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Standard Guide for Specification, Design, Verification, and Application of Single-Use Systems in Pharmaceutical and Biopharmaceutical Manufacturing[1]

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1. Scope

1.1 This guide is intended as a complement to Guide E2500.

1.2 This guide is applicable to the range of manufacturing systems described in Guide E2500, specifically all elements of single-use systems, or hybrids of single-use and traditional components, used for the manufacturing of pharmaceutical and biopharmaceutical products, including: materials of construction, components, assembly, manifolds, supporting utilities, associated process monitoring and control systems, automation systems, and controlled environment that have the potential to affect product quality and patient safety.

1.3 This guide is applicable for the implementation of changes to manufacturing system design for existing systems. It may be used for continuous improvement and changes in operation from clinical through to commercial scale.

1.4 For brevity, single-use systems are referred to as SUS throughout the rest of this guide.

1.5 The approach may be applied by the end user, the supplier of SUS, and raw materials sub-suppliers further back in the supply chain.

1.6 This guide is not intended to apply to the use of single-use technology for packaging, primary containers, combination products (products composed of any combination of a drug, device, or biological product) or devices.

1.7 This guide does not address specific local requirements, which remain the responsibility of the end user.

1.8 *This guide does not address employee health and safety, environmental, nor other good engineering and manufacturing practices (GXP) requirements. This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

[1] This guide is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.07 on Single Use Systems.

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2. Referenced Documents

2.1 *ASTM Standards:*[2]

D4169 Practice for Performance Testing of Shipping Containers and Systems

E2363 Terminology Relating to Manufacturing of Pharmaceutical and Biopharmaceutical Products in the Pharmaceutical and Biopharmaceutical Industry

E2500 Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

2.2 *United States Pharmacopeia:*[3]

USP<788> Particulate Matter in Injections

USP<790> Visible Particulates in Injections

2.3 *International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH):*[4]

ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients

ICH Q8 (R2) Pharmaceutical Development

ICH Q9 Quality Risk Management

ICH Q10 Pharmaceutical Quality System

2.4 *ISO Standards:*[5]

ISO 13485:2003 Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes

ISO 14644 Cleanrooms and Associated Controlled Environments

ISTA 3A General Simulation Performance tests

[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[3] Available from U.S. Pharmacopeial Convention (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

[4] Available from International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), ICH Secretariat, 9, chemin des Mines, P.O. Box 195, 1211 Geneva 20, Switzerland, http://www.ich.org.

[5] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

2.5 *U.S. Food and Drug Administration (USFDA):*[6]
Guidance for Industry Process Validation: General Principles and Practices
Pharmaceutical cGMPs for the 21st Century, A Risk-Based Approach
2.6 *European Medicine Agency:*
Commission Directive 2003/94/EC of 8 October 2003
2.7 *Other Publications:*
PDA Technical Report No. 66 Application of Single-Use Systems in Pharmaceutical Manufacturing
Consensus Quality Agreement Template for Single-Use Biopharmaceutical Manufacturing Products BioProcess Systems Alliance[7]
TAPPI Standard Practice T 564 sp-11

3. Terminology

3.1 *Definitions:*

3.1.1 For definitions of terms used in this guide, refer to Terminology E2363, Guide E2500, and PDA Technical Report No. 66. Terms requiring special consideration as they relate to SUS are detailed below.

3.1.2 *design reviews, n*—purpose of design reviews is still to evaluate design against standards and requirements, identify problems, and propose corrective actions.

3.1.2.1 *Discussion*—However, the scope of the review may differ depending on whether the end user is considering a standard design, configured variants of standard designs which maintain adherence to the supplier's design space, or customized designs, which incorporate one or more features that are outside of the supplier's design space. Such features may include components, design layout, design dimensions, or materials of construction. The end-user should first consider the requirements for any given SUS based on the application (for example, product or process contact, temperature, volumes, flow rates, mixing, requirements for sensors and controls etc. as applicable) and define them clearly in a document such as a user requirement specification (URS). In the case of standard or configured designs, the review will address the supplier's criteria for selection of materials, components, and functional design and align these against the URS. In the case of end-user-specified custom designs, the design review should affirm that the combination of supplier- and user-derived design attributes aligns with the URS. Additionally, the review should evaluate the risk taken in deviating from the supplier design space, and the possible need for risk mitigation, which generally will be the end user's responsibility. The risk assessment should be retained as part of the development history. Conditions and expectations should be covered in a quality agreement. The quality agreement should outline the responsibilities of the supplier and the end user with respect to the quality assurance of the system manufactured or supplied or both by the supplier to the end user. Quality agreement templates are available from various industry groups (for example, Consensus Quality Agreement Template for Single-Use Biopharmaceutical Manufacturing Products BioProcess Systems Alliance).

3.1.3 *modular, adj*—SUS can consist of assemblies of components or subassemblies that can be built or reconfigured or both in a modular manner provided that connectors are compatible with each other.

3.1.4 *subject matter experts, n*—individuals with expertise in a particular area or field, which will include, but are not limited to, material sciences, plastics and molding technologies, sterilization, particulate assessment, and leachables and extractables.

3.1.5 *verification, n*—verification is a systematic approach to verify that SUS, acting singly or in combination, are fit for intended use, have been properly installed, and are operating correctly.

3.1.5.1 *Discussion*—The manufacturing process for an SUS consists of multiple steps and verification activities should be appropriate for the stage of the SUS design and manufacturing process (for example, material selection versus component dimensions versus configuration) and the intended purpose of the component or finished assembly or both. Verification is an umbrella term that encompasses all types of approaches to assuring systems are fit for use including qualification, commissioning and qualification, verification, system validation, or other and extends across the supply chain as materials and components are integrated into the completed SUS. Given that each system is partially or completely replaced after use, it is important to confirm that components have been assembled correctly, none of the critical attributes of the assembly are damaged during installation, and no leaks that may compromise the SUS are evident before use. Suppliers of SUS and their materials and components should apply similar rigor and change control procedures to their sub-suppliers to ensure consistent quality over the lifetime of the SUS (see also 8.2, Change Management).

4. Summary of Guide

4.1 This guide is based on a similar risk-based and science-based approach taken in Guide E2500 and is similar in purpose, content, and organization.

4.2 The objective of this guide is to provide additional information to support defined and controlled processes relevant to SUS, or hybrid traditional SUS to enable the production of products that consistently meet defined quality requirements. A further objective is to support supplier manufacturing capability that meets quality requirements of SUS or User Requirement Specifications (URS) or both as applicable.

4.3 The approach described within this guide supports continuous process capability improvements and facilitates incorporation of new capabilities as technology evolves.

4.4 The main elements of this guide are:

4.4.1 The underlying key concepts,

4.4.2 A description of the specification, design, and verification process, and

4.4.3 A description of the required supporting processes.

[6] Available from U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD 20993, http://www.fda.gov.

[7] Available from BioProcess Systems Alliance, http://www.bpsalliance.org.

5. Significance and Use

5.1 Application of the approach described within this guide is intended to satisfy international regulatory expectations in ensuring that SUS are fit for their intended use and to satisfy requirements for sourcing, supply, design, specification, installation, operation, and performance.

5.2 The approach described in this guide applies concepts and principles introduced in the FDA initiative, Pharmaceutical cGMP's for the 21st Century – A Risk-Based Approach. It supports and is consistent with the framework described in FDA Guidance for Industry, Process Validation: General Principles and Practices, in ICH Q7, ICH Q8 (R2), ICH Q9, and ICH Q10.

5.3 This guide includes concepts developed in the PDA Technical Report No. 66.

5.4 This guide may be used independently or in conjunction with other ASTM Committee E55 proposed standards to be published by ASTM International.

5.5 Specific standard practices about extractables, leachables, particulate matter, and integrity testing/leak detection, biocompatibility, and raw materials as available should be used by suppliers and end users and applied to their own manufacturing process facilities.

6. Key Concepts

6.1 This guide follows similar key concepts to those covered by Guide E2500 focusing on clarification and discussion of SUS, good engineering practice, good manufacturing practice, and use of supplier and end user documentation. The concepts are listed in the following:

6.1.1 Risk-based approach,

6.1.2 Science-based approach,

6.1.3 Critical aspects of SUS,

6.1.4 Quality by design,

6.1.5 Good engineering/manufacturing/distribution/documentation practices,

6.1.6 Subject matter expert,

6.1.7 Use of supplier documentation,

6.1.8 Continuous improvement and change management, and

6.1.9 Supply chain.

6.2 *Risk-Based Approach:*

6.2.1 The underlying principle of risk management focuses on the issues which have the highest probability of occurring or have the greatest effect on the product quality and consequently patient safety.

6.2.2 Risk management underpins the specification, design, verification, and documentation activities as described in Guide E2500 and in ICH Q9.

6.2.3 SUS are an integral part of the drug manufacturing process and it is critical that SUS suppliers provide SUS in a timely manner. Special consideration should be given to mitigating the risk of an interruption of the supply chain of SUS, which may have an impact on the security of supply of drug to patients.

6.3 *Science-Based Approach:*

6.3.1 Product and process information, as it relates to product quality and patient safety, remain the basis for making science- and risk-based decision that ensure that the SUS are designed and verified to be fit for their intended use.

6.3.2 Examples of end-user product and process information to consider include: critical quality attributes (CQAs), critical process parameters (CPPs), process control strategy information, and prior production experience. For SUS, these can include extractables information, certificates of analysis, sterilization records, change control documents, and product design specifications.

6.3.3 Additional information to consider is the processing parameters and materials for the SUS themselves. Materials and designs should be selected and developed based on the intended use of the SUS (for example, cell culture, buffer bag, and product container) using quality by design approaches, such that sources of variability are understood and are managed such that they do not impact the performance of the end user's process or product quality.

6.3.4 Special consideration should be given to the supplier's evaluation and selection of materials of construction (for example, films, tubing, and connectors) as related to their fitness for intended use based on parameters such as physicochemical properties, mechanical strength, optical properties, and anticipated operating temperature. Materials should be robust and compatible with product and process fluids and should not be excessively prone to damage, which compromises structural integrity. The shedding of any materials, either as solid particles or soluble leachables, that impact product quality or process performance should be well characterized. For SUS, this is particularly important since changes may be made in the construction materials, production and sterilization processes, additives such as anti-oxidants and dyes, and material origin based on their availability over the lifetime of a given process. Such changes should be evaluated with the appropriate diligence based on the risk to the product or the process.

6.3.5 Consideration should be given to the possible impact of materials of construction or in-process leachables from materials of construction, or both, on product quality or process performance.

6.4 *Critical Aspects of SUS:*

6.4.1 Critical aspects of SUS are typically functions, features, abilities, and performance or characteristics necessary for the manufacturing process and systems to ensure consistent product quality and patient safety. They should be identified and documented based on scientific product and process understanding for both the SUS manufacturing process and the end-user process.

6.4.2 SUS often consist of multiple combinations of individual components. Often, multiple design configurations can be considered with varied materials and components, each of which can be demonstrated as capable of meeting the critical performance requirements for a given system such as volume, compatibility, low bioburden, freedom from leaks, and mixing if required.

6.4.3 Adopting a modular design approach allows for the interchangeable use of functionally equivalent components and

provides flexibility, which can be used to the advantage of both end user and supplier to manage the risk to supply continuity, subject to the appropriate qualification of alternative suppliers, materials, components, and designs and the existence of a well-planned connectivity strategy.

6.4.4 Critical aspects of SUS may be compromised throughout the lifetime of an SUS, which extends across component manufacturing, final assembly, sterilization, transportation, receiving, warehousing, installation, deployment, and use.

6.4.5 A risk-based approach analyzing potential points and types of failures through the lifetime of an SUS from fabrication, shipment, installation, deployment, and operation should be used to determine the appropriate controls and testing to be used at each point.

6.4.6 Additional activities to qualify alternative components and suppliers should be documented to facilitate improvements to the design or as part of change control in response to discontinuation of supply. This is detailed in following sections.

6.4.7 Where suppliers provide standard designs for specific unit operations, the supplier should provide documentation to support the selection and qualification of materials, components, or functional design, or combination thereof, in relation to its intended use (for example, cell type, fed-batch versus perfusion, mixing and sparging, temperature shift ramp rates, and so forth).

6.4.8 Where the end user has requested a custom design based on specific preferences for components, or a different combination of inlets, outlets, or ports, the responsibility for traceability of individual components and the performance of various parts of the assembly should be defined in the URS or a specific quality agreement as appropriate, along with the supply agreement and technical diligence as appropriate.

6.4.9 SUS are susceptible to variances in appearance because of creases made throughout assembly, packing, handling, transit, inspection and deployment. End users and suppliers should establish what constitutes normal and acceptable cosmetic variances.

6.5 *Quality by Design:*

6.5.1 SUS are heavily reliant on quality by design concepts. The degree to which post-installation verification can be applied to SUS is limited. Quality depends upon clearly stated expectations defined in a URS; design specifications that match expectations; a qualified design and manufacturing process; the supplier's quality and supply chain systems; and proper handling, deployment, and use procedures.

6.5.2 The critical aspects of the design and associated acceptance criteria should be documented in the URS.

6.5.3 Assurance that manufacturing systems are fit for intended use should not rely solely upon verification after installation but also be achieved by a planned and structured verification approach applied throughout the system lifecycle.

6.5.4 Suppliers should apply and maintain a similar level of stringency and scrutiny as is applied to them to their own sub-suppliers to provide a higher degree of assurance that the critical aspects of the SUS can be routinely and reliably met.

6.5.5 The end user should work with the supplier to be knowledgeable of potential sources of variation in the raw materials used to make the SUS to determine any potential effects that such raw material variation may have on their process and product quality. Variability can arise from changes in sources of materials and processing conditions, both planned and inadvertent, and should be managed by effective change management communication and transparency on the part of the supplier.

6.6 *Good Engineering, Manufacturing Practices:*

6.6.1 Good engineering and manufacturing practices (GXP) should underpin and support the specification, design, and verification activities.

6.6.2 The extent to which suppliers and sub-suppliers adhere strictly to GXP may vary. Many may also manufacture medical devices and adhere to other relevant standards (for example, ISO 13485).

6.6.3 The end user should engage in quality audit and technical due diligence activities to ensure that suppliers have defined designs and specifications and implemented quality management systems that are appropriate for the intended purpose of the SUS.

6.6.4 Appropriate distribution practices should be implemented and ensured throughout the entire lifecycle of the SUS to minimize damage to assemblies. (Good manufacturing practice and good distribution practice compliance, European Medicines Agency)

6.7 *Subject Matter Experts (SMEs)*—The role of subject matter experts is the same in this guidance as for Guide E2500. Specific areas of subject matter expertise may differ with knowledge of material properties, extractables and leachables, and particulate generation being particularly important. Qualified suppliers are an important source of SMEs as they have industry-wide exposure to SUS performance and best practices.

6.8 *Use of Supplier Documentation:*

6.8.1 Clear and comprehensive documentation between the end user and supplier is critical to define the design, specification and performance of the SUS and clarify other expectations (for example, technical support).

6.8.2 The end user of SUS is considerably more dependent on supplier documentation than traditional reusable systems that are verified by the end-user. In some cases the supplier may be the only practical source for justifying designs and confirming ongoing quality (for example, pre-sterilized assemblies). Supplier documentation, including test documentation, may be used as part of the verification documentation providing the regulated company has assessed the supplier and has evidence of:

6.8.2.1 An acceptable supplier quality system,

6.8.2.2 Supplier technical capability, and

6.8.2.3 Supplier application of appropriate practices (GXP, ISO) such that information obtained from the supplier will be accurate and suitable to meet the purpose of verification.

6.8.3 It is incumbent on the end user to understand the supplier's product testing strategy and release criteria, as this technical understanding will form the basis of an overall risk assessment on the use of supplier documentation. One should be aware that suppliers may take different, but equally valid,

approaches to controlling and testing for SUS critical quality attributes. The end-user assessment should focus on the desired outcome relative to the URS or specification.

6.8.4 The supplier and end user should also develop a shared understanding of the end-user's acceptance criteria to ensure alignment between the supplier's capabilities, the functional requirements of the SUS, and the relevance of the testing methods used.

6.8.5 The end user may mitigate potential inadequacies in quality systems or GXP by applying specific, targeted additional checks or other controls, which may be extended to sub-suppliers, rather than repeating supplier activities and replicating documentation.

6.8.6 The supplier's technical capability should be assessed through a technical diligence exercise. Suppliers should demonstrate sufficient technical capability to have control over their design, development and manufacturing processes. They benefit from being given an understanding of how their materials are used by the end user such that there is an understanding of the potential impact of any changes and ensure they are communicated, and should have sufficient technical resources and procedures to support investigations of complaints (Section 8). A technical diligence exercise differs from a quality audit in that it is an open ended exchange of information between SME's at the supplier and end user to provide a shared understanding of expectations and capabilities, rather than confirm compliance with a quality system.

6.8.7 The decision and justification to use supplier documentation to support the verification of critical aspects of the manufacturing element should take into consideration the intended use of the manufacturing system and its potential impact to product quality or process performance (for example, primary product containers versus upstream buffer containers). The assessment should be documented and approved by the appropriate SME(s) including the quality unit.

6.8.8 Understanding the supplier's testing strategy and release criteria is critical. Suppliers may take different, but equally relevant, approaches to qualifying and verifying a critical aspect of an SUS. Different approaches are acceptable if relevant and validated. The end user assessment should focus on the desired outcome relative to the URS or specification.

6.8.9 Effective management of suppliers shall include periodic review meetings involving analysis of the supplier's performance for quality and delivery performance during the preceding period. Suppliers should be able to provide information on the performance of standard or similar assemblies across the industry to help in identifying if an issue is related to the design or the specific application of the end user.

6.9 *Continuous Improvement and Change Management*—Over time, advances will be made in the materials used and designs of SUS. These changes may provide an opportunity for improvements in process performance but they may also impact critical aspects of SUS. Timely change notification and change management is required to mitigate any risks to end-user product quality or process performance. See also 8.2.

6.10 *Supply Chain:*

6.10.1 The supply chain for SUS is complex, starting with petrochemicals, and materials undergo multiple manipulations and processes before becoming a completed assembly.

6.10.2 To have good assurance of quality in the overall sourcing and management of materials and components, end users should assure that they understand sources of product and process risk that derive from their suppliers and sub-suppliers Such understanding will come through transparent dialog with suppliers and technical due diligence activities described in 6.8.

6.10.3 Special consideration should be given to the qualification of additional suppliers and alternative designs and materials in the event of a supply chain failure at a single supplier. This may be managed in part at the level of the supplier who should already have qualified alternatives for sub-supply of materials and components.

6.10.4 Many SUS are pre-sterilized process components or systems and often are implemented without pre-use testing by the end user. Therefore, the supply chain, especially packaging and transportation, should be qualified and controlled to assure that the SUS remains undamaged and that the leveraging of supplier activities and documentation remains relevant.

6.10.5 SUS have a finite shelf life, due to materials of construction and the resulting stress put on such by sterilization or bioburden reduction processes. Steps should be taken together with the supplier to ensure suitable storage conditions and inventory management. Attention should be given to planning and logistics.

6.10.5.1 SUS shelf life has two main phases:

(1) Raw materials, resins and components supply chain prior to assembly, and

(2) Finished SUS product shelf life.

6.10.5.2 Shelf life typically refers to post sterilization (if applicable and should be given highest consideration by all stakeholders).

6.10.5.3 Suppliers and assemblers should have systems in place to specify and maintain shelf life claims for component, and to manage inventory.

7. Process

7.1 *Overview*—The process of specification, design, and verification of manufacturing systems should include the following activities:

7.1.1 Requirements definition,

7.1.2 Specification and qualification of components,

7.1.3 Development of design from qualified components,

7.1.4 Verification,

7.1.5 Acceptance and release, and

7.1.6 Installation and deployment.

7.1.7 GXP and risk management should be performed throughout the process.

7.1.8 Design reviews should be performed throughout the lifecycle of the manufacturing system, notably in the event of changes in design or materials.

7.2 *Requirements Definition:*

7.2.1 *Quality Requirements*—A formal quality agreement, with or without a specifications document, should be provided by end users to suppliers to define overarching requirements

and expectations. A consensus template is available from BPSA Consensus Quality Agreement.

7.2.2 *User Requirement Specification (URS)*—Specific requirements should be identified and provide the basis of detailed specification, design, and verification of the SUS.

7.2.2.1 The specific requirements relative to product quality and patient safety should be based upon the following:

7.2.2.2 Product knowledge and understanding,

7.2.2.3 Process knowledge and understanding,

7.2.2.4 Materials knowledge and understanding,

7.2.2.5 Supply chain knowledge and understanding,

7.2.2.6 Regulatory requirements, and

7.2.2.7 Company quality requirements.

7.2.3 Product and process knowledge and understanding, including knowledge of sources of variability in the materials, product, and process should be based upon scientific data gathered during experimental and development work and manufacturing experience with the current or similar processes.

7.2.4 Multiple combinations of materials, components, and designs may exist that are capable of meeting the functional requirements of a specific manufacturing process. To mitigate risks in supply continuity, user requirements in the URS should be documented in such a way as to capture the important attributes or capabilities of a given design rather than a prescriptive solution to allow maximum flexibility in providing the desired outcome.

7.3 *Specification and Qualification of Components:*

7.3.1 A science- and risk-based approach can be taken to specifications, such that a range of materials and components (for example, films, tubing connectors, and so forth) can be used that are functionally equivalent and comparable in their ability to meet user requirements in terms of structural integrity, physicochemical properties, and biocompatibility without impacting process performance or patient safety.

7.3.2 Each of these components and their suppliers should be qualified for their fitness for purpose and ability to meet the quality requirements of the manufacturing process. Components may be qualified individually or as part of an assembly by end users or assemblers or both. If an SUS is qualified as an assembly, then it should be used as such and any change to the assembly should be managed through change control.

7.3.3 Suppliers may have made independent assessments of alternative sources of materials and components. The criteria for evaluation and assessment for performance should be documented by the supplier and reviewed and approved by the end user based on the intended use of the component/manufacturing system.

7.4 *Development of Design from Qualified Components:*

7.4.1 A modular approach driven by process performance and product quality requirements can be used to facilitate the development of the design of a SUS.

7.4.2 The design and specification for the SUS should focus on aspects that have been identified as being critical to product quality and patient safety. These aspects of a manufacturing system should be identified and documented by end-user subject matter experts.

7.4.3 The existence of a modular design based on functional requirements and qualified components rather than unique specifications can facilitate the replacement of components if they become discontinued or are superseded by superior designs.

7.5 *Verification:*

7.5.1 The performance of individual manufacturing systems/component assemblies may be the responsibility of the supplier, sub-supplier/assembler, or end user depending on where the assembly was completed and inspected.

7.5.2 The responsibility of verifying that final assemblies, acting singly or in combination, are fit for their intended use, have been properly installed, and are operating correctly is the responsibility of the end user and a systematic approach should be in place.

7.5.3 The verification approach should be defined, documented, and reviewed by independent experts. The extent of verification and the level of detail should be based on risk as detailed in Guide E2500.

7.6 *Acceptance and Release:*

7.6.1 Acceptance criteria should be defined by subject matter experts.

7.6.2 Acceptance of an SUS is initially based on acceptance of the design and acceptable variations in that design based on availability or preferences for qualified materials and component preferences.

7.6.3 Supplier's quality documentation will form the basis of acceptance of SUS as delivered to the end user. In many cases, a more detailed inspection of a given assembly may not be possible until immediately before installation based on packaging of components.

7.6.4 The reliability of the supplier's certificate of analysis should be established through confirmation of the results of the supplier's tests or examinations by repeating testing or by supplier audits.

7.6.5 The supplier's documentation shall include a description of the test or examination method(s) used, limits of the test or examinations, and actual results of the tests or examinations for the completed assembly or for components used in the assembly.

7.6.6 The end user shall reconfirm the supplier's documentation on a periodic basis. In addition, the end user may conduct a more exhaustive assessment of the supplier's procedures as part of supplier management. This could be by destructive testing in the case of smaller components, through an on-site observation of manufacturing and testing processes at the supplier's facility, or, in certain circumstances, through post-use inspection or investigation of non-conformances.

7.7 *Installation and Deployment:*

7.7.1 In contrast to traditional multi-use systems, SUS are installed anew each time they are used.

7.7.2 Pre-use testing post-installation is limited for practical reasons; the act of testing may itself be damaging (for example, inflation-re-inflation cycles, detecting small perforations in large assemblies). The end user should develop and qualify detailed procedural measures to ensure, for example, continued structural integrity of assemblies and sterility (where an