

Progress Report March 2011

LNE/G-MED: Sharing a Passion for Progress

Sterile Medical Device Packaging: International and European Rules

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Naturally, manufacturers of sterile devices must validate their method of sterilization. However, the essential requirements also require such products to remain sterile throughout transport until their eventual use.

European (EU) and International (ISO) standards address this requirement taking into account a variety of factors.

This newsletter explores packaging for sterile medical devices, including:

- applicable European directives
- relevant international (ISO) standards
- specific testing requirements
- examples of packaging failures

Medical Devices Can Face Harsh Conditions

The distribution of medical devices can involve a variety of diverse methods, each with its own potential hazards. Depending on the vehicle (plane, train, automobile, etc.) and destination, packaged devices are subjected to countless mechanical stresses, such as vibration, shock, perforation, pressure, abrasions and falls.

The packaging is also subject to the effects of temperature, humidity, air pressure variations and other conditions, such as microbiological environment.

A device's sterile barrier system must stand up to the relevant hazards, retain its integrity over time and not interact in a detrimental way with the device over time.

International Standard - ISO 11607: 2006

The applicable harmonized standard covering this requirement *ISO 11607: 2006 -- Packaging for terminally sterilized medical devices* -- is the best tool to methodically analyze and demonstrate the relevance of the packaging system for sterilized devices. These standards specify the requirements and test methods for packaging that are intended to maintain sterility of

Medical Device Packaging: European Directives and Requirements

The European Directives address the packaging of sterile medical devices, with the following:

Directive 93/42/EEC (Article 3): The devices must meet the essential requirements in Annex I which apply to them, taking into account the intended destination.

Directive 93/42/EEC (Essential Requirement 1 of Annex I): The devices must be designed and constructed so that, when used under conditions and for the purposes intended, they will not compromise the clinical condition or the safety of the patient, or the safety and health of users..."

Essential Requirement 8.3: "Devices delivered in a sterile state must be designed, manufactured and packed . . . according to appropriate procedures to ensure they are sterile when placed on the market and remain sterile . . . until the protective packaging is damaged or opened."

EN 868, Parts 2 to 10: Specifies particular requirements for a range of materials commonly used, which can be used to demonstrate compliance with one or more of the requirements of ISO 11607-1.

The manufacturer must be able to demonstrate that the methods of sterilization and packaging are efficient and reproducible and meet the essential requirements of European directives for medical devices.

medical devices that are sterilized at the end stage until point of use. The standard contains two parts:

- Part 1: Requirements for materials, sterile barrier systems and packaging systems
- Part 2: Validation requirements for forming, sealing and assembly processes

Technical File Requirements

Complying with this harmonized standard (EN ISO 11607; 2 parts) gives presumption of compliance to the corresponding essential requirements of the European Medical Device Directives. (See box above.)

General requirements for the control of packaging for sterile devices include the need for a quality system. Methods used to demonstrate the compliance to this standard must be validated and be based on sound statistical approach, with documented evidence of compliance.

The elements to be addressed in the technical file are as follow:

- Choice of the material, including:
 - Microbiological barrier properties
 - Biocompatibility and toxicological characteristics
 - Physical and chemical characteristics
 - Compatibility with the forming and sealing processes
 - Compatibility with the considered sterilization process
 - Restraints on shelf life for warehousing, before and after sterilization
- Compatibility with the labeling
- Warehousing and transport
- Design of the packaging system, demonstrating the ability to present the product aseptically
- Performance testing of the packaging system, demonstrating the integrity of the packaging system after sterilization
- Stability testing, demonstrating by real time and accelerated studies the maintenance of the integrity of the packaging system during the shelf life of the medical device.

Address Your Testing Needs Through LNE's High-Tech Lab

LNE offers you an economical way to address your medical device packaging with convenience, through LNE/G-MED America, of a local point of contact.

Our state-of-the-art testing facilities, responsive technical teams and competitive rates give you a smart solution for:

- Analysis of container-content interaction and compatibility
- Characterization of materials: sensory analysis, permeability tests, mechanical resistance, etc.
- Simulation of transport and distribution stresses
- Analysis of packaging suitability (consumer appeal, convenience, etc.)

LNE also provides a comprehensive range of tests and technical expertise to characterize your medical devices.

Our test methods are based on the harmonized standards implemented by European Directives 93/42/EEC and 90/385/EEC.

Contact LNE/G-MED regarding certification to ISO 11607: 2006 or the above testing needs at www.LNE-America.com/testing or call (301) 495-0477.

The validation of testing methods in the validation of the packaging will justify the choice of the tests, with regards to the packaging system, determination of the acceptance criteria, the repeatability, reproducibility and sensitivity of the testing method.

The validation of all packaging-related processes must include installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) in this order.

The EN ISO 11607 also specifies traceability requirements to consistently demonstrate the maintenance of sterility of the packaging system.

Laboratory simulation testing

Medical device packages are subject to a testing program (e.g. mechanical and climate) to simulate all of the constraints of a distribution chain.

The main test programs are described in:

- The American standard ASTM D 4169,
- The technical guide of the International Safe Transit Association (ISTA; of which LNE is a member)
- The standard EN ISO 4180 (November 2010).

The choice of program depends on the particular type of package used (weight, dimensions, etc.), the mode of transport selected, the distribution chain and destination.

The following tests among others are included in these programs:

- Vibration testing for road transportation, pressure testing for air transportation.
- Evaluation of the microbial barrier properties, biocompatibility and toxicity, as well as the effects of sterilization on the chemical and physical properties of materials, and compatibility with systems forming and sealing.
 - For impervious materials, demonstration of the impermeability of the material is sufficient to demonstrate the microbial barrier properties.
 - For porous materials, there is no universal method to demonstrate the microbial barrier properties of materials. EN ISO 11607 indicates that the samples may be subjected to the action of aerosolized bacterial spores or particulates under a set of test conditions specifying the flow of air through the material, microbial resistance of the sample and the test duration.

After testing, packaging will be considered satisfactory if the product has retained its usability and if the package can still be handled by common means. Integrity testing and/or peelability will be performed to verify the integrity of the products such as the maintenance of sterility.

The documentation for this packaging process for maintaining a sterile condition until use at minimum must include performance data, specifications, test results, protocols and testing of Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ).

Examples of Sterile Medical Device Packaging Failures

Here are some examples of where medical device packaging fails to adequately maintain sterility:

- A major pharmaceutical laboratory recalled all their syringes intended for the injection of orthopedic cement. Customer complaints indicated that up to 10% of the pouches were not strong enough to maintain their integrity and the sterility of the syringes. Package redesign and validation took more than a year.
- A device with a sharp edge was able to perforate the weak sealing line under a very mild pressure.
- An IVD device shipped at low temperature with ice packs. The resulting CO₂ gas interfered with the reagents leading to erroneous tests, leading to the need for a package redesign.

Editor's Note: Get a customized proposal for testing services related to your medical devices. Go www.LNE-America.com/medical or call (301) 495-0477.