cleaning shall be compatible with cleaning chemicals as per SD-2.4.4.2.
(c) Materials exposed to a sterilization method shall conform to SU-9.

**SC-5.6 Valve Performance**
(a) The valve assembly manufacturer shall specify and qualify valve performance. Performance specifications could include process temperature limits, system pressure limits, material compatibility, and duration of use.

**SC-5.7 Identification Requirements**
(a) Process contact materials shall conform to SU-6. Interchangeable parts that can affect form, fit, or function shall be identified for their intended purpose (e.g., tubing size, material, material hardness).
PART SI
SINGLE-USE PROCESS INSTRUMENTATION

SI-1 PURPOSE AND SCOPE  The purpose of this Part is to provide the requirements for process instrumentation and their supporting components for single-use applications.

SI-2 SINGLE-USE PROCESS INSTRUMENTATION GENERAL REQUIREMENTS  Process instrumentation for single-use applications includes, but is not limited to, sensors and supporting components (e.g. optical viewing windows and port plates).
(a) Inert-gas shielded welding processes do not produce slag. See GR-8 and AWS A3.0 for definition of slag.

(b) Welds on stainless steel tubing can produce a thin film that appears as localized islands on the surface of the weld. In welds on nickel alloys, stainless steels, or welds alloyed with nickel filler metals, these films have been identified as high-melting-point nonmetallic oxides, typically referred to as oxide islands.

(c) Oxide islands encountered on welds in stainless steels and nickel alloys identified in Tables MM-2.1-1 through MM-2.1-3 are commonly found in one of the following forms:

1. On stainless steels, a small, round, black spot at the termination of the weld bead, on the outside or inside surface, or both. This spot is generally unavoidable.

2. On products made from cast or wrought stainless steels and nickel alloys, a thin film, gray or the same color as the weld surface, may be evident because it covers the weld ripples.

3. Stainless steels welded with alloys having varying color with tints from gray to dark brown, may be evident because it covers the weld ripples.

(d) Slag in or on welds may be the result of faulty weld preparation, such as contamination, poor cleaning, or faulty tack welding procedures.

(e) Slag may also result from melting base metals of certain compositions that include elements not normally reported on Material Test Reports. These elements include, but are not limited to, aluminum, calcium, cerium, and zirconium.

(f) The owner/user and contractor should investigate the origin of any slag found during weld examination, determine its acceptability, and agree on any corrective action.
Table E-3.2-1
Minimum Surface Requirements for Process Qualification Samples

<table>
<thead>
<tr>
<th>Material</th>
<th>Test Method</th>
<th>Cr/Fe Ratio</th>
<th>Oxide Depth</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNS S31600 or UNS S31603</td>
<td>AES</td>
<td>1.0 or greater</td>
<td>15 Å min.</td>
</tr>
<tr>
<td>UNS S31600 or UNS S31603</td>
<td>GD-OES</td>
<td>1.0 or greater</td>
<td>15 Å min.</td>
</tr>
<tr>
<td>UNS S31600 or UNS S31603</td>
<td>XPS/ESCA</td>
<td>1.3 or greater</td>
<td>15 Å min.</td>
</tr>
</tbody>
</table>

**NOTES:**

(1) Test method as per SEMI F72, Test Method for Auger Electron Spectroscopy (AES) Evaluation of Oxide Layer of Wetted Surfaces of Passivated 316L Stainless Steel Components.

(2) Test method as per SEMI F60, Test Method for ESCA Evaluation of Surface Composition of Wetted Surfaces of Passivated 316L Stainless Steel Components.

(3) XPS (X-ray photoelectron spectroscopy), also known as ESCA (electron spectroscopy for chemical analysis), testing at the weld, including the worst discoloration area in the weld and heat-affected zone, and on the base metal to meet the requirements of Table E-3.2-1.
Table E-3.2-2
Passivation Processes (Cont’d)

<table>
<thead>
<tr>
<th>Process Type</th>
<th>Process Description [Notes (1), (2)]</th>
<th>Comments [Note (3)]</th>
<th>Conditions of Process [Notes (4), (5)]</th>
<th>Chemistry [Note (6)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passivation processes (Cont’d)</td>
<td>Electropolishing</td>
<td>This process is generally limited to components rather than installed systems. Process should be performed according to a qualified procedure. This process removes metal from the surface. Electropolishing should be performed in such a way as to meet or exceed ASTM B912.</td>
<td>Exposure time shall be calculated to ensure 5 μm to 10 μm material removal from all surfaces requiring passivation. Rinsing shall include a step to ensure removal of residual film that may adversely affect the appearance or performance of the product.</td>
<td>Phosphoric acid-based electrolyte</td>
</tr>
<tr>
<td>Oxidation processes</td>
<td>Hydrogen peroxide</td>
<td>Oxidizes metal surface and sanitizes</td>
<td>30 min to 2 hr at ambient to 104°F (40°C)</td>
<td>3% to 10% hydrogen peroxide</td>
</tr>
<tr>
<td>Hydrogen peroxide with peracetic acid blends</td>
<td>Oxidizes metal surface and sanitizes</td>
<td></td>
<td></td>
<td>1% to 2% blend</td>
</tr>
</tbody>
</table>

NOTES:
(1) Application methods include fluid circulation, gelled applications for welds or surfaces, and spraying methods for vessels and equipment.
(2) Special attention should be directed to removal of metal shavings and construction debris from locations such as sprayballs, diaphragm valves, heat exchangers, etc.
(3) These passivation processes may produce hazardous wastes based on the metals content, and local and state regulations.
(4) The time and correlating temperatures in the Table are in direct relation to the percent by weight of the base reactant(s). A change in a formulation may change those corresponding requirements.
(5) A deionized water rinse shall immediately follow each of the chemical treatments.
(6) Chemical percentages are based on weight percent.

E-4.2 Certificate of Passivation Conformance

The passivation provider shall supply a Certificate of Conformance for each system or set (type) of component(s) that shall include, but not be limited to:
(a) customer’s name
(b) description of system or component(s)
(c) vendor company name
(d) qualified passivation method used
(e) documentation of passivation process, as follows:
   (1) written qualified procedure
   (2) documentation of process control of essential variables
   (3) instrument calibration records
   (4) certificates of analysis for all chemicals used
   (5) process testing and verification
(f) postpassivation verification method(s) used

tation generated during the process (listed in E-4.2) should provide assurance that the components or system has received the specified treatment. As a guide to owner/users and others, to help determine whether an acceptable surface has been achieved following a particular cleaning or chemical passivation procedure, Table E-5-1 has been developed.

E-5.1 Acceptance Criteria for Cleaned and Passivated Process Contact Surfaces (See Table SF-2.6-1)

Table E-5-1 may be used as a guide for acceptance criteria for cleaned and passivated components or systems. This matrix is a simplified compilation of testing methodologies that an owner/user may want to use in selecting a test or as a means to interpret a proposal from a testing company.

The matrix is divided into groups of four types of testing methods:
(a) gross inspection of cleaned and passivated parts per ASTM A380/A967 (Pass/Fail)
(b) precision inspection of cleaned and passivated parts under ASTM A380/A967 (Pass/Fail)
(c) electrochemical field and bench tests

E-5 EVALUATION OF CLEANED AND PASSIVATED SURFACES

There are no universally accepted tests to ensure that a component or system has been passivated or is in a passive condition. If the system/component has received the proper chemical passivation treatment, the documentation generated during the process (listed in E-4.2) should provide assurance that the components or system has received the specified treatment. As a guide to owner/users and others, to help determine whether an acceptable surface has been achieved following a particular cleaning or chemical passivation procedure, Table E-5-1 has been developed.
Table E-5-1
Test Matrix for Evaluation of Cleaned and Passivated Surfaces (Cont’d)

<table>
<thead>
<tr>
<th>Type of Test</th>
<th>Test Description</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron spectroscopy for chemical analysis (ESCA) also known as X-ray photoelectron spectroscopy (XPS) (PT, RT)</td>
<td>Using X-ray as an excitation source, photoelectrons are ejected from the inner-shell orbital of an atom from the target material. The ejected photoelectrons are then detected and analyzed by means of XPS. The method by which the ejected photoelectrons are then detected and analyzed is ESCA (or XPS). Useful for surface analysis to a depth of 10 Å to 100 Å. Provides quantitative analysis in measuring the following: (a) Elemental composition of the surface (10 Å to 100 Å usually) (b) Empirical formula of pure materials (c) Elements that contaminate a surface (d) Chemical or electronic state of each element in the surface (e) Uniformity of elemental composition across the top of the surface (also known as line profiling or mapping) (f) Uniformity of elemental composition as a function of ion beam etching (also known as depth profiling)</td>
<td>The specimen chamber shall be maintained at ultra-high vacuum (UHV) Instrument is not readily available The specimen shall be electronically conductive Expertise is needed for data interpretation</td>
<td></td>
</tr>
<tr>
<td>GD-OES (glow discharge–optical emission spectroscopy) (PT, RT)</td>
<td>GD-OES uniformly sputters material from the sample surface by applying a controlled voltage, current, and argon pressure. Photomultiplier tube detectors are used to identify the specific concentrations of various elements based on the wavelength and intensity of the light emitted by the excited electrons in each element when they return to the ground state. The GD-OES method is particularly useful for rapid, quantitative depth profiling of thick- and thin-film structures and coatings</td>
<td>Relatively expensive Instrument not widely available</td>
<td></td>
</tr>
</tbody>
</table>

(d) surface chemical analysis

Groups 1 and 2 of Table E-5-1 reflect the two main divisions in ASTM A380 and ASTM A967. The most obvious type of examination of these methods is visual. The examiner shall look for a clean surface free of oxides, scale, weld discoloration/heat tint, stains, dirt, oil, grease, or any deposits that could prevent the chemical passivation solution from reaching the metal surface.

The test results from ASTM A967, which are exclusively for passivation, are all based on visual detection of staining or discoloration indicative of the presence of free iron. These test results are subjective and nonquantifiable. However, for some applications this may be all that is required. The visual acceptance criteria in ASTM A380 and ASTM A967 apply.

Groups 3 and 4 of Table E-5-1 reflect two distinct methods of quantitative testing. These tests are not contained in either of the ASTM standards. These tests are designed to provide a more quantifiable analysis of a passivated surface. The electrochemical field and bench tests in Group 3 in Table E-5-1, with the exception of cyclic polarization, are suitable for field tests such as those used for passivation testing of installed piping systems and welded surfaces.

Passivation is capable of dramatically increasing the chromium-to-iron (Cr/Fe) ratio on the surface of 316L-type stainless steel when properly applied. One measurement of the degree of enhancement of the layer following a chemical passivation treatment is the Cr/Fe ratio as determined by AES, GD-OES, or ESCA. The procedure is not readily adapted to field use but may be useful in developing the passivation procedure.

A Cr/Fe acceptance ratio, regardless of test method, should be 1.0 or greater (see Table E-3.2-1); because of variability in accuracy, identical results obtained with the different test methods are not expected. The surface chemical analysis tests in Group 4 in Table E-5-1 include methods for evaluation of the thickness and chemical state of the passive layer on stainless steel. Cyclic polarization measurements (Group 3 in Table E-5-1) may also be used to provide a quantitative evaluation of the level of passivation. Cyclic polarization as well as the methodologies in Group 4 in Table E-5-1 might be applied to sacrificial coupons placed in systems subject to the complete passivation process.
<table>
<thead>
<tr>
<th>ASTM Standard</th>
<th>Purpose of Test</th>
<th>Data Obtained</th>
<th>Typical Alloys Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASTM A262</td>
<td>Practice A (oxalic acid test)</td>
<td>Qualitative test to determine susceptibility to intergranular attack associated with chromium carbide precipitates. Tests the effectiveness of final heat treatment. Used to screen specimens intended for testing in Practices B, C, and E.</td>
<td>Comparative, visual examination of microstructure after testing only</td>
</tr>
<tr>
<td></td>
<td>Practice B (ferric sulfate-sulfuric acid test)</td>
<td>Quantitative test measuring weight loss due to intergranular corrosion associated with chromium carbide precipitates. Also tests for sigma phase in 321-type alloys. Tests the effectiveness of final heat treatment.</td>
<td>Report weight loss only</td>
</tr>
<tr>
<td></td>
<td>Practice C (nitric acid test)</td>
<td>Quantitative test measuring weight loss due to intergranular corrosion associated with chromium carbide precipitates. Also tests for sigma phase in 316-, 316L-, 321-, and 347-type alloys. Tests the effectiveness of final heat treatment.</td>
<td>Report weight loss only</td>
</tr>
<tr>
<td></td>
<td>Practice E (copper-copper sulfate-sulfuric acid test)</td>
<td>Qualitative test to determine susceptibility to intergranular attack associated with chromium carbide precipitates. Tests the effectiveness of final heat treatment.</td>
<td>Pass or fail</td>
</tr>
<tr>
<td>ASTM A923</td>
<td>Method A (sodium hydroxide etch test)</td>
<td>Detection of the presence of detrimental intermetallic phases. Used to screen specimens intended for testing in Method B and Method C.</td>
<td>Visual examination, Pretest for subsequent methods</td>
</tr>
<tr>
<td></td>
<td>Method B (Charpy impact test)</td>
<td>Used to test toughness characteristics that may result from processing irregularities.</td>
<td>Impact toughness energy</td>
</tr>
<tr>
<td></td>
<td>Method C (ferric chloride test)</td>
<td>Detects a loss of corrosion resistance associated with a local depletion of Cr, Mo, or both, as a result of the precipitation of chromium-rich and possibly molybdenum-rich phases.</td>
<td>Report weight loss only</td>
</tr>
<tr>
<td>ASTM G48</td>
<td>Methods A and B (ferric chloride test)</td>
<td>Resistance to pitting or crevice corrosion. Define the minimum temperature at which pitting or crevice corrosion initiates. Test the effects of alloying elements, final heat treatment, and surface finish of final product.</td>
<td>Report weight loss</td>
</tr>
<tr>
<td></td>
<td>Methods C and D (ferric chloride test)</td>
<td>Resistance to pitting or crevice corrosion. Define the minimum temperature at which pitting or crevice corrosion initiates. Test the effects of alloying elements, final heat treatment, and surface finish of final product.</td>
<td>Report critical temperature</td>
</tr>
<tr>
<td></td>
<td>Methods E and F (ferric chloride test)</td>
<td>Resistance to pitting or crevice corrosion. Define the minimum temperature at which pitting or crevice corrosion initiates. Test the effects of alloying elements, final heat treatment, and surface finish of final product.</td>
<td>Report critical temperature</td>
</tr>
<tr>
<td>ASTM G28</td>
<td>Method A</td>
<td>Tests the susceptibility to intergranular attack associated with composition and processing.</td>
<td>Report weight loss only</td>
</tr>
<tr>
<td></td>
<td>Method B</td>
<td>Tests the susceptibility to intergranular attack associated with composition and processing, specifically subsequent heat treatments</td>
<td>Report weight loss only</td>
</tr>
<tr>
<td>Standard</td>
<td>Purpose of Test</td>
<td>Data Obtained</td>
<td>Typical Alloys Tested</td>
</tr>
<tr>
<td>----------</td>
<td>----------------</td>
<td>---------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>ISO 3651-2</td>
<td><strong>Method A</strong>&lt;br&gt;(copper-copper sulfuric acid test)&lt;br&gt;Qualitative test to determine susceptibility to intergranular attack associated with chromium carbide precipitates. Tests the intrinsic material resistance to intergranular corrosion or the effectiveness of final heat treatment.</td>
<td>Pass or Fail</td>
<td>Austenitic steels with &gt; 16% Cr and ≤ 3% Mo&lt;br&gt;Ferritic steels with 16-20% Cr and ≤ 1% Mo&lt;br&gt;Duplex steels with &gt; 16% Cr and ≤ 3% Mo.</td>
</tr>
<tr>
<td></td>
<td><strong>Method B</strong>&lt;br&gt;(35% sulfuric acid-copper sulfate test)&lt;br&gt;Qualitative test to determine susceptibility to intergranular attack associated with chromium carbide precipitates. Tests the intrinsic material resistance to intergranular corrosion or the effectiveness of final heat treatment.</td>
<td>Pass or Fail</td>
<td>Austenitic steels with &gt; 20% Cr and 2-4% Mo&lt;br&gt;Duplex steels with &gt; 20% Cr and &gt; 2% Mo</td>
</tr>
<tr>
<td></td>
<td><strong>Method C</strong>&lt;br&gt;(40% sulfuric acid-copper sulfate test)&lt;br&gt;Qualitative test to determine susceptibility to intergranular attack associated with chromium carbide precipitates. Tests the intrinsic material resistance to intergranular corrosion or the effectiveness of final heat treatment.</td>
<td>Pass or Fail</td>
<td>Austenitic steels with &gt; 17% Cr and &gt; 3% Mo&lt;br&gt;Austenitic steels with &gt; 25% Cr and &gt; 2% Mo&lt;br&gt;Ferritic steels with &gt; 25% Cr and &gt; 2% Mo&lt;br&gt;Duplex steels with &gt; 20% Cr and ≥ 3% Mo</td>
</tr>
<tr>
<td>ASTM A1084</td>
<td><strong>Method A</strong>&lt;br&gt;(oxalic acid etch test)&lt;br&gt;Exploratory test for detection of the presence of detrimental intermetallic phases. Not used for screening specimens intended for testing in other methods.</td>
<td>Visual examination</td>
<td>Lean duplex stainless steels</td>
</tr>
<tr>
<td></td>
<td><strong>Method B</strong>&lt;br&gt;(Charpy impact test)&lt;br&gt;Used to test toughness characteristics that may result from processing irregularities</td>
<td>Impact toughness energy</td>
<td>Lean duplex stainless steels</td>
</tr>
<tr>
<td></td>
<td><strong>Method C</strong>&lt;br&gt;(inhibited ferric chloride test)&lt;br&gt;Detects a loss of corrosion resistance associated with a local depletion of Cr, Mo, or both, as a result of the precipitation of chromium-rich and possibly molybdenum-rich phases</td>
<td>Report weight loss only</td>
<td>Lean duplex stainless steels</td>
</tr>
</tbody>
</table>
Table F-3-1
PRE Numbers for Stainless Steels per Table MM-2.1-1
and for Nickel Alloys per Table MM-2.1-2 (Cont’d)

<table>
<thead>
<tr>
<th>UNS Number</th>
<th>EN Designation</th>
<th>JIS Designation</th>
<th>PRE Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>S30400</td>
<td></td>
<td></td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>1.4301</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>SUS304</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>S30403</td>
<td>1.4307</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4306</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>SUS304L</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>S31600</td>
<td></td>
<td></td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>1.4401</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>SUS316</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>S31603</td>
<td>1.4404</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4435</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>SUS316L</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>N08904</td>
<td></td>
<td></td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>1.4539</td>
<td></td>
<td>36</td>
</tr>
<tr>
<td>N08367</td>
<td></td>
<td></td>
<td>43</td>
</tr>
<tr>
<td>S31254</td>
<td>1.4547</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>S31256</td>
<td>1.4529</td>
<td></td>
<td>42</td>
</tr>
<tr>
<td>S32101</td>
<td></td>
<td></td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>1.4162</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>S32205</td>
<td></td>
<td></td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>1.4462</td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>N06625</td>
<td></td>
<td></td>
<td>41</td>
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<tr>
<td></td>
<td>2.4856</td>
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<td>41</td>
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<td></td>
<td>NCF625</td>
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<td>41</td>
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<td>N10276</td>
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<td>NW0276</td>
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<td>N06022</td>
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<td>2.4602</td>
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</tr>
<tr>
<td></td>
<td>NW6022</td>
<td></td>
<td>46</td>
</tr>
</tbody>
</table>

GENERAL NOTES:
(a) Alloys listed between horizontal lines are not equivalent, but comparable.
(b) The below are industry-accepted formulas. Other formulas may be used at the owner/user’s discretion.

$32750$ $...$ $...$ $...$ $41$
$...$ $1.4410$ $...$ $41$
NONMANDATORY APPENDIX H
ELECTROPOLISHING PROCEDURE QUALIFICATION

H-1 SCOPE

This Appendix defines a method for qualifying the electropolishing process used for electropolishing component(s) surfaces that will be exposed to the process fluids in bioprocessing and pharmaceutical systems and ancillary equipment.

H-2 PURPOSE

This Appendix is intended to provide general guidelines for qualification of the electropolish methods used to achieve required surface improvements. Electropolishing is used to impart a surface that

(a) shall be free of oxide contamination and undesirable metallurgical conditions

(b) takes advantage of a material’s surface chemical characteristics minus any damage or degradation from the component(s) manufacturing process

(c) exhibits a surface that is free of the surface irregularities that result from prior machining and forming processes

(d) optimizes corrosion resistance

H-3 ELECTROPOLISH PROCEDURE QUALIFICATION

H-3.1 Method Procedure

This Appendix is intended to provide general guidelines for qualifying the electropolish process used to provide the surface improvements of component(s) required.

The electropolish vendor shall produce sample component(s) or coupons from each electropolish method used (e.g., submersion, spot, in situ) for the purpose of demonstrating that the method is capable of providing the required surface characteristics.

The electropolish vendor shall also demonstrate the ability to reproduce the method used on the qualification component(s) or coupons on the production component(s) and/or equipment for which the method is being qualified.

The electropolish vendor shall have a written quality control program that shall describe, as a minimum, the following:

(a) prepolish inspection process

(b) precleaning process

(c) specific gravity at operating temperature of electrolyte bath (minimum and maximum)

(d) bath analysis data (last date analyzed, iron/water concentrations of electrolyte, adjusted specific gravity value)

(e) resistivity of final deionized rinse water (minimum and maximum)

Qualification will be supported by internal documentation for each method. The actual values of the essential variables listed above shall be documented, maintained, and available for customer review.

H-3.2 Essential Variables

The electropolish vendor shall develop an electropolishing procedure for each method used. The procedure will be developed to ensure that essential variables used to produce the qualification samples can be reproduced. The electropolishing procedure, as a minimum, shall include the following essential variables:

(a) amperage/time (minimum and maximum)

(b) temperature range of bath during process (minimum and maximum)

(c) electropolish process

(d) final rinsing/cleaning process

(e) final inspection requirements

H-3.3 Vendor Documentation

The electropolish vendor shall generate and maintain the following additional information:

(a) scanning electron microscope (SEM) records for each process qualification sample produced

(b) XPS (ESCA) records for each process qualification sample produced. These results must meet the criteria of Table H-3.3-1.

(c) actual sample(s) used to qualify the process

(d) process control records

(e) the electropolish procedure used

(f) final Rz (if required)

(g) copies of Certificate of Conformance (C of C) for each job
Table H-3.3-1
Minimum Surface Requirements for Process Qualification Samples

<table>
<thead>
<tr>
<th>Material</th>
<th>Cr/Fe-Ratio</th>
<th>Depth [Note (1)]</th>
<th>Surface-Photo [Note (2)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNS S31600</td>
<td>1-to-1-or-greater</td>
<td>15 Å minimum</td>
<td>150X</td>
</tr>
<tr>
<td>UNS S31603</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTES:
(1) Test method: X-ray photoelectron spectroscopy (XPS/ESCA) analysis.
(2) Scanning electron microscopy (SEM).

H-3.4 Certificate of Conformance

The electropolish vendor, if requested by the customer, shall provide a Certificate of Conformance with each type of component(s) that shall include but is not limited to:
(a) vendor’s company
(b) customer’s name
(c) description of component(s)
(d) identification of the electropolish procedure used
(e) final surface finish report ($R_a$ if required by the customer)

NONMANDATORY APPENDIX H has been replaced with next 5 pages.
H-1  SCOPE
This Appendix defines a method for qualifying an electropolishing procedure.

H-2  PURPOSE
The purpose of this appendix is to describe a standard method for qualifying an electropolishing procedure, including the minimum required tests and acceptance. The qualification process is not a guarantee that the final product will meet customer requirements.

Electropolishing is used to impart a surface that:

(a) Is free of contamination and undesirable metallurgical conditions.
(b) Takes advantage of a material's surface compositional characteristics by removal of damage or degradation from the component's manufacturing process.
(c) Optimizes corrosion resistance.

H-3  ELECTROPOLISHING PROCESS
The electropolisher shall describe the overall process steps in a written document. This document identifies the processes required to produce an electropolished finish and should provide or reference information regarding:

(a) Precleaning process
(b) Electropolishing Procedure Specification(s)
(c) Electrolyte conditions
(d) Current density & time
(e) Electrolyte solution controls
(f) Rinsing process
(g) Post-cleaning process
(h) Final rinsing process
(i) Inspection process

H-4  ELECTROPOLISHING PROCEDURE QUALIFICATION
The electropolisher shall develop a procedure for each method and generate the following document types:

(a) Electropolishing procedure specification (EPPS)
(b) Electropolishing procedure qualification record (EPQR)

The EPPS is a written qualified procedure specification which shall contain, as a minimum, the essential variables described herein. Each EPPS shall be qualified by testing with test results recorded on an EPQR. Both documents shall be retained by the electropolisher to demonstrate that the process parameters used were tested and produced acceptable results for the application intended. These documents should be made available for review at the electropolisher’s facility when audited.

To qualify a procedure, the electropolisher shall electropolish sample components or coupons using each electropolishing technique (e.g., submersion, spot, in situ) for the purpose of demonstrating the method is capable of producing the required surface characteristics.

The documentation format for the EPPS and EPQR can be customized to accommodate a specific technique. Forms EPPS-1 and EPQR-1 are suggested formats that would be suitable for the submersion technique.
**H-4.1 Electropolishing Procedure Specification**

The EPPS is a written qualified electropolishing procedure specification prepared to provide direction for the person performing the operation. The document is used to identify the range of process parameters that are essential to assure quality standards are met. The specification shall:

(a) Identify alloy type: (list of alloys that can be electropolished with this process)

(b) Reference the supporting EPQR.

(c) Specify the acceptable ranges of the following essential variables.

1. Initial cleaning process: (identify procedure used, minimum temperature and time)
2. Temperature range of electrolyte during process (minimum and maximum)
3. Electrolyte Specific Gravity: (adjusted specific gravity range)
4. Current density range: (the range in amperes/ft\(^2\) (amperes/m\(^2\))
5. Voltage type and range: (the type of voltage applied {AC, DC positive or DC negative})
6. Current exposure time: (the range of time that surface is exposed to current)
7. Technique of electropolishing process (submersion, spot, moving cathode, moving anode, etc.)
8. Final rinsing/cleaning process: (identify procedure used, minimum temperature and time)

(d) Describe the essential variables for each technique used. (e.g. submersion, spot, moving anode, moving cathode)

The electropolisher may also include any other information that may be helpful in achieving an acceptable electropolished surface.

**H-4.2 Electropolishing Procedure Qualification Record**

The EPQR is a record of the variables recorded during the electropolishing of the qualification component or coupon and the test results of the tested specimens. Recorded variables normally fall within a small range of the actual variables that will be used in production and identified on the EPPS used. The record shall:

(a) Document the essential variables for each technique to be qualified. Other variables used during the qualification process may be recorded at the organization’s option.

(b) Be certified accurate by the organization. The certification is the organization’s verification that the information is a true record of the variables that were used during the electropolishing qualification process and that the test results conform with H-4.4

(c) Document the testing method performed the qualification component or coupon shall be tested by using methods in H-4.4 or other methods producing the same data and shall meet the acceptance criteria in Table H-4.4-1 and SF-2.2.

(d) Record the following data:

1. alloy type
2. final Ra
3. thickness of material removed
4. total Cr/Fe ratio after electropolishing
5. depth of passive layer after electropolishing
6. before and after photographs at 150X minimum
**H-4.3 Procedure Qualification Acceptance Criteria**

Procedure qualification acceptance criteria shall include the contents of Table H-4.3-1. The surface condition of the test specimen shall also meet acceptance criteria of the targeted surface finish designation defined in Part SF.

**Table H-4.3-1 Procedure Qualification Acceptance Criteria for Test Coupons**

<table>
<thead>
<tr>
<th>Material</th>
<th>Minimum Material Removal</th>
<th>Surface Designation [Note (3)]</th>
<th>Total Cr/Fe Ratio</th>
<th>Depth [Note (1)]</th>
<th>Documented surface quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austenitic Stainless Steels [Note (2)]</td>
<td>0.0002 in. (5µm)</td>
<td>SF6 or Better</td>
<td>1 to 1 or greater</td>
<td>15 Å minimum</td>
<td>Before and after photos at 150X minimum magnification</td>
</tr>
<tr>
<td>Superaustenitic Stainless Steels [Note (2)]</td>
<td>0.0002 in. (5µm)</td>
<td>SF6 or Better</td>
<td>1 to 1 or greater</td>
<td>15 Å minimum</td>
<td>Before and after photos at 150X minimum magnification</td>
</tr>
<tr>
<td>Duplex Stainless Steel [Note (2)]</td>
<td>0.0002 in. (5µm)</td>
<td>SF6 or Better</td>
<td>N/A</td>
<td>N/A</td>
<td>Before and after photos at 150X minimum magnification</td>
</tr>
<tr>
<td>Nickel Alloys [Note (4)]</td>
<td>0.0002 in. (5µm)</td>
<td>SF6 or Better</td>
<td>N/A</td>
<td>N/A</td>
<td>Before and after photos at 150X minimum magnification</td>
</tr>
</tbody>
</table>

**Notes:**
(1) Depth of chromium enriched passive layer
(2) Stainless steels listed in Table MM-2.1-1 and Table MM-2.1-3
(3) See Table SF-2.4.1-1 for Electropolished $R_a$ Max. acceptance criteria.
(4) Nickel alloys listed in Table MM-2.1-2 and Table MM-2.1-3

**H-4.4 Testing Methods**

Techniques to measure the test specimen include, but are not limited to, one of the following testing methods for each criterion.

(a) Minimum material removal
   (1) Calculated thickness removal using material density, specimen surface area, and measured mass loss due to electropolishing.
   (2) Measured thickness removal due to electropolishing

(b) Surface designation
   (1) Visual examination and surface roughness measurement after electropolishing

(c) Total Cr/Fe Ratio
   (1) X-Ray photoelectron spectroscopy (XPS/ESCA)
   (2) Auger electron spectroscopy (AES)

(d) Minimum passive layer depth
   (1) X-Ray photoelectron spectroscopy (XPS/ESCA)
   (2) Auger electron spectroscopy (AES)

(e) Documented surface quality
   (1) Before and after photos at 150X minimum magnification
   (2) Final condition photos using scanning electron microscopy (SEM)
Form EPPS-1 Suggested Format for Electropolishing Procedure Specification (EPPS)

Procedure Identification

EPPS No. ____________ Revision ____________ Date ____________

Supporting EPQR(s) ____________ Technique ____________ Precleaning ____________

Base Metal

Material Category ____________ UNS No. ____________ Product Form ____________

Electrolyte

Product Name

Manufacturer

Composition

Specific Gravity of Electrolyte (range)

Temperature of electrolyte (range)

Electrical Characteristics

Voltage Type ____________ Cathode material type ____________

<table>
<thead>
<tr>
<th>Units</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voltage Range</td>
<td>volts</td>
<td></td>
</tr>
<tr>
<td>Current Density Range</td>
<td>amperes / ft² (amperes / m²)</td>
<td></td>
</tr>
<tr>
<td>Cathode to Anode Distance</td>
<td>in. (mm)</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>minutes</td>
<td></td>
</tr>
</tbody>
</table>

Technique

Pre-EP Finish Method

Initial Cleaning

Electropolish

Rinse

Final Cleaning

Company Name

Created by: ______________________ Date: ______________________

(Title)
Form EPQR-1 Suggested Format for Electropolishing Procedure Qualification Record (EPQR)

**Procedure Identification**

<table>
<thead>
<tr>
<th>EPQR No.</th>
<th>Revision</th>
<th>Date</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>EPPS No.</th>
<th>Technique</th>
<th>Pre-cleaning</th>
</tr>
</thead>
</table>

**Base Metal**

<table>
<thead>
<tr>
<th>Material Category</th>
<th>UNS No.</th>
<th>Product Form</th>
</tr>
</thead>
</table>

**Electrolyte (actuals)**

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer</th>
<th>Composition</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Specific Gravity of Electrolyte</th>
<th>Percentage Metal in Electrolyte</th>
<th>Temperature of Electrolyte</th>
</tr>
</thead>
</table>

**Electrical Characteristics**

<table>
<thead>
<tr>
<th>Voltage Type</th>
<th>Cathode material type</th>
<th>Units</th>
<th>Actual</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Voltage</th>
<th>volts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Density</td>
<td>amperes / ft² (amperes / m²)</td>
</tr>
<tr>
<td>Cathode to Anode Distance</td>
<td>in. (mm)</td>
</tr>
<tr>
<td>Time</td>
<td>minutes</td>
</tr>
</tbody>
</table>

**Surface Conditions Before EP**

<table>
<thead>
<tr>
<th>Pre-EP Finish Method</th>
<th>Material Thickness or Weight</th>
<th>150X Photo, Y/N</th>
</tr>
</thead>
</table>

**Surface Conditions After EP**

<table>
<thead>
<tr>
<th>Visual</th>
<th>Material Thickness or Weight</th>
<th>Roughness Ra</th>
<th>150X Photo, Y/N</th>
</tr>
</thead>
</table>

**Test summary**

<table>
<thead>
<tr>
<th>Total Cr/Fe Ratio</th>
<th>Passive Depth</th>
<th>Amount of Material Removed</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Operator Name</th>
<th>ID no.</th>
<th>Witness By</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Test Evaluation by</th>
<th>Company</th>
<th>Lab test #</th>
</tr>
</thead>
</table>

We hereby certify that the statements in this record are correct and that the test coupons were prepared and tested in accordance with the applicable requirements of ASME BPE Appendix H.

Certified by: ___________________________ Date: ________________

(Title)
NONMANDATORY APPENDIX N
COMMENTARY: UNS S31603 WELD HEAT-AFFECTED ZONE DISCOLORATION ACCEPTANCE CRITERIA

(a) The acceptance criteria for discoloration on weld heat-affected zones were developed by making autogenous square groove welds on 2-in.-diameter UNS S31603 stainless steel tube-to-tube butt joints whose inside diameters were purged with argon containing controlled amounts of oxygen. The oxygen levels were measured on the downstream side of the sample numbers listed in Figures MJ-8.4-2 and MJ-8.4-3, the oxygen contents were as follows:
   (1) #1a and #1b — 10 parts per million (ppm)
   (2) #2 — 25 ppm
   (3) #3 — 35 ppm
   (4) #4 — 50 ppm
   (5) #5 — 80 ppm

(b) All welds were made with the gas-tungsten arc welding (GTAW) process using 95% argon — 5% hydrogen shielding gas.

(c) The electropolished tubing used for the test welds had an SF4 surface finish (15 μin. Ra max.) and the mechanically polished tubing had an SF1 surface finish (20 μin. Ra max.).

(d) The photos shown in Figures MJ-8.4-2 and MJ-8.4-3 were taken using a camera having direct visual access to the weld surfaces.

(e) The corrosion resistance determined by both ASTM G150, Critical Pitting Temperature Test, and the modified ASTM G61, Potentiodynamic Polarization Corrosion Test.

(f) ASTM G150 determines the voltage-independent critical pitting temperature (CPT) by way of a potentiostatic technique that determines the temperature above which pitting corrosion proceeds on its own under standardized test conditions. Higher CPTs indicate increased resistance to pitting corrosion.

The modified ASTM G61 determines the voltage (potential) at which the anodic current increases rapidly during a standardized cyclic polarization test at room temperature. The voltage determined, referred to as the E_{PIT}, is a measure of resistance to pitting corrosion. Higher, or more noble, values of E_{PIT} indicate increased resistance to pitting corrosion.

Neither the CPT nor the E_{PIT} values determined are material properties per se; rather, they are the result of standardized tests designed to rank different materials or different surface finishes of the same material in their resistance to the stable propagation of pits in a standard test environment.

(g) The acceptance criteria for discoloration, not on the oxygen levels of the internal purge gas used during welding. As a result, the photographs in Figures MJ-8.4-2 and MJ-8.4-3 should be used to identify the oxygenation by number, but not to specify the oxygen level in the backing gas.

(h) All welds were tested in the as-welded condition, with no postweld conditioning.

(i) For the electropolished tubing in Figure MJ-8.4-2, acceptable levels of heat-affected zone discoloration were those that exhibited corrosion resistance similar to unwelded, electropolished UNS S31603 base metal in the ASTM G150 test.

(j) For the mechanically polished tubing in Figure MJ-8.4-3, acceptable levels of heat-affected zone discoloration were those that exhibited corrosion resistance similar to that of a cold-rolled, mill-finished, UNS S31603 base metal.

(k) It is generally accepted that as-welded heat-affected zones on mechanically polished tubing having the same level of discoloration as weld heat-affected zones on electropolished tubing will exhibit lower resistance to pitting than the heat-affected zone on electropolished tubing.

(l) The user is cautioned that the amount of discoloration and its appearance can be influenced by factors other than oxygen, as listed below:

   (1) High levels of moisture in the backing gas can increase the degree of discoloration.

   (2) Other contaminants, such as hydrocarbons, moisture, and some types of particulates on the surface prior to welding, can affect discoloration levels.

   (3) Hydrogen in the argon backing gas can significantly reduce the amount of discoloration.

   (4) The metal’s surface finish can also affect the appearance of the discoloration.

With both G150 and G61 testing, exposed coupons were examined to determine the location and severity of the attack.
NONMANDATORY APPENDIX O
GUIDANCE WHEN CHOOSING POLYMERIC AND NONMETALLIC MATERIALS

O-1 GENERAL

Polymer materials can be divided into two general classes: thermoplastics and thermosets. The composition, form, and construction of these materials determine their suitability for use in their various applications, and the systems designer should be aware of their strengths and limitations.

Polymer materials may be manufactured from a single monomer (homopolymer) or multiple monomers (copolymers). They may be filled or unfilled. They may be elastomeric or rigid. They may exist in an amorphous, crystalline, or semicrystalline state. They may consist of either single or multiple microphases, be manufactured as composites, and include adhesive materials.

Nonmetallic materials may be rigid or flexible, amorphous or crystalline, exist in single or multiple microphases, and formed into complex mixtures and composites. These materials can offer a range of unique properties (e.g., extreme hardness, chemical inertness, self-lubrication, or transparency). The system designer and owner/user should be aware of the broad range of physical and chemical properties of these materials.

O-2 PARTICULATES

O-2.1 Characterization

Particulates are characterized by several attributes including, but not limited to, size, morphology/shape, hardness, and chemical composition. These attributes may affect the ability to detect, measure, capture, identify, and control the particulates.

(a) Physical Form. Particulates may be of varying shapes. Some may be long and thin while others may be short and round. A majority of the particulates are irregular shapes with complex geometries.

(b) Material Makeup. Intrinsic particulates are native to the single-use system and include materials of construction or ingredients in the process formulation. Extrinsic particulates are foreign to the single-use system and come from the manufacturing environment or process personnel.

(c) Hardness. Particulates may be rigid or soft.

(d) Chemical Composition

O-2.2 Levels of Acceptance

Acceptable levels of particulate quantity and size distribution in single-use components and assemblies should be determined by their intended use. Owner/users should use established industry standards for the end product to quantify acceptable particulate criteria. Some of the industry standards available as acceptance criteria for drug products include USP <1>, USP <787>, USP <788>, USP <790>, EP 2.9.19, EP 2.9.20, JP 6.06, and JP 6.07.
1.1 Thermoplastic Polymers. Thermoplastic polymers will melt and flow to form desired shapes when sufficiently heated. They can be melt-processed into a wide variety of shapes by molding, extruding, thermoforming, etc., and can be re-formed and shaped with heat and/or pressure. Thermoplastic materials are often used for fittings, tubing, piping, diaphragms, seals, liners for vessels, column tubes, filter media and capsules, etc. Examples of thermoplastic polymers are shown in Table 1.1.1.

Some thermoplastics, such as thermoplastic elastomers, combine an elastomer such as ethylene propylene diene monomer (EPDM) with a plastic such as polypropylene, giving the resulting thermoplastic compound properties of flex endurance and sealability so it can be used for tubing, seals, diaphragms, etc. Thermoplastic elastomers (TFE) combine the features of melt processability and flexibility. Many polymeric materials are described in ASTM standards that detail their composition and mechanical properties. It is the owner/user’s responsibility to select materials that are appropriate for their applications.

Filler materials may be used to enhance the properties of thermoplastic polymers. Fillers may be carbon based, inorganic, metallic, organometallic, etc., as needed for performance. Additives for thermoplastic polymers may be used to aid in thermal stability, flexibility, gamma stability, extrudate performance, crystallization control, oxidative stability, mold release, plasticization, and adhesion. Additives may be used in the bulk of the polymer as well as the surface, as required.

1.2 Thermoset Polymers. Thermosets are polymers that, in their final state after processing, are rendered substantially insoluble and infusible. Fully processed thermosets cannot be re-softened or re-formed by exposure to heat. Exposure to excessive heat will cause degradation. Thermoset polymers are processed from a liquid or malleable state and are converted to the solid state by irreversible curing with heat, catalysis, or other means. Chemical cross-links are formed between polymer chains during the curing process. This results in an interconnected polymer network with the cross-link junctions restricting flow of the polymer when exposed to thermal or mechanical stresses.

Thermoset polymers can be classified into either thermoset elastomers or thermoset resins, with the elastomers being more common. Thermoset elastomers are often elastic and soft materials and are used for seals, gaskets, tubing, diaphragms, hoses, etc. Examples of thermoset polymers are shown in Table 1.2.1.

Most thermoset polymeric materials contain reinforcing fillers and other additives to meet required use conditions. Fillers may be carbon based, inorganic, metallic, organometallic, etc., as needed for performance.

Elastomer formulations typically contain 5% to 50% filler to achieve optimum properties.
### Table O-1.1-1

#### Common Thermoplastic Polymers and Applications

<table>
<thead>
<tr>
<th>Type of Polymer</th>
<th>Example Polymers</th>
<th>Example Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>General thermoplastics</td>
<td>Polyester (PET)</td>
<td>Fittings, connectors, filter housings,</td>
</tr>
<tr>
<td></td>
<td>Polyamide (nylon)</td>
<td>piping and rigid tubing, column</td>
</tr>
<tr>
<td></td>
<td>Polycarbonate (PC)</td>
<td>tubes, filter media</td>
</tr>
<tr>
<td></td>
<td>Polysulfones (PSI, FSS)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polyether ether ketone (PEEK)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic polyolefins</td>
<td>Polypropylene (PP)</td>
<td>Fittings, connectors, piping and rigid</td>
</tr>
<tr>
<td></td>
<td>Ultra-low-density polyethylene (ULDPE)</td>
<td>tubing, filter media and capsules, bags,</td>
</tr>
<tr>
<td></td>
<td>Low-density polyethylene (LDPE)</td>
<td>vessels, vessel linings, and coatings</td>
</tr>
<tr>
<td></td>
<td>High-density polyethylene (HDPE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ultra-high-molecular-weight polyethylene (UHMWPE)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic fluoropolymers</td>
<td>Fluorinated ethylene propylene (FEP)</td>
<td>Fittings, piping and tubing, flexible</td>
</tr>
<tr>
<td></td>
<td>Perfluoroalkoxy (PFA)</td>
<td>hose, filter media and capsules, pumps,</td>
</tr>
<tr>
<td></td>
<td>Polytetrafluoroethylene (PTFE)</td>
<td>vessels, vessel linings, and coatings</td>
</tr>
<tr>
<td></td>
<td>Ethylene tetrafluoroethylene (ETFE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polytinylidene fluoride (PVDF)</td>
<td></td>
</tr>
<tr>
<td>Thermoplastic elastomers (TPE)</td>
<td>Blends of EPDM with polypropylene</td>
<td>Tubing, bags</td>
</tr>
<tr>
<td></td>
<td>Styrene-iso-butylene-styrene block polymers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Copolymers of ethylene and octene</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethylene-vinyl acetate copolymer (EVA)</td>
<td></td>
</tr>
</tbody>
</table>

### Table O-1.2-1

#### Common Thermoset Polymers and Applications

<table>
<thead>
<tr>
<th>Type of Polymer</th>
<th>Example Polymers</th>
<th>Example Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermoset elastomers</td>
<td>Ethylene propylene diene (EPDM)</td>
<td>Tubing, seals, gaskets, diaphragms,</td>
</tr>
<tr>
<td></td>
<td>Ethylene propylene rubber (EPKR)</td>
<td>and hoses</td>
</tr>
<tr>
<td></td>
<td>Silicone (VMQ)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluororesistomers (FKM)</td>
<td></td>
</tr>
<tr>
<td>Rigid thermosets</td>
<td>Fiber-reinforced polymer (FRP/GRP) composites</td>
<td>Tanks and pipes</td>
</tr>
</tbody>
</table>

(Record 22-525)-cont.
PM-2 Revision
### Table PM-213-1

<table>
<thead>
<tr>
<th>Examples of Nonmetals</th>
<th>Types of Nonmetallic</th>
<th>Example Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass</td>
<td>Amorphous inorganic nonmetallic material</td>
<td>Sight glasses, vessel lights, optical sensors, glass electrodes</td>
</tr>
<tr>
<td>Borosilicate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soda-lime</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sintered materials</td>
<td>Crystalline inorganic nonmetallic material</td>
<td>Mechanical seals, bearings, process sensors</td>
</tr>
<tr>
<td>Aluminum oxide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon carbide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon nitride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungsten carbide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zirconium dioxide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction-bonded materials</td>
<td></td>
<td>Mechanical seals</td>
</tr>
<tr>
<td>Silicon carbide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon nitride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Siliconized carbon-graphite</td>
<td></td>
<td>Mechanical seals</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resin-impregnated carbon-graphite</td>
<td></td>
<td>Mechanical seals</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cemented materials</td>
<td>Crystalline inorganic nonmetallic in a metallic matrix</td>
<td>Mechanical seals, bearings</td>
</tr>
<tr>
<td>Tungsten carbide with alloyed binder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungsten carbide with nickel binder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungsten carbide with cobalt binder</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Per Record 19-2115

components that conform to the ASME BPE Standard
(c) Manufacturers of polymeric or other nonmetallic material shall maintain a change management and notification system for any process contact component per PM-2.2.3.

For manufacturers of metallic tubing and fittings

For record 19-3266, add “referenced” in between “applicable” and “product”

clarification change of (b) to Z-3.2 (b)
Notes to Editor in BLACK. Changes in RED

Per record 20-505, in (-e) remove unnecessary capitalization and italics.

Per record 19-2115

Approving suppliers through surveys and audits.

conformance to
Notes to Editor in BLACK. Changes in RED

Editor: for Z-3.1(f) Link needs to be updated to proper location

Grammatical change – in Z-3.10 (b) “cause (s)” needs to be changed to “cause(s)”

taken. These provisions shall include a method for reviewing all measurements or tests performed with that device since the last successful periodic calibration to determine if applicable requirements have been met.

(2) When a device fails to calibrate during a periodic check, provisions need only address measurements or tests performed since the last successful periodic check. The method and frequency used for the periodic checks are described in calibration procedures.

Z-3.10 Nonconformances and Corrective Actions

(a) Items and services that do not conform to specified requirements shall be controlled to prevent inadvertent installation or use. Controls shall address identification, documentation, evaluation, segregation when practical, and disposition of nonconforming items, as well as the notification of affected organizations.

(b) Measures shall be established to ensure that conditions that do not conform to specified requirements, such as failure, malfunction, deviation, defective material and equipment, nonconformance, and other quality system deficiencies, are identified, reported to appropriate levels of management, and promptly corrected. These measures shall also ensure that the root cause (s) responsible for these nonconformances be determined and corrected.

(c) The identification of conditions causing recurring nonconformances; the cause of these conditions; and the corrective action taken shall be documented and reported to appropriate levels of management.

Z-3.11 Storage, Shipping, Handling, and Packaging

Controls shall be established for the cleaning, preservation, packaging, storage, and shipping of finished components.

(22) Z-3.12 Control of Documents and Record Retention

(a) Provisions shall be established to ensure that documents that are to be maintained throughout the design and manufacture of the component is shipped shall be established.

(b) These provisions shall also require that manufacturer's Data Reports, MTRs, and C of C shall be retained for a minimum period of 5 yr from the date the component is shipped.

(c) Document retention requirements shall extend to records of personnel training, qualification, and certification, for which the minimum retention time shall be 5 yr after their employment ceases. Personnel providing outsourced services in accordance with Z-3.1(f) provisions shall be established for the Certificate Holder to have access to their personal records, as needed.

Z-3.13 Sample Forms

The use of forms shall be described in the QMS manual. Typical examples, referred to as “exhibits” shall be included and marked “Sample.” These samples should be completed in a manner typical of that expected for actual production documents.

Z-3.14 Internal Audits

Requirements shall be established for internal audits. Those requirements should address the following, as a minimum:

(a) The frequency of internal audits shall be specified. These audits shall be conducted in accordance with a written procedure by qualified auditors not having direct responsibility for the areas being audited. All elements in the QMS shall be internally audited at least once during each certification period.

(b) Audit reports shall be documented by auditing personnel and reviewed by management having responsibility over the areas being audited. This documentation shall bear the signatures of the responsible management personnel.

(c) Corrective actions taken in response to deficiencies or nonconformances shall be documented. Follow-up actions shall be required after corrective actions have been taken to ensure the problem has been corrected. These follow-up actions may include a re-audit of deficient areas.

Z-3.15 Management Performance Assessments

Management personnel with assigned responsibility shall review the organization’s QMS at least annually to ensure its continued suitability, adequacy, and effectiveness. The input from management review shall include information on the results of audits, process performance and product conformity, the status of preventative and corrective actions, and customer feedback, as appropriate.
NONMANDATORY APPENDIX AA
STATIC SEALS APPLICATION GUIDE
FOR COMPENDIAL WATER SYSTEMS

AA-1 GENERAL

Table AA-1-1 provides a guide to static seal selection, which is intended to give readers general information about chemical, physical/mechanical, and maintenance considerations related to selecting materials suitable for static seals used in compendial water systems. Evaluations presented in the Table generally describe compounds in the specified material class. Different compounds within a material class, different compounds from particular suppliers, and articles manufactured from the same compounds in different ways may vary significantly. Seal location within the system may also affect seal performance. Some performance data for this application can be developed using test methods listed in Nonmandatory Appendix L. Chemical compatibility/suitability of a particular compound may be verified through the material supplier. Maintenance characteristic evaluations are expert opinions based on testing (see Nonmandatory Appendix K) and experience using these compounds. The scope of this Appendix cannot address all possible materials. Materials other than those listed may be suitable for compendial water applications provided they meet the requirements of Part PM.

The intent of this Appendix is to guide communication between the owner/user and the supplier to find a balance of properties needed for the application. This information may give initial guidance for material selection. However, due to the inherent variability of materials, compound processing, and use, the owner/user should qualify individual materials and suppliers based on performance data.

AA-2 MATERIAL CLASS DESCRIPTIONS

AA-2.1 Synthetic Rubbers (Elastomers)

EPDM (Ethylene Propylene Diene Rubber) – peroxide-cured systems: EPDM is one of the more widely used and varying materials in bioprocessing equipment, including compendial water systems. VMQ (Silicone) – peroxide-cured and platinum-cured systems: Silicone is often preferred for single-use applications due to its relative simplicity of formulation, low toxicity, and optical clarity. Peroxide-cured silicone systems generally have more reaction by-products, which may be extractable, than platinum-cured systems.

FKM (Fluoroelastomers): FKM materials can be separated into types, based on the monomers used and their ratio(s). In general, the higher the fluorine level, the better the chemical resistance. Different curing systems within the same type can affect performance significantly.

AA-2.2 Plastics and Composites

PTFE (Polytetrafluoroethylene) and Composites: PTFE has long been used in bioprocessing equipment due to its relative high purity, chemical inertness, nonstick properties, and long seal life. However, as a plastic, PTFE seals are susceptible to irreversible deformation under load/compression (cold-flow/creep). PTFE seals can vary in geometry due to warping and/or process variation, and fit may be less predictable than elastomeric seals. PTFE seals and their variants generally require higher compressive forces (fastener torque) to form a seal than their elastomeric counterparts. They are more susceptible to degradation due to gamma-irradiation (sanitization) than other commonly used materials. PTFE seal properties can also vary with PTFE grades (molecular weight and particle size distribution) and manufacturing variables.

PTFE and its composites are used widely for compendial water applications.

AA-2.3 Modified PTFE

Modified PTFE has lower vapor phase transmission, without sacrificing chemical resistance, than standard PTFE. Modified PTFE is often substituted for PTFE in static seals (see AA-2.2).
Table AA-1-1
Static Seals for Use in Compendial Water Systems (MC-2.2.1)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Chemical [Note (2)]</th>
<th>Maintenance</th>
<th>Physical/Mechanical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hot DI Water</td>
<td></td>
<td>Permeability</td>
</tr>
<tr>
<td></td>
<td>Acidic</td>
<td></td>
<td>Compression Set</td>
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<tr>
<td></td>
<td>Alkaline</td>
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<td></td>
<td>Oxidizing/Corrosion</td>
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<td></td>
<td>Steam</td>
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<tr>
<td></td>
<td>Ease of Instaling/Removal/Cleaning</td>
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<tr>
<td></td>
<td>Length of Service</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Need for Retightening</td>
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<tr>
<td></td>
<td>Resistance to Cold Flow (Creep) During Thermal Cycling and/or Compression</td>
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<tr>
<td></td>
<td>Resistance to Erosion</td>
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<tr>
<td></td>
<td>Tear Resistance</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Ease of Forming Seal (Sealability/Modulus)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Material [Note (1)]</td>
<td>EPDM (Ethylene Propylene Diene Rubber)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>VQM (Silicone)</td>
<td></td>
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<tr>
<td>Peroxide-Cured</td>
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<tr>
<td>Platinum-Cured</td>
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<tr>
<td>PTFE (Polytetrafluoroethylene)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Modified PTFE</td>
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<td></td>
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<tr>
<td>PTFE composites</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Elastomer/PTFE</td>
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<tr>
<td>Elastomer/PTFE</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>envelope</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonded</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTFE/inorganic fillers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FKM (Fluoroelastomers)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1: low fluorination ~66%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2: medium fluorination ~68%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2: high fluorination ~70%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Preferred
- Acceptable
- Unacceptable

++ Best
+ Good
- Caution
### Table AA-1-1

**Static Seals for Use in Compendial Water Systems (MC-2.2.1) (Cont’d)**

<table>
<thead>
<tr>
<th>GENERAL NOTES:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Recommendations are for static seals located within the compendial water envelope (see MC-5.3).</td>
</tr>
<tr>
<td>(b) Relative importance to this application (see MC-5.3) is defined as follows:</td>
</tr>
<tr>
<td>C = critical</td>
</tr>
<tr>
<td>I = important</td>
</tr>
<tr>
<td>S = secondary (importance depends on owner/user specifics)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NOTES:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Comments made here are generally true with compounds in this class currently available. Different compounds within a class vary between seal suppliers. Different compound numbers from a particular supplier may also vary. Communication between user and supplier is recommended to find the balance of properties needed for the owner/user.</td>
</tr>
<tr>
<td>(2) Passivation chemicals are occasionally used in compendial water systems. Consult with supplier.</td>
</tr>
</tbody>
</table>
NONMANDATORY APPENDIX AA
SEAL APPLICATION MATERIAL SELECTION GUIDE

AA-1 GENERAL
This section provides guidance for sealing component material selection for common applications. Each component material is recommended for its suitability for the particular application, and the selection reflects current common industry practice.

Sections describing each seal type may list additional characteristics of the system and equipment necessary to ensure proper application of that component.

Seal performance (chemical resistance, physical properties, and maintenance considerations) varies significantly with both material class (e.g., EPDM, FKM, PTFE) and each supplier’s formulation and manufacturing choices.

Assembly/fitting details (e.g., torque settings, choice of clamping mechanism, and alignment) significantly affect the performance and longevity of static sealing components and should be considered (see also ASME B31.3). For example, overtightening of these clamps may damage seals or cause excessive intrusion (see MC-4.2).

Evaluations presented in the following tables generally describe compounds in the specified material class. Different compounds within a material class, different compounds from particular suppliers, and articles manufactured from the same compounds in different ways may vary significantly.

The scope of this Appendix cannot address all possible materials. Materials other than those listed may be suitable for the specified applications provided they meet the requirements of Part PM. The intent of this Appendix is to guide communication between the owner/user and the supplier to find a balance of properties needed for the application.

This information may give initial guidance for material selection. However, due to the inherent variability of materials, compound processing, and use, the owner/user should qualify individual materials and suppliers based on performance data.

Seal location within the system may also affect seal performance. Performance data for applications can be developed using test methods listed in Nonmandatory Appendix L. Chemical compatibility/suitability of a particular compound may be verified through the material supplier. Maintenance characteristic evaluations are expert opinions based on testing (see Nonmandatory Appendix K).

AA-1.1 Guidance Limitations
Every component has its own limited process capabilities and service life for each application in which it is used. Application characteristics such as size, speed, pressure, temperature, cycles, and cycle time help define an application envelope and will determine the suitability of a particular component. Appropriate component selection requires understanding of the application requirements and component capabilities.

In order to use the component selection guidance in this section
(a) The owner/user should collect the required application data (e.g., Form S-1, Application Data Sheet).
(b) If the owner/user’s application data fall inside the component’s application envelope, then the guidance provided is valid.
(c) If the owner/user’s application data fall outside the component’s application envelope, then the owner/user should consult with the vendor to find the appropriate component.

AA-1.2 Understanding the Charts

AA-1.2.1 Static Seal Charts

[Reserved for future content]

AA-1.2.2 Mechanical Seal Charts
The instructions to select mechanical seal face materials using Table AA-3.2.3-1 are as follows:

(1) Select the material for one of the seal faces in the “Material List” column.
(2) Verify the material selection is suitable using the grading system in the “Material Characteristics” column.
(3) Select a mating face material based on the grade indicated in one of the “Face Pair Compatibility” columns.
(4) Verify the mating face material is preferred or accepted in the “Material Characteristics” columns.
AA-2 MATERIAL CLASS DESCRIPTIONS¹

AA-2.1 Synthetic Rubbers (Elastomers)

*EPDM (Ethylene Propylene Diene Rubber) – peroxide-cured systems:* EPDM is one of the more widely used and varying materials in bioprocessing equipment.

*VMQ (Silicone) – peroxide-cured and platinum-cured systems:* Silicone is often preferred for single-use applications due to its relative simplicity of formulation, low toxicity, and optical clarity. Peroxide-cured silicone systems generally have more reaction by-products, which may be extractable, than platinum-cured systems.

*FKM (Fluoroelastomers):* FKM materials can be separated into types, based on the monomers used and their ratio(s). In general, the higher the fluorine level, the better the chemical resistance. Different curing systems within the same type can affect performance significantly.

AA-2.2 Plastics and Composites

*PTFE (Polytetrafluoroethylene) and Composites:* PTFE has long been used in bioprocessing equipment due to its relative high purity, chemical inertness, nonstick properties, and long seal life. However, as a plastic, PTFE seals are susceptible to irreversible deformation under load/compression (cold-flow/creep). PTFE seals can vary in geometry due to warping and/or process variation, and fit may be less predictable than elastomeric seals. PTFE seals and their variants generally require higher compressive forces (fastener torque) to form a seal than their elastomeric counterparts. They are more susceptible to degradation due to gamma-irradiation (sanitization) than other commonly used materials. PTFE seal properties can also vary with PTFE grades (molecular weight and particle size distribution) and manufacturing variables.

AA-2.3 Modified PTFE

Modified PTFE has lower vapor phase transmission, without sacrificing chemical resistance, than standard PTFE. Modified PTFE is often substituted for PTFE in static seals (see AA-2.2).

AA-3 Compendial Ambient/Hot-Water Distribution Systems

AA-3.1 Envelope

The application and selection of sealing components are based on compeial water at temperatures between 68°F and 185°F (20°C and 85°C) and pressures greater than 0 psig (0 barg) up to 87 psig (6 barg). Systems may be exposed to hot-water sanitization and/or intermittent steam at up to 266°F (130°C).

These systems are typically constructed of metallic materials.

Sealing components used in compeial water systems should be selected based on requirements for long-term seal reliability in a continuous-duty cycle.

(a) Most compeial water systems are sanitized with hot water (self-sanitizing). When systems are steam-sanitized, the owner/user should select appropriate materials/fittings based on operational requirements.

(b) Seals used in systems that are periodically heated for sanitization should be selected to accommodate thermal cycling.

AA-3.2 Seal types

AA-3.2.1 Static Seals

Table AA-3.2.1-1 provides a guide to static seal selection, which is intended to give readers general information about chemical, physical/mechanical, and maintenance considerations related to selecting materials suitable for static seals used in compeial water systems.

¹ Reference ASTM D1418, Standard Practice for Rubber and Rubber Latices - Nomenclature
Table AA-3.2.1-1: Polymeric Static and Dynamic Seal Selection for Use in Compendial Water Systems

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Chemical [Note 2]</th>
<th>Maintenance</th>
<th>Physical/Mechanical Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance to Static Seals</td>
<td>C</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Importance to Dynamic Seals</td>
<td>C</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

|--------------------|----------------------------------------|------------------------|---------------|----------------|---------------------------------------|-----------------------|-------------------------|------------------------------------------|---------------------|------------------------|----------------------|
|                    | ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ●
C = Critical
I = Important
S = Secondary

NOTES:
(1) Comments made here are generally true with compounds in this class currently available. Different compounds within a class vary between seal suppliers. Different compound numbers from a particular supplier may also vary. The optimal balance of characteristics in material selection for dynamic seals varies by type and application. For example, a dynamic O-ring, a weir diaphragm, and a radial diaphragm interact differently with mating surfaces and process solutions in the course of installation and operation. Communication between user and supplier is recommended to find the balance of properties needed for the owner/user.
(2) Passivation chemicals are occasionally used in compendial water systems - Consult with supplier
(3) Not recommended for certain dynamic O-ring applications.
(4) Recommendations represent predicted performance based on similar applications.
(5) Primarily applies to dynamic applications, but some properties may also be important in static applications (e.g., Resistance to adhesion applies to maintenance of static seals as well).
AA-3.2.2 Valves

A polymer seal material is acceptable provided that the manufacturer rates the valve assembly for the pressure and temperature limits and the material is compatible with the service stated in AA-3.1.

(a) Diaphragm valves, which have nonsliding seals, as designated in MC-2.3.1.2(a) through MC-2.3.1.2(c), are preferred.

(b) Other valve types with nonsliding seals are acceptable [e.g., pinch valves designated in MC-2.3.1.8; bellows seals like those shown in Figure MC-2.3.1.2-2, illustration (c); membrane or diaphragm seals like those shown in Figure MC-2.3.1.2-4, illustrations (b) and (c), FigureMC-2.3.1.2-5, or Figure MC-2.3.1.4-1, illustration (a)].

(c) Valves with sliding seals in process contact are not acceptable (e.g., ball, butterfly, or plug valves) unless the design enables maintaining both sides of the sliding seal in a clean and sanitized condition or the valves are used in a continuously self-sanitizing system.

(d) Valves with nonsliding and sliding seals are acceptable if only the nonsliding seal is in process contact (e.g., needle, control, or rising stem valves with O-ring seals).

AA-3.2.3 Mechanical Seals

Table AA-3.2.3-1 will help the reader select a face pair (consisting of a rotating face and a stationary face) for a compendial water pump mechanical seal.

The most common mechanical seal face materials are listed under the “Material List” column in Table AA-3.2.3-1. The materials listed are generic and do not specify the many grades available. Other seal face materials and combinations not listed in the Table may be suitable.

For information about material availability, face pair combinations, or specific grades, contact the equipment vendor.

(a) The “Material Characteristics” column offers insight into application-specific attributes of the material. The materials for both faces in the face pair should have preferred or accepted ratings in the Material Characteristics column.

(b) The “Face Pair Compatibility” column of Table AA-3.2.3-1 addresses the tribological characteristics of the face pair. The face pair is lubricated by the process fluid. The grading system is a direct indication of expected seal performance including service life, weepage rate, and particle generation.

(c) The grading system for material characteristics and face pair compatibility is explained in the General Notes for Table AA-3.2.3-1.

AA-3.2.3.1 Flush Plans

Flush Plan numbers 01, 02, 03, and 11, as defined in MC-2.3.2.4, are recommended. Compensial water is the seal face lubricant.
### Table AA-3.2.3-1: Mechanical Seal Face Material Selection for Compendial Water Pumps

<table>
<thead>
<tr>
<th>Material List</th>
<th>FACE Pair Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resin Impregnated Carbon</td>
<td>Pure Impregnated Carbon</td>
</tr>
<tr>
<td>Siliconized Graphite (Carbon Substrate with Silicon Layer)</td>
<td>Siliconized Graphite</td>
</tr>
<tr>
<td>Sintered Materials</td>
<td>Silicon Carbide Direct Sintered</td>
</tr>
<tr>
<td>Aluminum Oxide</td>
<td>Silicon Carbide with Graphite</td>
</tr>
<tr>
<td>Silicon Carbide with Porosity</td>
<td>Silicon Carbide with Porosity</td>
</tr>
<tr>
<td>Cemented Materials</td>
<td>Tungsten Carbide Cobalt</td>
</tr>
<tr>
<td>Tungsten Carbide Nickel</td>
<td>Tungsten Carbide Cobalt</td>
</tr>
<tr>
<td>Reaction Bonded</td>
<td>Tungsten Carbide Alloy</td>
</tr>
<tr>
<td>Glass-Filled PTFE</td>
<td>PTFE</td>
</tr>
</tbody>
</table>

**GENERAL NOTES:**

(a) Solid circles indicate the material is preferred for the column characteristic. Half-filled circles indicate accepted material for operating in compendial water. Performance issues may exist specific to the characteristic listed in the column heading. Open circles indicate materials should not be used.

(b) Solid circles indicate the preferred face pairs for operating in compendial water. Half-filled circles indicate accepted face pairs for operating in compendial water. This face pair can operate in a satisfactory manner for a period of time but will likely have more wear, friction, heat, and debris over a shorter period of time than the preferred face pairs. Open circles indicate materials and face pairs that are not recommended for operating in compendial water. It is expected that this face pair will cause damage to one or both seal faces with the greatest amount of particle generation, heat, and wear.

### AA-4 Pure Steam

#### AA-4.1 Envelope

The application and selection of sealing components is based on pure steam with pressures to 45 psig (3.1 bar), at 292°F (145°C) (saturated steam) in high-pressure distribution areas, and 25 psig (1.7 bar), at 267°F (130°C) (saturated steam) in low-pressure distribution areas.

Seals used in service conditions beyond these limits require special consideration.

Sealing components used in pure steam distribution systems should be selected based on requirements for long-term seal reliability in a continuous-duty cycle.

Pure steam systems should be designed to provide access for examination and replacement of sealing components as many seal types used with pure steam lines may leak after thermal cycling.
**AA-4.2 Seal types**

**AA-4.2.1 Static Seals**

Static seals used for pure steam applications should be selected for their ability to
(a) resist pure steam
(b) withstand continuous high temperatures
(c) minimize retightening

Hardware for use with static seals in pure steam systems should be selected to accommodate creep (cold flow) when plastic seals (e.g., PTFE or PTFE composites) are used.

**AA-4.2.2 Valves**

A polymeric seal material is acceptable provided that the manufacturer rates the seal material for the pressure and temperature limits and the service conditions stated in AA-4.1.

(a) Valve design and materials of construction should be rated for the pressure and temperature ranges of the service stated in AA-4.1.

(b) Valve types with nonsliding or sliding seals are acceptable (e.g., diaphragm, ball, rising stem, steam trap, pressure control, check, pressure relief, and plug valves).
**NONMANDATORY APPENDIX BB**

**MECHANICAL SEAL FACE MATERIAL SELECTION FOR COMPENDIAL WATER PUMPS**

**BB-1 GENERAL**

Figure BB-1-1 will help the reader select a face pair (consisting of a rotating face and a stationary face) for a compendial water pump mechanical seal.

The most common mechanical seal face materials are listed under the "Material List" column in Figure BB-1-1. The materials listed are generic and do not specify the many grades available. Other seal face materials and coatings are shown in Figure BB-1-2.

### Material List

<table>
<thead>
<tr>
<th>Material Type</th>
<th>Chemical Compatibility</th>
<th>Thermal Shock Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resin-impregnated carbon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Siliconized graphite (Carbon substrate with silicon layer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sintered materials Aluminum oxide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon carbide direct sintered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon carbide with graphite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon carbide with porosity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cemented materials Tungsten carbide nickel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungsten carbide cobalt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tungsten carbide alloy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction bonded Silicon carbide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicon carbide, graphite loaded</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coatings Chromium oxide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>316/316L SS (UNS S31600/UNS S31603)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH 17-4 (UNS S17400)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duplex 2205 (UNS S31803/UNS S32205)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glass-filled PTFE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FACE PAIR COMPATIBILITY**

- Preferred
- Accepted
- Not recommended

**GENERAL NOTES:**

(a) Solid circles indicate the material is preferred for the column characteristic. Half-filled circles indicate accepted material for operating in compendial water. Performance issues may exist specific to the characteristic listed in the column heading. Open circles indicate materials should not be used.

(b) Solid circles indicate the preferred face pairs for operating in compendial water. Half-filled circles indicate accepted face pairs for operating in compendial water. This face pair can operate in a satisfactory manner for a period of time but will likely have more wear, friction, heat, and debris than over a shorter period of time than the preferred face pairs. Open circles indicate materials and face pairs that are not recommended for operating in compendial water. It is expected that this face pair will cause damage to one or both seal faces with the greatest amount of particle generation, heat, and wear.
combinations not listed in the Figure may be suitable. For information about material availability, face pair combinations, or specific grades, contact the equipment vendor.

(a) The "Material Characteristics" column offers insight into application-specific attributes of the material. The materials for both faces in the face pair should have preferred or accepted ratings in the Material Characteristics column.

(b) The "Face Pair Compatibility" column of Figure BB-1-1 addresses the tribological characteristics of the face pair. The face pair is lubricated by the process fluid. The grading system is a direct indication of expected seal performance including service life, wearpage rate, and particle generation.

(c) The grading system for material characteristics and face pair compatibility is explained in the General Notes for Figure BB-1-1.

(d) The instructions to select mechanical seal face materials using Figure BB-1-1 are as follows:

(1) Select the material for one of the seal faces in the "Material List" column.

(2) Verify the material selection is suitable using the grading system in the "Material Characteristics" column.

(3) Select a mating face material based on the grade indicated in one of the "Face Pair Compatibility" columns.

(4) Verify the mating face material is preferred or accepted in the "Material Characteristics" columns.
FF-1. Concept of Maximum Allowable Leakage Limit (MALL) for Single-use-System:
For single-use systems, the MALL is associated with the barrier property of the single-use system (i.e., prevent any risk to product safety, product quality or operator and environmental safety). For more details, see also ASTM E3244. To identify the MALL associated to microbial integrity, typically a destructive test method (e.g., microbial ingress testing), is used in the development and qualification phases of the single-use system.
### Table FF-1

#### Leak Test, Nondestructive Methods

<table>
<thead>
<tr>
<th>Type of Test</th>
<th>Test Description</th>
<th>Disadvantages</th>
<th>Reference</th>
<th>Typical Defect Size Limit of Detection, μm</th>
<th>Typical Test Time, min</th>
<th>Typical Test User</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helium tracer gas</td>
<td>Assembly or component is placed in a vacuum chamber, followed by chamber evacuation. The helium tracer gas is then admitted to inside of the assembly. Any leaks will be detected via a mass spectrometer with a helium sensor. <em>has been shown</em> High sensitivity; Correlation to microbial challenge is possible. Specialized equipment required; Not suitable for complex systems; Complicated handling and maintenance; Impacted by material gas permeability; Preuse only.</td>
<td>ASTM F2391, Standard Test Method for Measuring Package and Seal Integrity Using Helium as the Tracer Gas. ASTM E3336: Standard Test Method for Physical Integrity Testing of Single-Use Systems.</td>
<td>22 5 to 15 for assembly for connectors components</td>
<td>Assembly manufacturer; component manufacturer owner/user</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure decay with restraining plates</td>
<td>Bag body is placed between two plates and connected to a pressurized air supply, inflated to a defined pressure, and monitored for pressure drop over a defined time. Pass/fail results are based on specified pressure decay rates. <em>has been shown</em> Mid to high sensitivity.</td>
<td>Specialized equipment required; Preuse only; Requires a filter for testing post irradiation; Limited volume range; Leaks may be masked by the assembly support hardware walls/grid.</td>
<td>ASTM E2095, Standard Test Method for Pressure Decay Leak Test for Flexible Packages With and Without Restraining Plates. ASTM E3336: Standard Test Method for Physical Integrity Testing of Single-Use Systems.</td>
<td>210 5 to 10</td>
<td>Assembly manufacturer; component manufacturer owner/user</td>
<td></td>
</tr>
<tr>
<td>Volume-dosed flow measurement Gas</td>
<td>Assembly is installed at point of use, connected to the test instrument for testing, and inflated to a defined pressure. Pressure is maintained while monitoring flow-of-air. Gas flow is measured while keeping test pressure constant in the inflated assembly. <em>Requires</em></td>
<td>Specialized equipment required; Preuse only; May require a filter for post-gamma irradiation; Limited volume range; Leaks may be masked by the assembly support hardware walls/grid.</td>
<td>ASTM E2930, Standard Practice for Pressure Decay Leak Test Method. ASTM E3336: Standard Test Method for Physical Integrity Testing of Single-Use Systems.</td>
<td>230 10 to 15</td>
<td>Assembly manufacturer; owner/user</td>
<td></td>
</tr>
</tbody>
</table>

Note: better sensitivity can be reached in lab configuration.
and Integrity


GENERAL NOTE: More detailed information on test setups, procedures and method validation can be found in ASTM E3336.

### Table FF-1
Leak Test, Nondestructive Methods (Cont'd)

<table>
<thead>
<tr>
<th>Type of Test</th>
<th>Test Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Reference</th>
<th>Typical Defect Size Limit of Detection, μm</th>
<th>Typical Test Time, min</th>
<th>Typical Test User</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure decay without restricting plates</td>
<td>Assembly or component is connected to a pressurized air supply, inflated to a defined pressure, and monitored for pressure drop over a defined time. Pass/fail results are based on specified pressure decay rates.</td>
<td>Simple handling and operation Test can also be performed in situ at point of use No further handling before use Requires and volume for testing</td>
<td>Sensitivity limited by assembly pressure tolerance Preuse only (postuse possible with limitations) May require a filter post-gamma irradiation Sensitivity declines as volume increases Larger bag volumes require a large workspace Significant risk of damage during testing</td>
<td>ASTM E2095, Standard Test Methods for Pressure Decay Leak Test for Flexible Packages With and Without Restraining Plates</td>
<td>≥50</td>
<td>15 to 30 [Note (1)]</td>
<td>Assembly manufacturer; component manufacturer; owner/user</td>
</tr>
<tr>
<td>Visual inspection</td>
<td>Visual inspection is conducted for the assembly or component.</td>
<td>No specialized equipment required Requires skilled operators Lack of clear pass/fail criteria Defects in folds or seams of assembly may not be visible</td>
<td></td>
<td>ASME BPVC, Section V, Article 9 (Visual Examination)</td>
<td>≥100</td>
<td>5</td>
<td>Assembly manufacturer; component manufacturer; owner/user</td>
</tr>
</tbody>
</table>

**Note:** (1) This does not include filling time.
<table>
<thead>
<tr>
<th>Type of Test</th>
<th>Test Description</th>
<th>Methodology</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microbial challenge testing</td>
<td>by liquid</td>
<td>unit into a liquid</td>
<td>Correlation of Physical barrier sensitivity to microbial growth</td>
<td>Complicated setup, high cost</td>
<td>Typically qualitative</td>
</tr>
<tr>
<td>Microbial challenge testing</td>
<td>by air</td>
<td>assembly unit into a specially designed and sealed chamber, charging the atmosphere within the chamber with a specified period of time, and examining the unit for microbial growth</td>
<td>Correlation of Physical barrier sensitivity to microbial growth</td>
<td>Complicated setup, high cost</td>
<td>Typically qualitative</td>
</tr>
</tbody>
</table>

**Table FF-2: Leak Test, Destructive Methods**

<table>
<thead>
<tr>
<th>Test</th>
<th>Limit of Detection</th>
<th>Typical Test Time</th>
<th>Typical Test User</th>
<th>Assembly manufacturer: component manufacturer:</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Record 22-1287**

- cont.

NMA FF Revision
**GENERAL NOTE:** More detailed information on test setups, procedures and method validation can be found in ASTM E3251.
## Physical and Functional Testing References Used to Characterize Single-Use Bags

### Table HH-1

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Test Level</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integrity (Leak) Test</strong></td>
<td>Confirmation of integrity for components at a given temperature. This includes pressure testing under operating conditions and at elevated pressures.</td>
<td>Component</td>
<td>ASTM E515 Standard Practice for Leaks Using Bubble Emission Techniques (modified)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Manufacturer defined method</td>
</tr>
<tr>
<td></td>
<td>Hydrostatic leak testing</td>
<td>Material</td>
<td>ASTM E1003 Standard Practice for Hydrostatic Leak Testing</td>
</tr>
<tr>
<td><strong>Puncture Resistance</strong></td>
<td>Puncture resistance testing predicts the durability of the film while in use. Films with high puncture resistance correspond with materials that can absorb the energy of an impact by both resistance to deformation and increased elongation. Puncture resistance, measured in energy units, evaluates the film strength and extensibility properties. Puncture resistance is similar to toughness.</td>
<td>Material</td>
<td>ASTM D7192 Standard Test Method for High Speed Puncture Properties of Plastic Films Using Load and Displacement Sensors</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Puncture Test Federal Test Method Standard (FTMS) 101C- Method 2065.1</td>
</tr>
<tr>
<td><strong>Tear Strength</strong></td>
<td>Tear strength measures the resistance to propagation of a rip or tear once the rip has been initiated.</td>
<td>Material</td>
<td>ASTM D1004 Standard Test Method for Tear Resistance (Graves Tear) of Plastic Film and Sheeting</td>
</tr>
<tr>
<td><strong>O₂ and CO₂ Permeability</strong></td>
<td>Determines the steady-state rate of transmission of O₂ through material.</td>
<td>Material</td>
<td>ASTM D3985 Standard Test Method for Oxygen Gas Transmission Rate Through Plastic Film and Sheetig Using a Coulometric Sensor</td>
</tr>
<tr>
<td></td>
<td>Determines the steady-state rate of transmission of CO₂ through material.</td>
<td>Material</td>
<td>ASTM F2476 Standard Test Method for the Determination of Carbon Dioxide Gas Transmission Rate (CO₂TR) Through Barrier Materials Using an Infrared Detector</td>
</tr>
<tr>
<td><strong>Tensile Strength</strong></td>
<td>A measure of the force (stress) required to stretch a material to its breaking point.</td>
<td>Material</td>
<td>ASTM D882 Standard Test Method for Tensile Properties of Thin Plastic Sheeting</td>
</tr>
<tr>
<td><strong>WVTR</strong></td>
<td>Water Vapor Transmission Rate.</td>
<td>Material</td>
<td>ASTM F1249 Standard Test Method for Water Vapor Transmission Rate Through Plastic Film and Sheetig Using a Modulated Infrared Sensor</td>
</tr>
<tr>
<td><strong>Chamber Integrity Test</strong></td>
<td>Used to measure manufactured product and seal barrier performance of a variety of package types and forms, as well as seal or closure types.</td>
<td>Component</td>
<td>ASTM E3244 Standard Practice for Integrity Assurance and Testing of Single-Use Systems</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BPE section SU-3</td>
</tr>
<tr>
<td><strong>Seal Integrity Peel</strong></td>
<td>Performed to ensure that functional strength requirements are met.</td>
<td>Component</td>
<td>Manufacturer defined method typically aligned with ASTM F88/F88M Standard Test Method for Seal Strength of Flexible Barrier materials, or risk assessment</td>
</tr>
<tr>
<td><strong>Thickness &amp; layer composition</strong></td>
<td>Film thickness and materials composition to be defined.</td>
<td>Material</td>
<td>ASTM D1777 Standard Test Method for Thickness of Textile Materials</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BPE section SC-3.1</td>
</tr>
<tr>
<td><strong>Visual Observation Library</strong></td>
<td>List of potential visual observations regarded as defects vs cosmetic imperfections. Observations should consider secondary packaging materials that may contribute to visual observations, as well as the installation state of the biocontainer at the time such inspections would typically be performed.</td>
<td>Component</td>
<td>BioPhorum &quot;Disposables: Single-use systems bag assembly leakage and defect toolkit&quot; (Oct 2020)</td>
</tr>
</tbody>
</table>
# Functional Testing References Used to Characterize Single-Use Bags

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Test Level</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Package Testing/ Transportation Shipping</td>
<td>Qualify that product packaging will protect the product during shipping. Standard practice for performance testing of shipping containers and systems to provide a uniform basis of evaluating, in a laboratory, the ability of shipping units to withstand the distribution environment.</td>
<td>Component</td>
<td>ASTM D4169 Standard Practice for Performance Testing of Shipping Containers and Systems</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ISTA 2A, 3A, 3B, 3E</td>
</tr>
<tr>
<td>Accelerated Aging (Shelf Life)</td>
<td>Accelerated or real life studies to determine the effects, if any, due to the passage of time and environmental effects on the properties of product, and on the sterile integrity of packages and the physical properties of their component packaging materials.</td>
<td>Component</td>
<td>ASTM F1980 Standard Guide for Accelerated Aging of Sterile Barrier Systems and Medical Devices</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BPE section SU-10</td>
</tr>
<tr>
<td>Particulate Matter</td>
<td>Evaluates the presence of particulates in or on a sample.</td>
<td>Component</td>
<td>USP &lt;788&gt; Particulate Matter in injections</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BPE section SU-11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BPSA Recommendations for Testing, Evaluation, and Control of Particulates from Single-Use Processing Equipment</td>
</tr>
<tr>
<td>Break at Cold Temperature test</td>
<td>Determines cold crack temperature of plastic film.</td>
<td>Material</td>
<td>ISO 8570 Plastics – Film and sheeting – Determination of cold-crack temperature</td>
</tr>
<tr>
<td>Low Temperature Brittleness</td>
<td>Determines the temperature at which plastics and elastomers exhibit brittle failure.</td>
<td>Material</td>
<td>ASTM D1790 Standard Test Method for Brittleness Temperature of Plastic Sheet by Impact</td>
</tr>
<tr>
<td>Dart Drop</td>
<td>Test method covers the determination of the energy as part of mechanical properties that causes plastic film to fail under specified conditions of impact of a free-falling dart.</td>
<td>Material or Component</td>
<td>ASTM D1709 Standard Methods for Impact Resistance of Plastic Film by the Fee-Falling Dart Method</td>
</tr>
<tr>
<td>Gelbo (flex crack resistance)</td>
<td>Determines the flex resistance of materials by the formation of pinholes.</td>
<td>Material or Component</td>
<td>ASTM F392/F392M Standard Practice for Conditioning Flexible Barrier Materials or Flex Durability</td>
</tr>
<tr>
<td>Glass Transition Temperature</td>
<td>Determines the glass transition temperature (Tg) of materials. The Tg is the temperature where the polymer goes from a hard, rigid state to a rubber-like, flexible state.</td>
<td>Material</td>
<td>ASTM E1640 Standard Test Method for Assignment of the Glass Transition Temperature by Dynamic Mechanical Analysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ASTM D3418 Standard Test Method for Transition Temperatures and Enthalpies of Fusion and Crystallization of Polymers by Differential Scanning Calorimetry</td>
</tr>
<tr>
<td>Plastic Containers Qualification of</td>
<td>Tests of plastic materials for use as containers for drug solutions. Tests ensure that the plastics do not change/degrade under conditions of normal use. They look for changes in physical characteristics, pH, or other changes associated with light, or chemicals.</td>
<td>Material</td>
<td>EP 3.2.2.1. Plastic Containers for Aqueous Solutions for Infusion</td>
</tr>
<tr>
<td>Parenteral/Ophthalmic - Aqueous Solutions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Table HH-2**
The following table provides a size comparison between common thermoplastic sizing standards and stainless steel tube sizes.

<table>
<thead>
<tr>
<th>Nominal Size</th>
<th>SS Tube</th>
<th>Sch 40</th>
<th>Sch 80</th>
<th>SDR 11</th>
<th>SDR 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>in.</td>
<td>in. mm</td>
<td>in.</td>
<td>in. mm</td>
<td>in.</td>
<td>in. mm</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>1/2</td>
<td>0.5</td>
<td>12.7</td>
<td>9.4</td>
<td>0.84</td>
<td>21.3</td>
</tr>
<tr>
<td>3/4</td>
<td>0.75</td>
<td>19.1</td>
<td>6.2</td>
<td>1.05</td>
<td>26.7</td>
</tr>
<tr>
<td>1</td>
<td>1.25</td>
<td>31.8</td>
<td>25.1</td>
<td>1.32</td>
<td>33.4</td>
</tr>
<tr>
<td>1-1/4</td>
<td>1.66</td>
<td>42.2</td>
<td>37.3</td>
<td>1.66</td>
<td>42.2</td>
</tr>
<tr>
<td>1-1/2</td>
<td>2</td>
<td>48.3</td>
<td>37.5</td>
<td>1.9</td>
<td>48.3</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>63.5</td>
<td>60.2</td>
<td>2.00</td>
<td>73</td>
</tr>
<tr>
<td>2-1/4</td>
<td>3</td>
<td>76.2</td>
<td>72.9</td>
<td>3.5</td>
<td>88.9</td>
</tr>
<tr>
<td>3</td>
<td>3.5</td>
<td>97.5</td>
<td>5</td>
<td>4.5</td>
<td>114</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>152</td>
<td>147</td>
<td>6.63</td>
<td>168</td>
</tr>
</tbody>
</table>

MOVED FROM PM-4.2.1