VALIDATION & VERIFICATION OF REUSABLE MEDICAL DEVICES

A

Dissertation Report

Submitted In Partial Fulfilment of The Requirement

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Master Of Technology

In Biotechnology

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To

Department Of Biotechnology

TIET, Patiala

2022

DECLARATION

I hereby declare that the work being presented in the dissertation report entitled "Validation & Verification of Reusable Medical Devices" submitted by me for the award of the degree of Masterof Technology in Department of Biotechnology, Thapar Institute of Engineering & Technology, Patiala is true and original record of my own independent and original research work carried outunder the supervision Aruna Devi P (SGTC). Further, I declare that no partof this dissertation has been submitted to any other University/Institute for theaward of any degree in India or abroad.

Date: 09-Sept-2022

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CERTIFICATE

This is to certify that the dissertation work entitled **"Validation & Verification of Reusable Medical Devices** "submitted by **Manasvi Jain (Roll No. 602004024)** in partial fulfillment for the award of degree of Master of Technology in Biotechnology from Thapar Institute of Engineering and Technology, Patiala Punjab is the record of the candidates own independent and original research work carried out under our supervision and guidance. The matter embodied in this dissertation has not been submitted in part to any other University/Institute for the award of any degree or diploma in India or Abroad.

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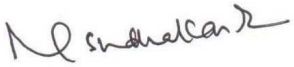

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ABBREVIATIONS

TERM	ABBREVIATIONS
SGTC	Stryker Global Technology Centre
R&D	Research and Development
T&E	Trauma and Extremities
QMS	Quality Management System
ISO	International standards organization
US	United States
EU MDR	European Union Medical Device Regulation
CER	Clinical Evaluation Report
QMS	Quality Management System
DQP	Design Quality procedure
QA	Quality Assurance
EU	European Union
MDR	Medical Device Regulations
EN standards	European National
EUDAMED	European databank on medical devices
IVDR	In Vitro Diagnostic Device Regulation
FDA	Food and Drug Administration
CE	Certification mark
CFU:	Colony-forming units.
OPA	Ortho-phthaldialdehyde
CNS	Central Nervous System
ROI	Regions of Interest
CDRH	Center for Devices and Radiological Health

TERMINOLOGY

Medical Device: It is basically a device intended to be used for medical purposes. It is used to benefit patients by helping health care providers diagnose and treat patients and helping patients overcome sickness or disease, improving their quality of life. Significant potential for hazards is inherent while using a device for medical purposes and thus they must be proved safe and effective with reasonable assurance before regulating governments allow marketing of the device in their country. A general rule, as the associated risk of the medical device increases the amount of testing required to establish safety and efficacy also increases.

Notified Body: It is an organization that has been designated by a member state to assess the conformity of certain products, before being placed on the E.U. market, with the applicable essential technical requirements. These essential requirements are to be publicized in European directives or regulations.

Design Quality procedure: This describes a design control system to ensure that safe & effective products result from new product development projects. It is designed to establish a common process for all the product development activities at Stryker Trauma & Extremities. The procedure which defines the general workflow as well as a step-by-step description of the product development process. It specifies the work steps for each development phase and assigns responsibilities.

Food and Drug Administration: The Food and Drug Administration also called as (FDA or USFDA) is a federal agency of the United States Department of Health and Human Services, one of the United States federal executive departments. It is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, medications, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices, etc.

Legacy product: Products that are already existing in the market for customers under the same brand and intended use.

Biological Indicator (BI): A test system that contains viable microorganisms which provides a defined resistance to a specified sterilization process.

Cleaning: It is the physical removal of soil and contaminants from an item to the extent necessary for further processing or for the intended use.

Design History File (DHF): It is a compilation of all records which describes the design history of a finished device.

Disinfectant: It is an agent that destroys pathogenic and other kinds of microorganisms by chemical or physical means. Generally, disinfectant destroys most recognized pathogenic microorganisms, but not necessarily all microbial forms, such as bacterial spores.

Disinfection: It is a process that destroys pathogens and other microorganisms by physical or chemical means. The lethality of the disinfection process might vary, depending on the nature of the disinfectant.

Subcategories:

a. **High Level Disinfection**: A lethal process that kills all forms of microbial life except for large numbers of bacterial spores.

b**. Intermediate Level Disinfection**: It is a lethal process utilizing an agent that kills viruses, mycobacteria, fungi, and vegetative bacteria, but no bacterial spores.

c. **Low Level Disinfection**: It is a lethal process utilizing an agent that kills vegetative forms of bacteria, some fungi, and lipid viruses.

Process Validation: It is a process of establishing objective & evidence that a process consistently produces a result or product meeting its predetermined specifications.

Reprocessing: It is process to validate medical device, which has been previously used or contaminated, fit for a subsequent single use. These processes are designed in order remove soil and contaminants by cleaning and to inactivate microorganisms by disinfection or sterilization.

Reusable Medical Device: Device that is intended for repeated use either on the same or different patients, with appropriate cleaning, sterilization, and other reprocessing between uses.

Single-use Device (SUD): It is a device that is intended for one use or on a single patient during a single procedure.

Spore: It is the dormant state of a microorganisms, typically a bacterium or fungus, that exhibits a lack of biosynthetic activity, reduced respiratory activity, and has a resistance to heat, radiation, desiccation, and various chemical agents.

Sterilant: It is an agent that destroys all the viable forms of microbial life.

Sterile: It is a State of being free from viable microorganisms.

Sterility Assurance Level (SAL): SAL is the probability of a single viable microorganism occurring on an item even after sterilization.

Sterilization: It is a validated process that is used to render product free from viable microorganisms.

Sterilization Wrap: A sterilization wrap (pack, sterilization wrapper, etc.) is a device intended that is to be used to enclose another medical device that is to be sterilized by a health care provider. It's intended to allow sterilization of the enclosed medical device and to majorly to maintain sterility of the enclosed device until used.

Bioburden: Population of viable microorganisms on or in product and/or sterile barrier system.

Lumen: Cavity or channel within a tube.

Simulated aging cleaning validation: cleaning validation that occurs after functional testing to the expected life of a device.

Field aging cleaning characterization: A data-gathering study in which the same tests performed in a cleaning validation are performed on a device that has been used in the field.

Simulated aging cleaning validation: Cleaning validation that occurs after functional testing to the expected life of a device.

1. ABSTRACT

Medical devices have played a significant role towards healthcare. From sticking plasters to X-ray scanners, dentures to hip joints and in-vitro diagnostic Devices that monitor diabetes or identify infections etc. Medical devices have always played a crucial in Diagnosing, preventing, monitoring as well as treating illness, and overcoming various kinds of disabilities.

For any Medical Device to exist in the Market, ensuring the product is verified and validated according to the Regulation and relevant standards is important. Based on the nature and class of device, the extent of verification and validation test varies. Implants are considered to be the stringent medical devices existing in the market as they have to be maintained in their aseptic condition throughout their shelf life. This includes validation of the packaging material and the implant itself.

Non-Sterile product do not pose any special storing conditions as they are not intended to be in their aseptic condition during their shelf life. There are also Reusable devices (eg. Instruments) which can be used multiple times by reprocessing them after every use. The use life of any non-Sterile product is determined based on the number of cycles and wear & tear on the product.

Reprocessing of trays involves multiple steps like cleaning & disinfection, sterilization, storage. Cleaning can be done either manual or automated which will be followed by sterilization (Steam, EO, Gamma etc.) So, to ensure that the medical devices follow all the quality parameters certain validation tests are performed on the medical devices so that they pass all the quality check according to the medical device regulations and become customer usable.

Stryker T&E validation tests are performed in India as well as outside India, so after testing everything is documented and submitted to the respective regulatory bodies of that country in order to launch the product in that country.

The role assigned during this project is to perform activities related to Sterility Assurance, in this role, I was responsible for all sterility assurance tests and their documentation. The report therefore presents formal correctness and compliance to Stryker divisional and corporate procedures and requirements, which are based on International Standards.

The role also includes the adequacy of Design Verification and Validation of the Trays. The scope of this project is limited to reprocessing of trays i.e., Reusable medical devices supplied to the customers are sterile to the user and requiring the user to reprocess (i.e., clean and disinfect or sterilize) the device after initial use prior to the subsequent use on patient.

2. INTRODUCTION

2.1 MEDICAL DEVICE

Medical devices are any instrument, apparatus, or machine that is used in the prevention, diagnosis or treatment of illness or disease, or for detecting, determining, altering, or modifying the structure or function of the body for some health purpose.

Without medical devices, common medical procedures like bandaging a sprained ankle to diagnosing HIV/AIDS, implanting a manmade prosthesis or any surgical intervention – would not be feasible. They are used in many diverse settings, for example, by laypersons at home, by paramedical staff and clinicians in remote clinics, and by health-care professionals in advanced medical facilities, for prevention and screening. Such health technologies are used to diagnose, to monitor treatments, to assist disabled people and to intervene and treat illnesses, both acute and chronic.

As per Open sources, there are an estimated 2 million different kinds of medical devices on the world market, categorized into more than 7000 generic devices groups.

2.2 MEDICAL DEVICE REGULATION

Medical Device Regulation is a set of rules and/or Directives drafted and maintained by an authority. Every country has its own country specific Regulations to monitor the safety and performance of the medical devices sold within the region.

2.3 NEED FOR MEDICAL DEVICE REGULATION

The medical devices are the most important components of patient care. They may be uncomplicated devices employed during medical examinations, such as tongue depressors and thermometers, or sophisticated life-saving implants like heart stent & valves. As per GHTF harmonized definition, the term "medical device" means any tool, apparatus, implement, machine, use, implant, *in vitro* reagent or calibrator, software intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific resolution of diagnosis, prevention, monitoring, treatment or alleviation of disease or diagnosis, monitoring, treatment, alleviation of or compensation for an injury or investigation, replacement, modification, or support of the anatomy or of a physiological process or supportive or sustaining life or control of start or disinfection of medical devices.

In many countries medical device regulations rarely existed and there were limited regulatory controls to prohibit the use of low-quality devices. By then compulsion to draft regulatory policies on medical devices started to assess their quality, safety, and efficacy. Now with different regulations of the countries or region on medical devices, there is a need to harmonize regulations in order to reduce regulatory hurdles and accelerate access to high quality, safe and efficacious medical devices.

2.4 MAJOR MEDICAL DEVICE REGULATIONS ACROSS WORLD

- United States
- European Union
- Australia
- Canada
- Japan
- Brazil
- Russia
- India

- China

2.4.1 UNITED STATES

In US, the Federal Food Drug and Cosmetic Act regulate the medical device. The marketing application must be filed with the Food and Drug Administration (FDA) and approval received before marketing the medical device in the United States. Within FDA, the Center for Devices and Radiological Health (CDRH) is primarily accountable for pre- and post-market supervision of medical devices in the United States. The United States has adopted a risk-based classification for medical devices wherein the devices are classified according to the risk associated with the use of the device. Devices are classified into a Class I-lowest risk; Class II-intermediate risk and Class III highest risk.

2.4.2 EUROPEAN UNION

European Union Medical Device Directive (EU MDD) 93/42/EEC regulates the safety and marketing of medical devices in Europe since 1990s. In 2017, European Union introduced Medical Device Regulation (EU MDR), superseding Medical Device Directive (EU MDD) which is more vigilant regulation for marketing Medical devices in EU Market. In contrast to the United States, the European Union (EU) follows a four-class scheme. Devices are classified into class I (including Is and Im), IIa, IIb, and III. Class III are ranked as the highest and higher the classification the greater the level of scrutiny. Any Medical device cannot be marketed in the European Union without adhering to the stringent regulations of the European Union; one of these regulations is the affixation of the *Conformite "Europe"enne (CE) marking.*

2.4.3 AUSTRALIA

Therapeutic Goods Administration (TGA) regulates the medical devices marketed in Australia. Before being launched in the Australian market the medical devices must be recorded in the database of the Australian Register of therapeutic Goods (ARTG). In Australia, medical devices are classified into following classes; class I, class I- supplied sterile, class I- incorporating a measuring device, class IIa, class IIb, class III and Active Implantable Medical devices (AIMD). Class I pose a minimum risk whereas class I- supplied sterile, class I- incorporating a measuring device and class IIa poses low medium risk. Class IIb represents medium high risk whereas and class III and Active Implantable Medical devices the highest risk. There is a distinct classification system for *In vitro* Diagnostic medical devices (IVDs). A manufacturer has to prove that both the device and manufacturing process used to make the device adhere to the requirement of the therapeutic good legislation under conformity assessment of the medical device. The certificate granted by the regulatory body proving that a manufacturer has been assessed and has the proper system in place to manufacture the device is known as conformity assessment evidence. A conformity assessment certificate, a Declaration of Conformity and an application to include the medical device in the ARTG are the three documents essential to register a medical device in Australia.

2.4.4 CANADA

The medical device is classified based on the Canadian Risk-Based Classification System (RBCS), under the aegis of the Therapeutic Products Division (TPD) of Health Canada. Alike European Union, Health Canada has adopted a four-tier classification system for medical devices based on their risk to the human body. Class I pose the lowest risk to the human body and Class IV poses the highest risk. Because Health Canada employs a risk-based process for the regulation of medical devices, the scrutiny increases with the risk of the device. Class I devices are reckoned to be lower risk device and post market monitoring is adjudged to be enough. Class II devices are licensed and are subject to the safety and efficacy needs of the regulations. In addition, manufacturers must acquire a valid Quality Systems certification, along with the post market controls. The higher risk devices of Class III and IV have the added obligations and must fulfill the regulatory prerequisites of a premarket safety and efficacy assessment.

2.4.5 JAPAN

In Japan, the Pharmaceuticals Medical Devices Agency (PMDA), a regulatory agency founded in 2004, analyses, assesses and suggests decisions to the Ministry of Health, Labor and Welfare (MHLW). MHLW is a powerful central ministry amalgamating political authorization and accountability for the whole medical device regulatory scheme, in addition to the national health protection system, public health, medical facilities and labor and welfare matters.16 In 2005 a new law was introduced which was harmonized with international stipulations. The law is known as the New Pharmaceutical Affairs Law (PAL). The main difference with international stipulations is that Japan has additional needs for buildings and manufacturing spaces. A manufacturer must work as per the Market Authorization Holder (MAH) process. In this process the manufacturer is only accountable for production and the MAH is accountable for the launch of the product to the market.

In Japan, medical devices are classified into General Medical devices (Class I), Controlled Medical Devices (Class II) and Specially Controlled Medical Devices (Class III and IV). A manufacturer must also get a device notification, device certificate or device approval based on the class of device. Medical devices in class I need a device notification, medical devices in class II need a device certificate and medical devices class III and IV need a device approval. Clinical trials are not required for class I, in principle not necessary for class II, sometimes necessary for class III and in principle compulsory for class IV. In Japan it is compulsory to follow Good Vigilance Practice (GVP).

2.4.6 BRAZIL

The new regulation on GMP – Good Manufacturing Practices inspections for medical devices was announced as per Resolution RDC 16, of March 2013. This regulation integrated the regulations for both medical devices and IVD device. In August 2013, the National Health Surveillance Agency (ANVISA) announced RDC 39/2013. This resolution encompasses administrative procedures for Brazilian Good Manufacturing Practice (BGMP) permission, including those needing BGMP compliance for each product line. A different presidential order (Decree No. 8077/2013) advocates that in the future, ANVISA may adopt a more selective approach in deciding which medical devices need BGMP certification and which do not require such certification. Such a move could expedite the regulatory pathway for lower-risk devices.

2.4.7 RUSSIA

The Russian regulation of medical devices is intricate and includes several different regulatory authorities. Roszdravnadzor (Federal Service on Surveillance in Healthcare and Social Development) is the expert authority accountable for registration and assessing clinical safety and efficacy of all medical devices. GOST Standard (Federal Agency for Technical Regulation and Metrology) ensures that all medical devices fulfill well-established Russian benchmarks. A GOST-R quality certificate is needed for importing any medical device into Russia. A Sanitary- Epidemiology Conclusion (Hygiene Certificate) is also needed before any medical device can be imported into Russia. Rospotrebnadoz (Federal Service for Supervision in the Area of Consumer Rights and Welfare Protection) is make sure that all medical devices related with the human body, or which in other ways may adversely affect patients or doctors, fulfill sanitary and epidemiological standards. Russia applies a risk-based system for classifying medical devices into four classes (Class 1, 2a, 2b, and 3). The class 1 is the lowest risk device and class 3 the highest risk device

2.4.8 INDIA

The Central Drug Standards Control Organization which is a part of the Ministry of Health and Family Welfare currently regulates medical devices in India. Medical Devices Regulation Bill (MDRB) was introduced in 2006 with the aim to strengthen laws inline to medical devices and Medical Device Regulatory Authority of India. The intention of the bill was to create and sustain a national system of controls for the quality, safety and accessibility of medical devices in India. For import of medical devices in India, the procedure for registration and import license as prescribed under the Drugs and Cosmetics Rules shall be followed. Imported medical devices on the notified list that have already obtained approval from other countries (e.g. US, EU) are allowed on the Indian market without undergoing separate conformity assessment.

2.4.9 CHINA

The Chinese medical device regulatory pathway is very complicated. Albeit in 2013, China Food and Drug Administration (CFDA) took some major steps such as electronic validation, new approval regulations for innovative devices, and exclusions from China Compulsory Certification (CCC) Mark is required. Through new online system medical device registrants can solicit regulatory validation of their device classifications. Under new approval regulations for innovative devices, qualifying medical device products would be given preference review by the CFDA. But qualifying medical devices must be produced in China and must be the unique device to be registered in China.

Table 1 Compares salient features of medical device regulations of US and EU

	United States	European Union
Regulation of medical device	The Federal Food Drug and Cosmetic Act	Medical Device Regulation (MDR)
Pre- and post-market supervision of medical devices	Within FDA, CDRH is primarily accountable	The NBs are autonomous private enterprise to enact regulatory control over medical devices. NBs have the authority to grant the CE mark.
Approval system	Class I device: general controls Class II devices: premarket notification 510(k) process Class III devices need premarket approval (PMA)	Medical device manufacturers need to exhibit CE marking on their products to ensure that devices are safe and fit for their intended use

Table 2 Compares salient features of medical device regulations of Japan, Australia and Canada

	Japan	Australia	Canada
Pre- and post-market supervision of medical devices	Pharmaceuticals Medical Devices Agency (PMDA	The Therapeutic Goods Administration (TGA).	Therapeutic Products Division (TPD) of Health Canada
Approval system	• Class I need a device notification • Class II need a device certificate • Class III and IV need a device approval.	A manufacturer has to prove that both the device and manufacturing process used to make the device stick to the requirement of the therapeutic good legislation	Class I devices: only post market monitoring. Class II devices: safety, efficacy, quality and the post market control; Class III and IV: premarket safety and efficacy assessment

2.5 CLASSIFICATION OF MEDICAL DEVICE

2.3.1 BASED ON RISK

Table 3 Classification of Device based on Risk

	Low Risk	Medium Risk	Medium to High Risk	High Risk
USA	Class I	Class II		Class III
EU	Class I Class Ir Class Im Class Is	Class IIa	Class IIb	Class III
Australia	Class I	Class IIa	Class IIb	Class III

	Low Risk	Medium Risk	Medium to High Risk	High Risk
	Class I- supplied sterile, Class I- incorporating a measuring device			
Canada	Class I	Class II	Class III	Class IV
Japan	General Medical devices (Class I)	Controlled Medical Devices (Class II)	Specially Controlled Medical Devices IV).	Specially Controlled Medical Devices (Class IV).
India	Class A	Class B	Class C	Class D
China	Class I	Class II		Class III
Russia	Class 1	Class 2a	Class 2b	Class 3

2.3.2 BASED ON USAGE

REUSABLE MEDICAL DEVICE

Reusable medical devices are devices which health care providers can reprocess and use on multiple patients. Examples of reusable medical devices include endoscopes, surgical forceps, stethoscopes etc.

All reusable medical devices can be grouped into one of three types according to the degree of risk of infection related with the use of the device:

- Critical devices, such as surgical forceps, when comes in contact with the blood.
- Semi-critical devices, such as endoscopes, when come in contact with the mucus membranes.
- Non-critical devices, such as stethoscopes, when come in contact with the unbroken skin.

Some examples of reusable medical devices are:

- Surgical instruments, such as forceps and clamps
- Endoscopes, such as duodenoscopes, and colonoscopes, used to visualize areas inside the body
- Accessories to endoscopes, such as scissors etc.
- Laparoscopic surgery accessories, such as arthroscopic shavers etc.
- Trays

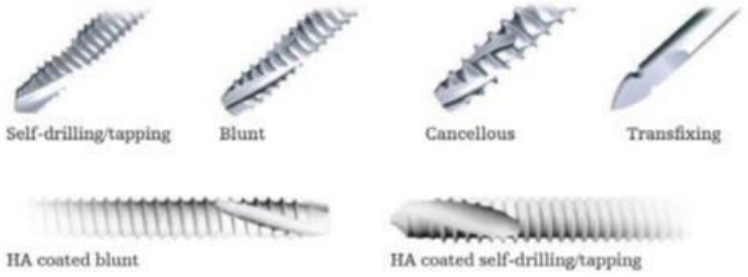


Figure 1 Examples of Reusable Medical Device

Trays can be categorized into different types:

Drawer Tray **Half Size Tray** **Full Size Tray (1/1 size)** **Insert Layer**

Figure 2 Different Types of Trays

SINGLE USE MEDICAL DEVICE

Single-use devices are the devices that are applied on one patient during only one process and then disposed of. Reusable medical devices are the devices that require reprocessing after a process, steps such as cleaning, disinfecting, and sterilization are performed. When selecting a single-use device (Implant) or disposable item over a reusable medical device, and vice-versa, the factors that need to be considered should be guided by any risk to patient wellbeing. In addition to such risks as contamination and infection, environmental impact, cost-efficiency, time-savings are other factors to consider.

Figure 3 Examples of Single Use Medical Devices

3. INTENDED PRODUCT

Gamma4 tray is a Hip Fracture Nailing System which is a two layered tray comprise of Base, Insert and Lid it is a metal container which is used to hold and protect surgical devices during the sterilization process. It consists of an interlocking tray and lid; both are perforated that allow the passage of sterilizing agent from outside the tray to the devices placed inside. The system is indicated for the treatment of stable and unstable fractures as well as for stabilization of bones and correction of bone deformities in the intracapsular, trochanteric, subtrochanteric and shaft regions of the femur (including osteoporotic and osteopenic bone).

Figure 4 Gamma 4 Implant

It consists of implants (Trochanteric/Intermediate/Long Nails including set screws, End Caps, Lag Screws), target devices, indication specific instrumentation and **Trays.**

Trays are metal containers used to hold and protect surgical devices during the sterilization process. They consist of an interlocking lid and tray, which are both perforated in order to allow the passage of sterilizing agent from outside of the tray to the devices placed inside. These are categorized under the category of Reusables i.e, the product can be used multiple times as it is not an Implant single use device.

Trays are used for the storage of Instruments that can be reused after following certain guidelines which medical device companies attaches with their products. These guidelines include proper process for cleaning, sterilization, storage etc at temperature, which reagent and many more things all these things are documented in a document called as IFU (Information for Use) which is provided with the product.

Gamma4 Tray consists of various Instruments like Plus Targeting Arm, Lag Screw Reamer, Lag Screwdriver, Anti-Rotation Clip, and many other that are kept inside this tray.

Plus Targeting Arm

Lag Screw Reamer

Lag Screwdriver

Anti-Rotation Clip

Figure 5 Examples of Instruments from Gamma4 Trays

Figure 6 shows fully equipped tray of Gamma4 where the Instruments can be reused by the customers (HCP, Clinicians etc.).

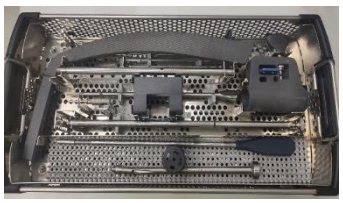


Figure 6 Gamma4 Fully Equipped Tray Base, Insert & Lid

4. PROJECT OVERVIEW

To manufacture a medical device and make it customer usable Quality Check plays a major role for medical device company. So, to check the quality and to manufacture the product different verification & validation tests are performed over these Trays, Instruments & Implants.

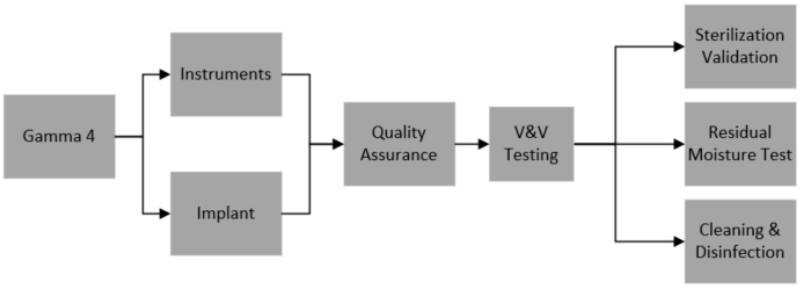


Figure 7 Process flow for Gamma 4 Implant/Instrument

The Project explains about the various tests performed for ensuring the verification and validation of Gamma4 Tray. The Verification and validation of Trays include Sterilization validation, Cleaning & disinfection Validation, Residual Moisture Test.

For reusable products like Trays that can be used multiple times by the hospitals follows reprocessing method given by the company & can be seen in flow chart below-

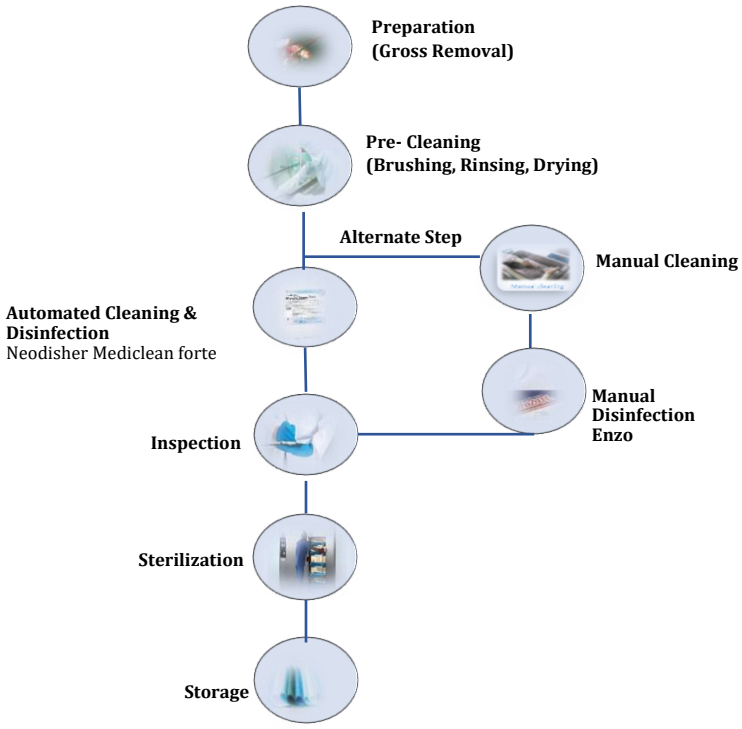


Figure 8 Reprocessing Cycle for Reusable Instruments

So, reprocessing cycle has been performed on Gamma4 trays which included cleaning, sterilization, and residual moisture test which is focused on the later stages.

The Project focuses on V&V of the trays and its Instruments and how it can be achieved. The results confirm that Gamma4 tray and its instruments have been verified and validated for multiple uses and is customer usable while also meeting all the regulatory requirements as criteria.

5. LITERATURE REVIEW

Costa, Dayane de Melo, et al. "Providing Sterile Orthopedic Implants: Challenges Associated with Multiple Reprocessing of Orthopedic Surgical Trays." *Hygiene* 2.1 (2022): 63-71. Costa, D. D. M., Vickery, K., Tipple, A. F. V., & Hu, H. (2022). Providing Sterile Orthopedic Implants: Challenges Associated with Multiple Reprocessing of Orthopedic Surgical Trays. *Hygiene*, *2*(1), 63-71.

Orthopedic implants, such as screws sometimes are provided in a non-sterile state that must be reprocessed before each use, therefore they may be exposed to multiple reprocessing cycles until they are used for the patient. The effect of these various reprocessing cycles on the quality and safety of these implants has been a subject of concern and discussion around the world. There are four main challenges associated with these non-sterile implants to the same standard, with respect to their quality and safety, as implants that are provided sterile: microbiological contamination, non-microbiological contamination, surface damage, and their acquisition in surgical trays from lender companies.

Seavey, Rose. "High-level disinfection, sterilization, and antisepsis: current issues in reprocessing medical and surgical instruments." *American journal of infection control* 41.5 (2013): S111-S117.

The complicated design of instruments, the design of instrument trays, and evidence-based practice says that there is a need for complicated and specific reprocessing references from instrument manufacturers. Patient safety depends on instruments whether they are appropriately cared for and effectively reprocessed. This article is concerned with the sterile reprocessing and operating of medical and surgical instruments.

Reprocessing plays a critical role in helping to prevent infections. Patient safety depends on instruments that are appropriately cared for and effectively reprocessed. Some of the most current issues that are related to reprocessing surgical and medical devices is following the manufacturer's written IFUs, including cycle parameters; the reason(s) for wet packs; being aware of latest updates in packaging.

Prince, Daniel, et al. "Challenges to Validation Of a Complex Nonsterile Medical Device Tray." Biomedical Instrumentation & Technology 48.4 (2014): 306-311.

Validation by steam sterilization of any reusable medical devices requires cautious attention to many factors that directly influence whether complete sterilization will occur or not. Complex implant/instrument tray systems have a range of configurations and components. Geobacillus stearothermophilus biological indicators is used in overkill cycles to simulate worst case conditions and are meant to provide substantial sterilization assurance level (SAL). Survival of G. stearothermophilus spores depends on access to steam and size of load in the chamber. By a small and reproducible margin, it was established that placement of the trays in a rigid container into minimally loaded chambers were more complicated to completely sterilize than maximally loaded chambers.

Schlautmann, Hannelore. "Reprocessing of Surgical Instruments." 101 of Surgical Instruments. Springer, Berlin, Heidelberg, 2022. 205-221.

The surgical instruments in all surgical departments have an immense financial value within the assets of a clinic, the purpose and value of the reusable medical devices must be maintained for many years. There are several guidelines and legal regulations that regulate the reprocessing by defined norms and to make it transparent and to document the reprocessing methods. The aim in reprocessing must be the maintenance of value, efficiency and to maintain hygiene.

Sheffield, George. "Responsibilities for effective medical device reprocessing procedures and instructions." Biomedical Instrumentation & Technology 46 (2012): 76.

In hospitals, the reprocessing of reusable medical devices and instruments is one of the daily requirements. Medical devices intended for reprocessing are made of materials that can withstand the multiple reprocessing steps that involve cleaning, disinfection, and sterilization. The cutting-edge technologies are a benefit to patients, but can also have a risk, as some of these devices are difficult to reprocess.

The responsibility for confirming correct reprocessing procedures and systematic instructions is shared by the FDA, the medical device industry, and healthcare facilities. This article provides as an introduction for healthcare professionals on responsibilities for optimizing the effectiveness of all reprocessing procedures and instructions in their facilities, , and to ensure patient wellbeing.

Manufacturer Requirements

As the increasing complexity of device designs and components, the FDA requires a cleaning validation studies for each device, from the device's manufacturer, to make sure adequate reprocessing of complex device designs and components. Manufacturers are also required to provide clear-cut processing guidelines for the user. Such procedures and instructions for use (IFU) are usually dispatched with each medical device. Manufacturer requirements include:

- Detailed cleaning instructions, including disassembly.
- Detailed disinfection and sterilization instructions, with specific sterilization parameters
- Expected end of life, and how this can be determined by the user
- Roles and responsibilities
- 21CFR 820.30—design controls
- 21CFR 820.70—production and process controls
- 21 CFR 820.75—process validation

6. DEVELOPMENT OF MEDICAL DEVICE

Medical Device Design & Development it is a multi-step process which involves various resources and massive investments and long timelines. This process has following stages of ideation, designing, development, packaging, labeling, and delivery.

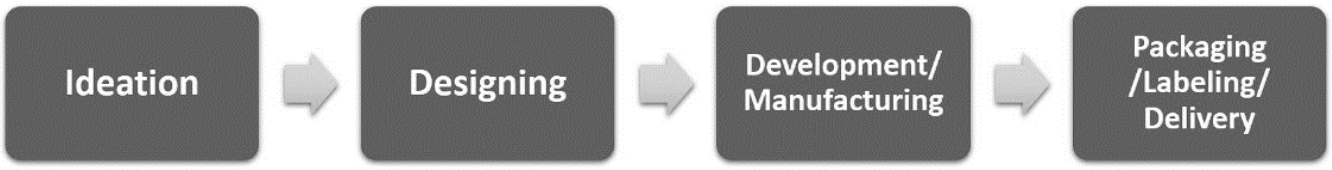


Figure 9 Sequence for Development of a Medical Device

Medical device design is the first step towards creating a medical device for the specific intended use (in compliance with regulatory requirement of the country). The product design should have a unique purpose, to deliver something more than already existing versions in the market.

The process of Medical Device Designing involves brainstorming and deep analysis to find out similar products exists in the market.

Every stage of the design process is done maintaining three things in mind:

- Market need
- Intended impact
- Safety & comfort of the end-user

6.1 MEDICAL DEVICE DESIGN CONTROL REGULATIONS

The most common method used for product development like Medical Devices has been the Waterfall Development Process, which takes a basic approach. In this approach, each phase must be completed before the next phase can begin. There should not be any overlap in the phases. The important aspect of this whole process requires linear and logical separation of phases.

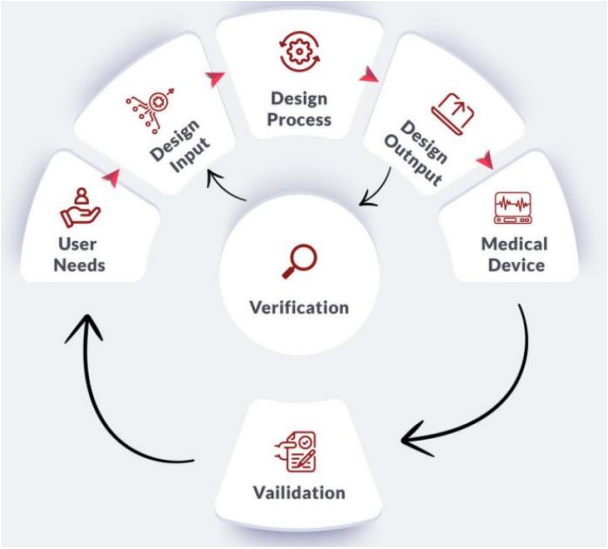


Figure 10 Waterfall model for Development of a Medical Device

6.1.1 USER NEEDS

This section describes the intended use and indications for the intended device. It must describe needs in enough detail to ensure the device can be defined operationally in the design input requirements.

This describe the product from the perspective of the user, whether it be a patient or doctor, and the product's intended use.

A user needs document must describe:

- Intended use of the product.
- Indications for use.
- How the product will be fitting with the environment in which it will be used.
- High-level performance.
- Details of functionality.
- Information about human factors and
- The target markets around the world (which will provide the basis for labeling, localization, and regulatory etc.).

This document provides the basis for performing a Hazard Analysis (HA) to identify potential hazards that may result during the intended usage of the product. Results from this analysis are taken into consideration in generating the design input requirements document.

6.1.2 DESIGN INPUT

Design input requirements are developed from the user needs and hazard analysis, as well as applicable input from Post market surveillance activity such as CAPAs, complaints, and other data. Design input requirements shall contain enough detail from an engineering standpoint so the product can be designed. Each requirement should be substantiated from a specific user need.

Requirements are usually detailed either in a single document, or multiple documents (e.g., system requirements and software requirements), and are refined and updated as needed during the project.

Design input requirements shall include whichever of the following requirements are applicable:

- Physical and Functional requirements.
- Product dependability requirements.
- Safety needs.
- Risk management needs.
- Regulatory and statutory requirements, including domestic and international requirements for the product
- Performance requirements.
- Voluntary and harmonized standard needs.
- Manufacturing needs.
- Labeling and packaging needs.
- Biocompatibility and Toxicity needs.
- Installation and servicing needs; and
- Sterility needs

6.1.3 DESIGN PROCESS

If the process is known, the design input is converted into high-level specifications and then incorporated as features in Medical Devices.

6.1.4 DESIGN OUTPUT

The manufacturer will establish and maintain procedures for defining and documenting the design output in terms that allow an adequate evaluation and giving conformance to design input needs. Design output procedures will contain, and they refer to the acceptance criteria and shall ensure that the design outputs that are necessary for the proper functioning of the device are identified. Design output will be documented, reviewed, and will be approved before its release. The approval includes the date and the signature of the individual approving the output which will be documented.

6.1.5 DESIGN VERIFICATION

Design verification stage shall:

- Provide appropriate information for purchasing, production, and for service provision
- Contain or reference product acceptance criteria, and
- Meet the input requirements for design and development,
- Specify the characteristics of the product that are essential for its safe and proper work.
- Records of the design and development outputs should be maintained.

Before implementing the user needs into actionable design inputs, all product stakeholders must sign off on the design inputs, including:

- Company management
- Product marketing
- Production
- Sales
- On-staff practitioners
- End-user representatives
- Shipping
- Regulatory
- Labeling
- Manufacturing

After confirmation from applicable parties with design inputs, the actual designing of the output begins.

Design outputs are the manifestation of specified design inputs in the medical device design. Verification ensures that medical device satisfies the required design inputs, involving the documentation of each of the design outputs as a evidence that the specified design inputs are accomplished.

Verification test during Product Development

There are several tests that can be conducted during the verification process to confirm the finished product meets its intended use in its intended environment, including:

- Thermal analysis of an assembly
- Fault tree analysis
- Failure modes and effects analysis,

- Packaging tests
- Biocompatibility testing
- Bioburden testing

This process involves the transferring to production facility for mass production. Design control regulation mandates the process of maintaining DHF (Design History File). The design history file should be traceable and available to all team members.

Design History File (DHF)?

It is a file which is a formal document with all the minor and major change details. This document contains the procedures followed and elements used in the device. The concerned accountable person details are also enclosed in the document. The file has two core purposes to serve:

- To enable traceability in case of any error.
- To trace the modifications done in the past and upgrade accordingly. DHR can have many other roles along with the purposes mentioned above.

6.1.6 DESIGN VALIDATION

According to Max Sherman, the editor of RAPS' recently published second edition of *The Medical Device Validation Handbook*, Validation is associated with the concept of verification.

The validation process starts when the parts are available, or first-off tooling parts. For instance, if the product is meant to be used in extremely cold environments, a test would be conducted by a user to manipulate and use the product in the frigid environment and details like whether the user can hold the device in his hand with his mittens on, or if hinges stick in the frigid environment would be validated.

Design Validation should be performed on any new processes that are being implemented, present processes that need to be fit on a regular basis and current processes that have been modified, experienced a downward trend in implementation or an increase in customer complaints.). Common examples of processes that must be proven are.

- Sterilization, packaging & sealing.
- Aseptic filling.
- Heat treating, plating, welding, painting etc.
- Lyophilization.

There are some processes where product verification is sufficient such as manual cutting processes, visual inspection of printed circuit boards and testing of wiring harnesses. In such cases output of the process can be verified with high reliability and precision.

To assure that a manufacturing process will consistently meet certain parameters, manufacturer must follow a systematic series of steps, such as shown below:

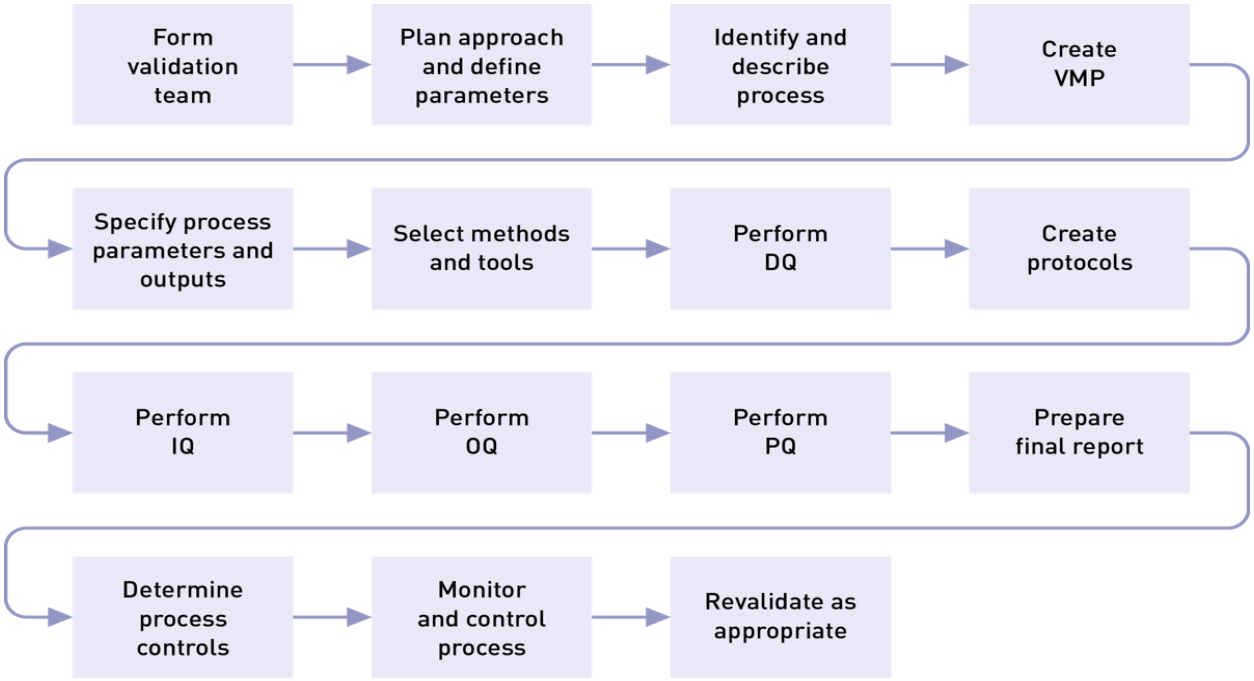


Figure 11 Design Validation process during development of medical Device

7. MATERIALS

7.1 INSTRUMENTS

7.1.1 AUTOCLAVE

Autoclave, also known as Steam sterilization, is the process of exposing the medical devices that are to be sterilized with saturated steam under pressure. Autoclaves also known as steam sterilizers and are typically used for healthcare or industrial applications. It is a machine that uses steam under pressure to kill harmful bacteria, viruses, fungi, and spores on items that are placed inside a pressure vessel. The moist heat facilitates the killing of all microorganisms, that includes heat-resistant endospores by heating the materials inside the autoclave at temperatures above the boiling point of water. According to the principle of gas laws, it can be achieved by raising the pressure inside the device.

Principle of an autoclave is moist heat sterilization. The high pressure inside the chamber which increases the boiling point of water for the sterilization of equipment. The higher pressure ensures the rapid penetration of heat into the deeper parts of equipment.

Figure 12 Types of Autoclaves

Components of Autoclave

- Pressure chamber
- Vessel
- Control System
- Safety Valve
- Thermostatic Trap
- Waste-Water Cooling Mechanism
- Vacuum System
- Steam Generator

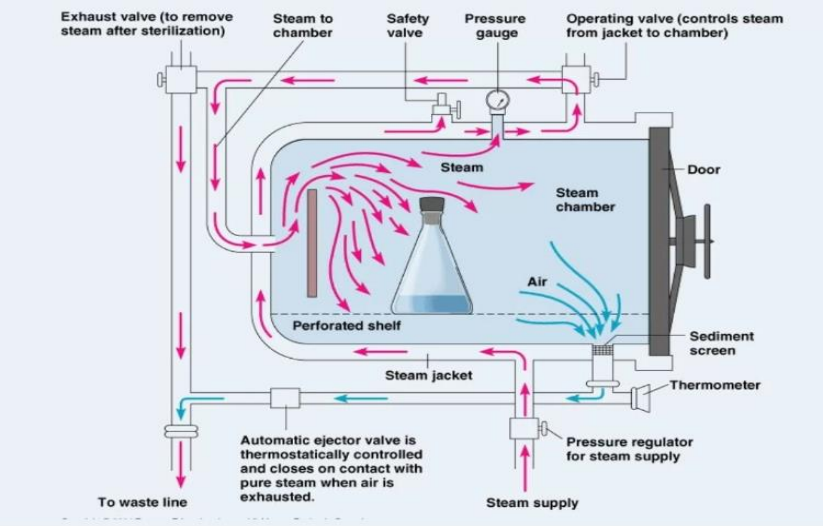


Figure 13 Working Principal of Autoclave

Uses of Autoclave:

Autoclaves rapidly eliminate a wide range of pathogens, even long-lived and resistant spores.

7.1.2 Washer Disinfector

A washer disinfector is used for the automated cleaning and disinfection of medical instruments in medical centers and hospitals. The automatic process of the liquid agents consisting of cleaning agent, neutralizer and rinse aid optimizes the cleaning and drying outcome. The instrument disinfection is accomplished by hot water over a prescribed period.

Figure 14 Washer Disinfector

Using a HEPA filter, the washer disinfector will ensure that no additional bacteria or microorganisms gets transmitted onto the equipment during the drying process.

Advantages of a washer disinfector:

- Ensure high levels of working efficiency in instrument reprocessing.
- The risk of sharps injuries incidents caused by manual cleaning and disinfection is reduced by the automated reprocessing with a washer disinfector.

- Higher degree of efficiency and effectiveness compared to the manual decontamination of instruments.
- Reduces the workload for the practice team because the cleaning, disinfection and drying is fully automated, the need for manual intervention is eliminated.

7.1.3 Laminar Air flow

A Laminar air flow cabinet is one of the enclosed workstations that is used to provide a contamination-free work environment by filters capturing all the particles entering the cabinet. These cabinets are designed to protect work from the environment and are most useful for the aseptic distribution of specific media and plate pouring. The principle of laminar flow cabinet is based on the laminar flow of air through the cabinet and the device works using inwards flow of air through one or more HEPA filters to create a particulate-free environment.

Figure 15 Laminar Air Flow

Components of Laminar Air Flow:

- Cabinet
- Working station,
- Filter pad/ Pre-filter
- Fan/ Blower
- UV lamp
- Fluorescent lamp
- HEPA filter

Uses of a laminar flow cabinet in the laboratory.

- Laminar flow cabinets are used in laboratories for contamination sensitive processes like Inoculation.
- Media plate preparation is done inside the chamber.
- Culture of organisms is performed inside the cabinet.
- Drug preparation techniques can be performed inside the cabinet.

7.1.4 Incubator

An incubator is an insulated and enclosed device that provides an optimal condition of humidity, temperature and other environmental conditions that are required for the growth of organisms. It is a piece of vital laboratory equipment necessary for cultivating microorganisms under artificial conditions. It can be used to cultivate both unicellular and multicellular organisms.

It is based on the principle that microorganisms require a particular set of parameters for their growth and development. All the incubators are based on the theory that when organisms are provided with the optimal condition of humidity, temperature, oxygen, and carbon dioxide levels, they grow and divide.

Figure 16 Incubator

Uses of an Incubator

- They are used to grow microbial culture or cell cultures.
- They can also be used to maintain the culture of organisms to be used later.
- Some of the incubators are used to increase the growth rate of organisms, having a prolonged growth rate in the natural environment.
- There are specific incubators that are used for the reproduction of microbial colonies and subsequent determination of biochemical oxygen demand.
- They also provide a controlled condition for sample storage before they can be processed in the laboratories.

7.2 TEST ACCESSORY / CONSUMABLES

7.2.1 STERISHEET

These are the sterilization wraps fit for use with all standard types of sterilization method and can be used in packaging also. There are different methods to wrap trays with sterisheets, T&E Stryker generally follows double wrap envelope method.

Figure 17 Sterisheet

Uses of Sterisheet;

- It allows safe and efficient for all standard sterilization cycles and protocols.
- It maintains sterility of the wrapped medical device.
- Limits the risk of contamination in hospital environment and ensures consistency of delivered material.

7.2.2 STERILE BAGS

Sterile, single service bags are made of heavy transparent polyethylene. Leak-proof and airtight. Puncture-proof tabs.

Figure 18 Steriking Pouches (Wipak)

Figure 19 Sterile Bag

7.2.3 BIOLOGICAL INDICATOR

Biological indicators are the test systems that contain viable microorganisms with a definite resistance to a specific sterilization process. They help in monitoring whether the necessary conditions were met to kill a specified number of microorganisms for the given sterilization process. Geobacillus stearothermophilus spores test steam and other unsaturated chemical vapor sterilizers. Geobacillus stearothermophilus produces Endospores, which possess high resistance towards steam sterilization process. Hence, this organism is commercially manufactured with a defined resistance and used in the steam sterilization process to check the efficiency of sterilization.

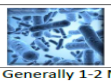
Characteristics	Thermophilic Organism/High Resistance to heat. Contain Endospores. (Hard to kill).
Temperature required for growth?	Optimum is 55-65 °C
Temperature/Exposure time required to kill/F Value	Varies depending upon the manufacturing process. Generally 121°C & ≥ 1.5 minutes.
Whether it can be used to verify other sterilization Process? (Example Dry Heat, EO)	No.
Microscopic view	
Size, Morphology	Generally 1-2 Micron, Gram Postitive rod.
Commercially available forms for lab usage	Strips, Vial suspension, Paper discs, SS Coupon, ProLine,SS Disc etc. (Some of them are shown in pictures)
Incubation	48 hours
ATCC Number	ATCC 7953 is generally used in industrial applications.
Population loaded	Generally 1.0 x 106

Figure 20 Details of Geobacillus stearothermophilus

Figure 21 Geobacillus Stearothermophilus

Figure 22 Bio Ball

Figure 23 Spore Strips

Figure 24 PRO Line

7.3 TOOLS

7.3.1 SLMS

Stryker learning and management system is a platform that enables to undergo training on all the required procedures and be therefore responsible for all the document handling before signing off any document. Compliance Wire is an integrated, cloud-based Learning Management System (LMS) that currentlyserves over 400 companies worldwide. The software was designed as a workforce training solution that meets both the compliance and performance needs of a global workforce in regulated manufacturing environments. So before working on or signing off any document you are actually trained on it with all the required procedures.

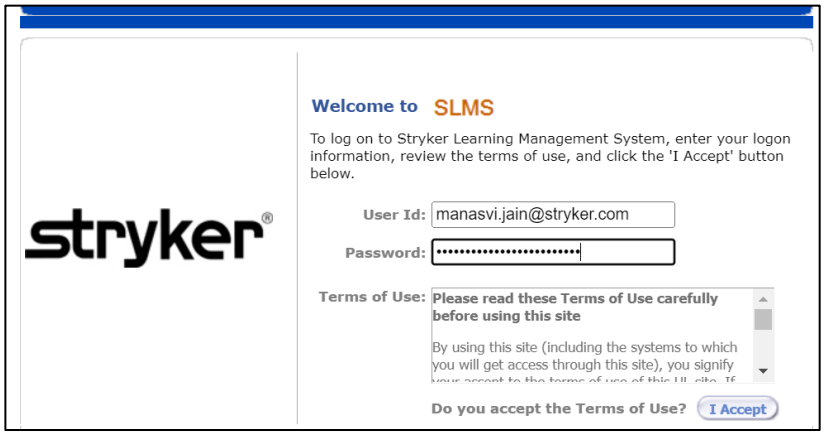


Figure 25 SLMS Portal

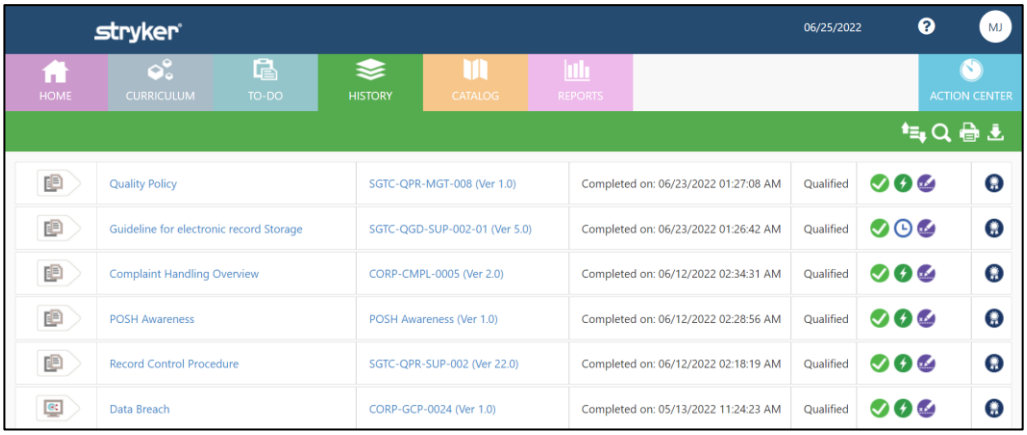


Figure 26 List of Trainings underwent in SLMS

7.3.2 onePLM

It is a repository for all the technical documents. It is a software and web based system thatcontains all the necessary information and technical documents needed in a new product developmentprocess. The system helps to get complete information of a project and its associated contents.

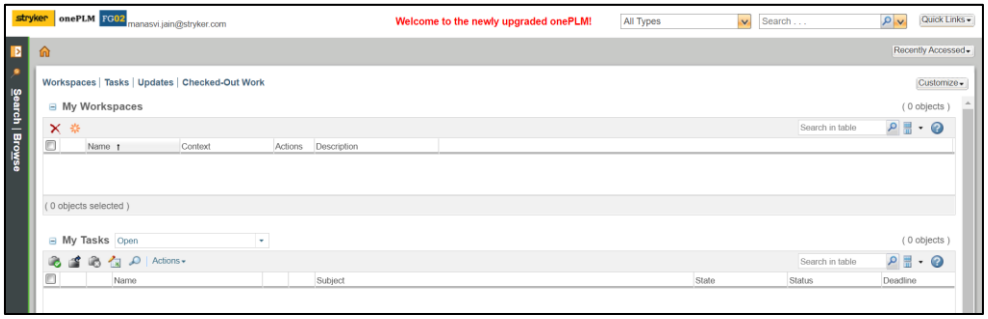
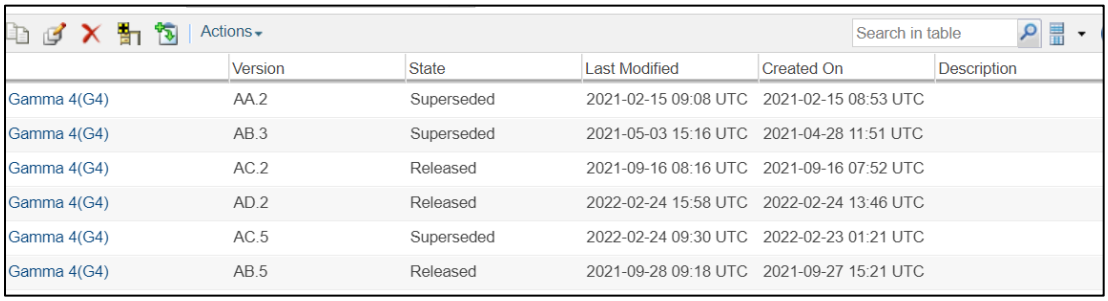


Figure 27 Snapshot of OnePLM portal



	Version	State	Last Modified	Created On	Description
Gamma 4(G4)	AA.2	Superseded	2021-02-15 09:08 UTC	2021-02-15 08:53 UTC	
Gamma 4(G4)	AB.3	Superseded	2021-05-03 15:16 UTC	2021-04-28 11:51 UTC	
Gamma 4(G4)	AC.2	Released	2021-09-16 08:16 UTC	2021-09-16 07:52 UTC	
Gamma 4(G4)	AD.2	Released	2022-02-24 15:58 UTC	2022-02-24 13:46 UTC	
Gamma 4(G4)	AC.5	Superseded	2022-02-24 09:30 UTC	2022-02-23 01:21 UTC	
Gamma 4(G4)	AB.5	Released	2021-09-28 09:18 UTC	2021-09-27 15:21 UTC	

Figure 28 onePLM document status

7.3.3 Quality Management System

Stryker Quality management system contains all the quality related documentsand procedures that are to be followed and complied to for carrying out any project. It gives an update regarding old and new revised procedures that are to be followed.

Figure 29 Snapshot of SharePoint Page

7.3.4 Techstreet

Techstreet helps you stay connected to essential industry codes and standards from around theworld. This streamlines your quality and compliance processes through the commercialization phase of theintellectual property (IP) lifecycle.

Figure 30 Snapshot of Techstreet front page

8. METHODS

8.1 CLEANING AND DISINFECTION

Cleaning is the process of removal of the foreign material (e.g., blood, bone, proteinaceous material, soil etc.) from medical devices and is normally done by using water with detergents or enzymatic products. Proper cleaning is required before high-level disinfection and sterilization because there might be inorganic and organic materials that may remain on the surfaces of instruments so that it does not interfere with the effectiveness of these processes. If soiled materials dry or bake onto the instruments, the removal process becomes difficult and the disinfection or sterilization process less effective or ineffective.

Two methods of cleaning that are followed by Stryker T&E's medical devices are as follows:

- An automated method using a washer disinfector and a manual method. Generally, automated method is preferred as it is more reliable, and staff is less exposed to the contaminated devices and the cleaning detergents used.
- Improper cleaning can cause surgical site infection, tissue damage, and other problems that impact patient safety on one hand and sometimes leads to corrosion of instruments also.

Cleaning encompasses the removal of both soil (patient secretions) and microorganisms (from the patient or from handling or water exposure during reprocessing). On completion of the cleaning process, it should be visually inspected for each item and carefully to detect any visible soil. Inspection using magnification can identify residues more readily than the unaided eye. The FDA houses the primary responsibility for developing and validating approaches for effective reprocessing of a reusable medical device. Two principles are involved in the verification of the cleaning process. The first consists of establishing, clarifying, and documenting a standard cleaning process based on published and validated recommended practices or guidelines. The second concerns measuring and evaluating the performance of the cleaning equipment used and/or the residual contaminants on medical devices after applying the established cleaning method.

Cleaning agents are used for the cleaning, these are those materials that are used to remove soil (organic, inorganic, and biological matter) from medical devices so that they can be processed for their final intended purpose. These materials include items used for the physicochemical removal of soils by wiping, brushing, or flushing with fluids that facilitates the cleaning process. Cleaning agents can be categorized as either enzyme-based or non-enzyme-based.

An ideal cleaning agent should be

- Non-abrasive,
- Low foaming,
- Free rinsing,
- Biodegradable and environmentally friendly,
- Provides for rapid soil dispersion or suspension,
- Non-toxic in the specified use dilution,
- Effective on clinically relevant soils under specified use conditions,
- Having a long shelf life,
- Cost-effective,
- Tested for effective concentration.

The sequence of steps required to prepare medical devices for re-use or to prepare new devices for initial use are summarized in the in the flowchart below-

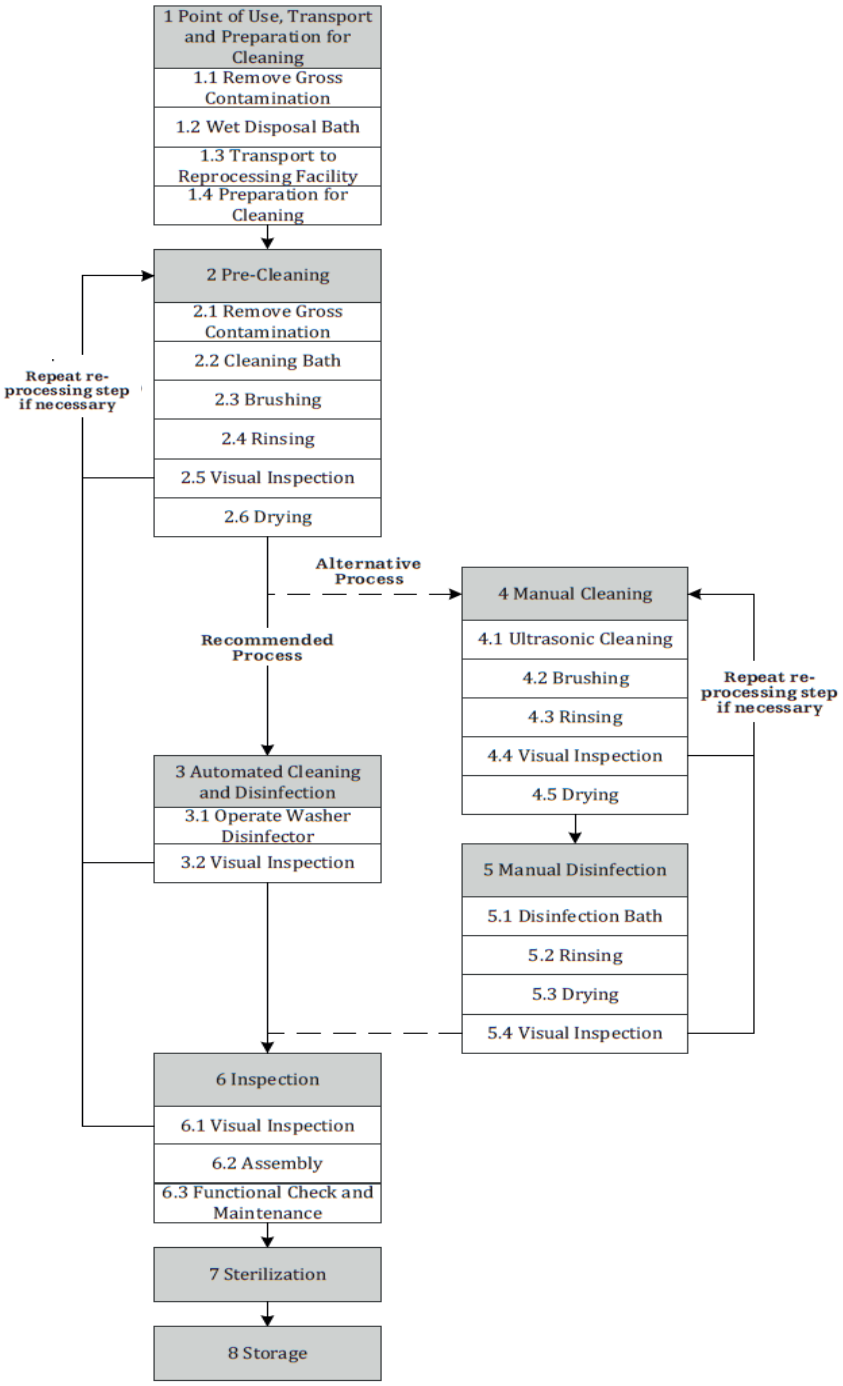


Figure 31 Flow chart of Reprocessing of Medical Devices

8.1.1 POINT OF USE, TRANSPORT, AND PREPARATION FOR CLEANING

Table 4 Description of Sub-Step

Sub-step	Description / Equipment / Parameters	Additional Information
Remove gross contamination	Absorbent lint-free single-use paper wipes, Running water: Sterile or germ-free purified water or highly purified water, Syringes,	The cleaning process shall be initiated directly after application to avoid drying of the contamination.

Sub-step	Description / Equipment / Parameters	Additional Information
	Remove gross contamination using absorbent lint-free single-use paper wipes and then rinse the device under running water for at least 1 minute. Rinse cannulations, blind holes, and similar features at least three times using a syringe.	
Wet disposal bath	Disinfectant, Demineralized water, Break-proof, disinfectable. Carefully put the device into the container to prevent organics from drying and then Open devices with joints and moving parts and fully immerse the device in the disinfectant solution.	The temperature of the solution shall be less than 40 °C to avoid protein fixation and Do not mix heavy devices with fragile ones in the container to avoid mechanical damage. Ensure that all the surfaces are wetted with disinfection solution:
Transport	Carefully transport all the devices in the container to the point where cleaning is to be performed.	
Preparation for cleaning	Disassemble the device.	Instructions are provided in the operative technique or separate information available from Stryker representative.

8.1.2 PRE-CLEANING

Table 5 Precleaning - Process

Sub-step	Description / Equipment / Parameters	Additional Information
Remove gross contamination	Cleaning detergent, Demineralized water, Container, Syringes, Absorbent lint-free single-use paper wipes are required. An effective cleaning solution according to the specifications of the detergent's manufacturer using demineralized water in an appropriate container. If contamination still visible, remove gross contamination using the paper wipes soaked in the cleaning solution.	A cleaning detergent intended for manual cleaning, which meets the criteria described by the company. Use a container large enough which allows complete immersion of the instruments. The temperature of the solution shall be less than 40 °C in order to avoid the protein fixation.
Cleaning bath	Open the devices with joints and moving parts. Fully immerse the devices in the cleaning solution. Follow the instructions.	Medical devices with flexible shaft: Recommended to conduct the following step in an ultrasonic bath. Ensure that all the surfaces are thoroughly wetted with cleaning solution: We can use a syringe to moisten all parts of the device, incl. cannulations, hinges and other shielded surfaces. No air should be trapped within the features of the device. Allow Full movement of the devices with joints and moving parts at least 3 times.
Brushing	Soft and firm plastic brushes, plastic bottle brushes, Firm plastic bristle brushes, Plastic cleaning wires etc are required. Brush the device thoroughly till no contamination is visible with unaided vision. Try to Bend and rotate flexible shafts during brushing to remove contamination between the windings. Brush the cannulations using a bottle brush.	Particular attention to rough surfaces, blind holes as well as hinges and joints between mating parts and features that may be shielded from the brushing action.
Rinsing	Running water- Sterile or germ-free with less than 10 germs/ml e.g. purified water or highly purified water, Syringes: Volume 1 to 50 ml depending on the size of the device be rinsed. Device is to be rinsed under running water for at least 1 min until all the traces of cleaning solution are removed.	N/A
Visual Inspection	Visually inspect that any remaining contamination is there and repeat the pre-cleaning steps if necessary.	N/A

Sub-step	Description / Equipment / Parameters	Additional Information
Drying	Absorbent lint-free paper wipes is required. Allow the device to drain on absorbent lint-free paper wipes or transfer immediately to the next cleaning step.	N/A

8.1.3 AUTOMATED CLEANING AND DISINFECTION

Table 6 Automated Cleaning and Disinfection

Sub-step	Description / Equipment / Parameters	Additional Information
Operate washer disinfector	Washer-disinfector with rinsing ports, cleaning detergent, Demineralized water for the washing step. Freshly prepared sterile or germ-free water with less than 10 germs/ml or endotoxin-free water or highly purified water for final rinsing / disinfection. Thermal disinfection program (A0 value > 3000 or – in case of older washer-disinfector – application of at least 5 min at 90 °C); with sufficient rinsing steps and filtered air for an active drying. Load the device into the washer. Connect cannulations to the rinsing ports of the washer and then Operate the washer-disinfector cycle.	Washer-disinfector with fundamentally approved efficiency (e.g., CE mark or FDA approval according to ISO 15883 series), properly installed, qualified and regularly subjected to maintenance and testing.
Visual inspection	On completion unload the washer-disinfector. Visually inspect each device for remaining contamination and dryness. If contamination remains repeat the cleaning process including the precleaning stage. Remaining wetness may be removed with medical grade compressed air, and absorbent, lint-free paper wipes (if required supplemented by post-drying at a clean place for up to 2 hours) or by heating in an oven below 110°C.	Chemical disinfection programs are not recommended due to the potential for chemical residues to remain on the instruments. These residues could interfere with sterilization efficacy.

8.1.4 MANUAL CLEANING

Table 7 Manual Cleaning

Sub-step	Description / Equipment / Parameters	Additional Information
Ultrasonic cleaning	Ultrasonic bath large enough to allow complete immersion of the device, frequency upto 25 – 50 kHz, cleaning detergent, Demineralized water An ultrasonic bath with a cleaning solution.	Cleaning detergent meant for manual cleaning and suitable for ultrasonic treatment which meets the criteria.
Brushing	Brush the device thoroughly until no contamination is visible anymore.	N/A
Rinsing	Running water- Sterile or germ-free with less than 10 germs/ml e.g., purified water or highly purified water, Syringes: Volume 1 to 50 ml depending on the size of the device be rinsed. Device is to be rinsed under running water for at least 1 min until all the traces of cleaning solution are removed.	Particular attention to rough surfaces, blind holes as well as hinges and joints between mating parts and features that may be shielded from the brushing action.
Visual inspection	Visually inspect the device if any remaining contamination and if required repeat the manual cleaning if necessary.	N/A
Drying	Allow the device to drain on absorbent paper wipes or transfer immediately to the next cleaning step.	N/A

8.1.5 MANUAL DISINFECTION

Table 8 Manual Disinfection

Sub-step	Description / Equipment / Parameters	Additional Information
Disinfection bath	Disinfectant, Demineralized water, Container, Syringe. Prepare a bath with a disinfectant solution concentration and temperature specified in the instructions. Immerse the device completely for at least the time specified. Rinse cannulations at least three times with a syringe using the solution.	Disinfectant intended for manual disinfection with the applied cleaning detergent.
Rinsing	Running water- Sterile or germ-free with less than 10 germs/ml e.g., purified water or highly purified water, Syringes: Volume 1 to 50 ml depending on the size of the device be rinsed. Device is to be rinsed under running water for at least 1 min until all the traces of cleaning solution are removed.	N/A
Drying	Absorbent lint-free paper wipes, Oven Absorbent lint-free paper wipes is required. Allow the device to drain on absorbent lint-free paper wipes step or by heating in an oven below 110 °C.	N/A
Visual inspection	Visually inspect the device and repeat complete manual cleaning and disinfection if necessary.	N/A

8.1.6 INSPECTION

Table 9 Inspection

Sub-step	Description / Equipment / Parameters	Additional Information
Visual inspection	Visually inspect all parts of the device for visible contamination and/or corrosion and repeat cleaning and disinfection if necessary.	Pay particular attention to: Contamination “traps” such as hinges, shafts of flexible.
Assembly	If required, re-assemble the device.	See instructions provided in the operative technique or separate information available from Stryker representative.
Functional check and Maintenance	Check functionality of devices with moving parts, straightness of rotating instruments, flexible instruments, e.g. reamer shafts, for damage to the spiral element.	N/A

8.1.7 PACKAGING

The cleaned, disinfected, and checked medical devices will be assembled into the dedicated trays provided. Stryker T&E Trays should be Double wrapped. The packaging for terminally sterilized medical devices should fulfill the following requirements: EN ISO 11607.

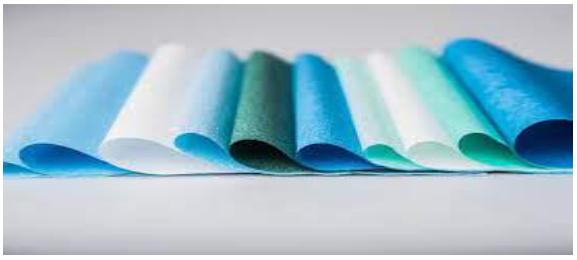


Figure 32 Wrapping sheets

Suitable for steam sterilization, Sufficient protection of the instruments as well as of the sterilization packaging’s to prevent mechanical damage.

Figure 33 Rigid Containers-Aseculap

Trays must not be stacked within the sterilization container or sterilization wrap and, in the autoclave, as it might impact sterilization.

Rigid sterilization container Aesculap JK and JN Series may be used for the same purpose to sterilize any reusable medical devices provided by Stryker T&E in stainless steel trays.

8.1.8 STERILIZATION

It is a process of killing of all forms of microbial life i.e., both vegetative and spore forms of life, which is carried out by several physical and chemical methods. Most of the medical and surgical devices used in healthcare are made of materials that are heat stable e.g., stainless steel, Titanium and therefore undergo heat, primarily steam, sterilization. There are some instruments in medical devices that require low temperature for sterilization. Ethylene oxide gas is used for the heat- and moisture-sensitive medical devices. Several new, low-temperature sterilization systems (e.g., hydrogen peroxide gas plasma, ozone) have been developed and are being used to sterilize the medical devices.

Sterilization destroys all microorganisms on ay device or in a fluid to prevent disease transmission associated with the use of that device. The use of inefficiently sterilized critical items represents a high risk of transmitting of pathogens.

The concept of the word “sterile” is measured as a probability of sterility for each item that needs to be sterilized. This probability is referred to as the sterility assurance level (SAL) of the product and is described as the probability of a single viable microorganism that might remain on a product even after sterilization.

SAL is expressed aa 10^{-n}. For example, if the probability of any spore surviving was one in one million, then the SAL would be 10^{-6}. SAL is the estimation of lethality of the entire sterilization process.

Medical devices that have contact with any sterile body tissues or fluids are considered critical items. These items should be sterile whenever used because any microbial contamination could result in disease transmission. Items such as surgical instruments, biopsy forceps, and implanted medical devices.

If these items are heat resistant, sterilization process recommended is **steam sterilization**, because of safety due to its reliability, consistency, and lethality.

There are different types of sterilization methods based on the devices which are described below.

8.1.8.1 STEAM STERILIZATION

Moist heat in the form of saturated steam under pressure is the most widely & dependable method. It is nontoxic, inexpensive, rapidly microbicidal, and heat penetrates rapidly.

The basic principle is accomplished in an autoclave, is to expose each item to direct steam contact at the required temperature and pressure for the specific time. Steam sterilization depends on 4 parameters: steam, pressure, temperature, and time.

The ideal steam for sterilization is the dry saturated steam and entrained water. Use of pressure is that it serves as means to obtain the high temperatures that is required to quickly kill microorganisms. Specific temperatures should be obtained to ensure the microbicidal activity. The two common steam-sterilizing temperatures are 134°C and 132°C. These temperatures are maintained for a minimal time to kill all the microorganisms.

The two basic types of steam sterilizers (autoclaves) are the

- Gravity displacement autoclave
- High-speed pre-vacuum sterilizer.

The gravity displacement autoclaves are primarily used for laboratory media, water, pharmaceutical products, regulated medical waste, and nonporous articles whose surfaces have direct steam contact.

The high-speed pre-vacuum sterilizers are related to the gravity displacement sterilizers as they are fitted with a vacuum pump (or ejector) that ensure air is removed from the sterilizing chamber and load before the steam is entered.

The Bowie-Dick test is used for detecting air leaks and inadequate air removal. A commercially available Bowie-Dick-type test sheet might be placed in the center of the pack. The test pack is placed horizontally in the front, bottom section of the sterilizer rack and near to the door and over the drain, in an otherwise empty chamber and run for around 134°C for 3 minutes. Sterilizer vacuum performance is acceptable when the sheet inside the test pack shows a uniform color change. Entrapped air will cause a spot to appear on the test sheet, because of the inability of steam to reach the chemical indicator. If the sterilizer fails the Bowie-Dick test, the sterilizer is not used until it is inspected by the sterilizer maintenance personnel and passes the Bowie-Dick test.

Another steam sterilization is a **steam flush-pressure pulsing** process, that removes air rapidly by repeatedly alternating a steam flush and the pressure pulse is above atmospheric pressure. Sterilization temperature is generally 132°C to 135°C with 3 to 4 minutes.

The effectiveness of steam sterilization is monitored by using a biological indicator containing spores of *Geobacillus stearothermophilus.*

Microbicidal Activity

Heat is the oldest and most recognized agent for inactivation of microorganisms. D-values (time to reduce the surviving population by 90% or 1 $\log_{10}$) which allows a direct comparison of the heat resistance of microorganisms.

Uses

Steam sterilizers also are used in healthcare facilities to sterilize medical devices and to decontaminate microbiological waste and sharps containers.

8.1.8.2 Ethylene oxide (ETO)

It is a colorless gas that is flammable and explosive. Used for sterilizing heat- and moisture-sensitive medical devices. The four essential parameters are: gas concentration; temperature; relative humidity; and exposure time and influences the effectiveness of ETO sterilization.

Figure 34 Ethylene Oxide

An increase in gas concentration and temperature may shorten the time necessary for achieving sterilization. The effectiveness of ETO sterilization can be changed by lumen length, diameter, inorganic salts & organic materials.

ADVANTAGES

It Can sterilize heat- or moisture-sensitive medical equipment without deleterious effects on the material used in the medical devices.

DISADVANTAGES

- ETO are the lengthy cycle time, the cost, and its potential hazards to patients and staff.
- Exposure to ETO might result in irritation (e.g., to skin, eyes, gastrointestinal or respiratory tracts) and CNS depression.

The basic ETO sterilization cycle consists of five stages that are as follows:

- Preconditioning and humidification,
- Gas introduction,
- Exposure,
- Evacuation
- Air washes.

Modern ETO sterilizers combine sterilization and aeration in the same chamber which makes it a continuous process. These ETO models minimize exposure to ETO during door opening and load transfer to the aerator.

MICROBICIDAL ACTIVITY

ETO inactivates all microorganisms although bacterial spores (especially *B. atrophaeus*) are more resistant than other microbes. *B. atrophaeus* is the suggested biological indicator.

USES

ETO is used in healthcare facilities to sterilize critical items that are moisture or heat sensitive and cannot be sterilized by steam sterilization.

8.1.8.3 GAMMA IRRADIATION

It uses Cobalt 60 radiation to kill microorganisms on a variety of different products in a specially designed cell. A key characteristic of gamma irradiation is that it has high penetration capability, which allows the delivery of target radiation dose to areas of products that may be greater in density.

The unit of absorbed dose- kiloGray, expressed as kGy. Delivery and absorption of dose is determined by product density, packaging size, dose rate, exposure time and facility design.

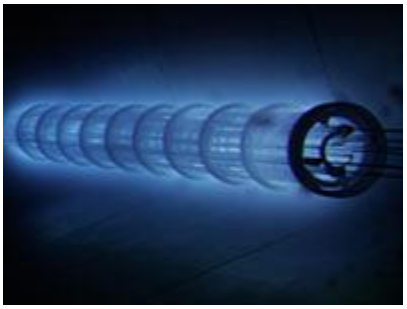


Figure 35 Gamma Irradiation

USES

It can effectively treat a wide variety of products composed of different materials, with varying densities, & configurations. Some examples where it is used:

- Medical devices
- Pharmaceuticals
- Combination drug/device products
- Packaging materials and many more.

BENEFITS OF GAMMA IRRADIATION

Gamma irradiation is safe, reliable, and highly effective in treating a wide variety of products with different densities. With the ability to penetrate products while wrapped in their final packaging, gamma irradiation also supports in the manufacturing and distribution process by enabling final packaged products as well as raw material needs, safeguarding full sterility of the product.

STANDARDS

Gamma sterilization is supported by the internationally recognized standard, ISO 11137, which defines the approach to validating a dose to achieve a well-defined sterility assurance level (SAL).

8.1.9 STORAGE

After sterilization, the medical devices are stored in the sterilization packaging's in a dry and dust-free place. The shelf life also depends on the sterile barrier employed, storage manner, environmental and handling conditions.

9. VERIFICATION & VALIDATION TESTS

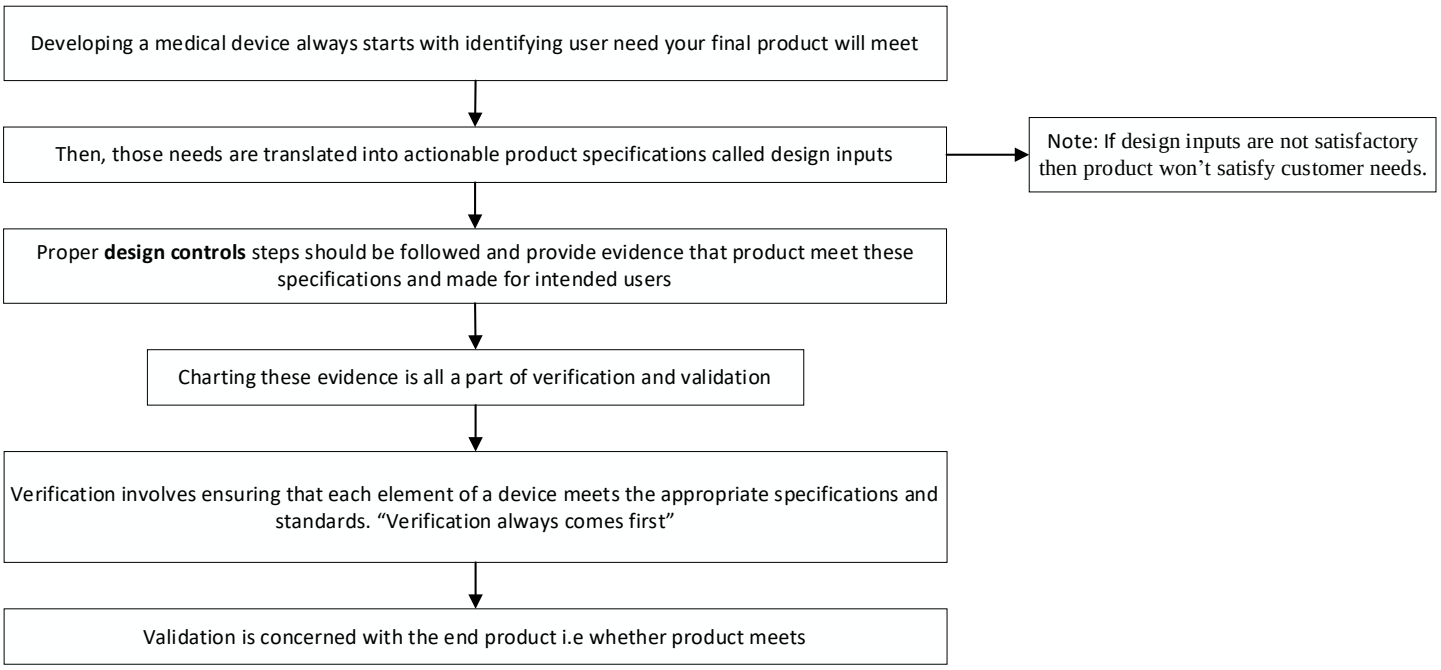


Figure 36 Process Flow of Verification & Validation Testing

9.1 STERILIZATION VALIDATION

Medical devices and health care products must be sterilized before use and sterilization cycle parameters must be defined through a sterilization validation process.

Medical device sterilization validation is very important aspects of medical device testing because an improper sterilization procedure could lead to severe diseases or even death. Devices have unique designs, densities, and packaging, sterilization conditions that might be sufficient and appropriate for one device might be inadequate for another. Therefore, sterilization processes must be validated depending on the device.

9.1.1 STEAM STERILIZATION VALIDATION

Moist Heat (Steam) sterilization validation testing is performed, using steam sterilizers (autoclaves). For the testing, devices are inoculated with a known population of microbes, and then the devices are autoclaved and then tested for sterility assurance.

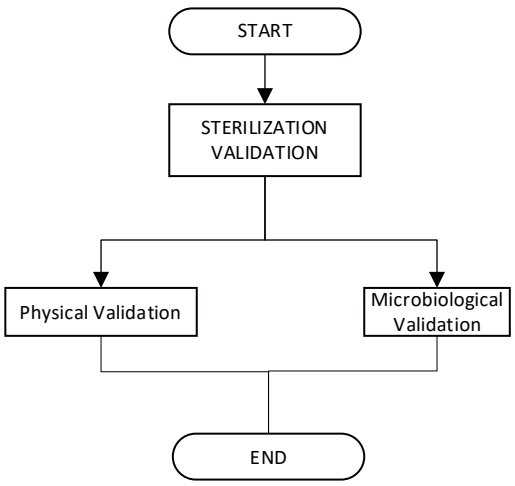


Figure 37 Sterilization validation Flowchart

Below are the steps that we perform for sterilization validation on trays:

9.1.1.1 Test Request from the Project Manager

When design inputs for the new device are ready then product comes to get verified and validate in order to know that it will follow all sterility parameters according to standard regulations and will be customer safe.


Trauma & Extremities Form

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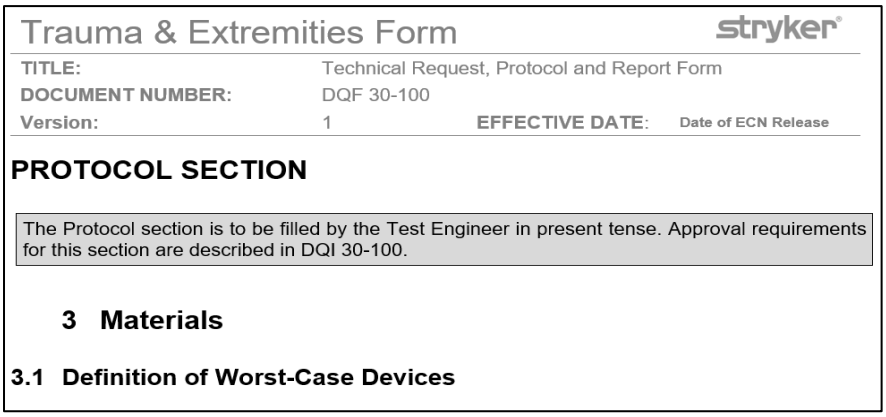
TITLE:	Technical Request, Protocol and Report Form		
DOCUMENT NUMBER:	DQF 30-100		
Version:	1	EFFECTIVE DATE:	Date of ECN Release

Figure 38 Internal Template for Test Request

9.1.1.2 CREATION OF PROTOCOL

- Test protocol creation includes worse case device assessments and worse case tray/kit configuration.
- Discussion and decision if an adoption should be performed or if validation shall be required.
- Test execution/coordination and project related communication to external vendors.
- Sterilization method, parameters, quantity of test samples, selection of inoculation areas (Table-13), etc.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Version:	1	EFFECTIVE DATE:	Date of ECN Release

PROTOCOL SECTION

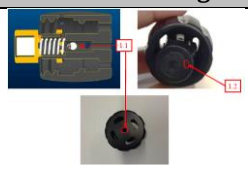
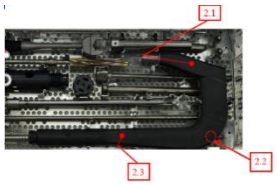
The Protocol section is to be filled by the Test Engineer in present tense. Approval requirements for this section are described in DQI 30-100.

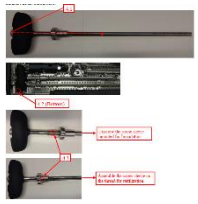
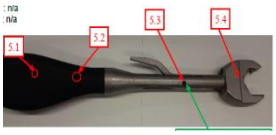
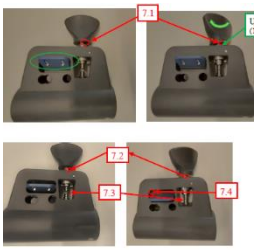
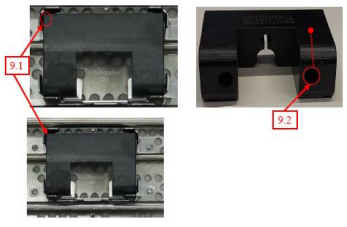
3 Materials

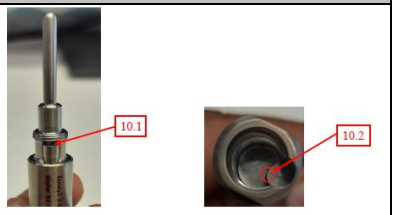
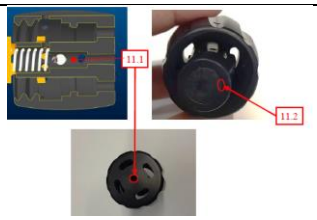
3.1 Definition of Worst-Case Devices

Figure 39 Protocol Template

Table 10 Inoculation Position for Instruments

Position	Name	Inoculated Sites	Reasons	Images
1.1	Targeting Sleeve	In the middle of the lumen	Insufficient steam spreading possible, Synthetic Material, Hidden Surface. Mechanism.	
1.2		In the gap		
2.1	Plus Targeting Arm	In the middle of the lumen.	Mass of the instrument, Hidden Surface, Insufficient steam spreading possible, Synthetic material (Low conductivity of heat).	
2.2		On the Surface of Targeting Arm		
2.3		In the middle of the lumen		

Position	Name	Inoculated Sites	Reasons	Images
3.1 **3.2**	Lag Screw Reamer	In the middle of the lumen Contact Surface between instrument shaft and clamping sleeve mechanism.	Insufficient steam spread possible, hidden surfaces, locked and bolted instrument.	
4.1 **4.2** **4.3**	Leg Screwdriver	In the middle of the lumen On the Surface (Bottom, in the corner) On the Thread	Mass of the instrument, Hidden Surface, Insufficient steam spreading possible, Synthetic material (Low conductivity of heat).	
5.1 **5.2** **5.3** **5.4**	Opening Reamer Handle	On the surface of the silicon handle Contact surface instrument / Metal-Bracket In the gap of the mechanism In the gap of the mechanism	Insufficient steam spreading possible, hidden surfaces, hidden surface, small gaps, assembled parts, tightened parts	
6.1	Counterbore Drill, Long	Contact Surface between Instrument and PP bracket	Insufficient Steam spreading Possible, hidden surface, synthetic material (low conductivity of heat).	
7.1 **7.2** **7.3** **7.4** **7.5**	Locking Adapter, Intermediate Nail	Gap between instrument knob /shaft (Adjusting Mechanism) Gap between instrument rod/shaft (adjusting mechanism) Between the closed gap of the upper and lower rod In the gap of chip corner. (Joint; moving mechanism) In the gap of the locking pin	Insufficient steam spreading possible, hidden surfaces during sterilization, small caps, capillary action.	
8.1	Anti-Rotation Sleeve	In the middle of the Lumen (Front end)	Insufficient steam spreading possible, size of diameter, deep length of lumen.	
9.1 **9.2**	Anti-Rotation Clip	Surface of the instrument at bottom In the blind hole	Mass of the Instrument, Insufficient steam spreading possible, hidden surface.	

Position	Name	Inoculated Sites	Reasons	Images
10.1 **10.2**	Adapter Implant Extraction Set	In the Gap In the Blind hole of Instrument.	Insufficient steam spreading possible, Hidden surface.	
11.1 **11.2**	Knob Mounted	In the middle of the lumen In the gap	Insufficient steam spreading possible, Synthetic Material, Hidden Surface	
12.1	G3 Flexible Screwdriver	On the surface oriented to the silicon mat	Insufficient steam spreading possible, Synthetic Material, Hidden Surface, stored on silicone mat	

9.1.1.3 PHYSICAL VALIDATION

A physical validation is only possible if the used thermos-sensors do not change the measuring points significantly, e.g., small instruments in silicon brackets.

- Sterilizer with adjusted limits for sterilization process.
- Thermometric recorder with minimum 4 temperature sensors is used.
- Single filter container modified to allow an airtight introduction of two thermos-sensors or double wrapped tray.
- Usually, a double wrapped tray is considered as a worst-case scenario.
- Fully loaded tray is used.

Physical Validation - Method

- Put fully loaded tray in container or double wrapped tray.
- Place one thermo sensor- 1 approximately in the geometric centre of the tray.
- Place a second sensor – 2 between tray lid and filter of container or the wrapping material.
- Close container lid or wrapping and insert tray in sterilizer.
- Place third sensor – 3 approximately 50 mm above the geometric centre of the tray surface.
- Place fourth sensor- 4 in draining opening of sterilizer.
- Place as much additional sensors as necessary for a full validation in tray. Put sensors at all critical positions.
- Critical positions are e.g., places where materials with different thermal properties come together and small cannulations.
- Run standard sterilization cycle with minimum parameters (time and temperature). Record temperatures of sensors during whole cycle.

9.1.1.4 MICROBIOLOGICAL METHOD

Identification of Instruments that can Fail the Parameters in the Tray

A tray consists of Base layer and Insert Layer in which Instruments are there as shown in Fig:10 Each and every Instrument

in the tray is studied and marked that might fail in the validation parameters.

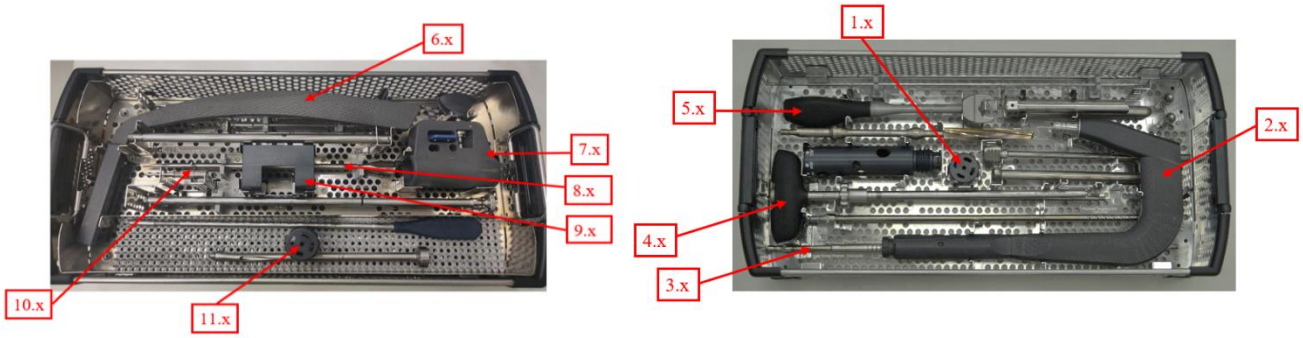


Figure 40 Base and Insert of a Gamma 4 Tray

Instruments that might fail are selected on different parameters like.

Table 11 Worst-Case selection Parameters

Feature type	Feature design	Examples
Material	Base material	Titanium, stainless steel, plastics
	Surface topology	Milled, grinded, blasted
	Surface finish	Electropolishing, anodization type X, coating
	Heat capacity	Titanium, stainless steel, plastics
Function	Hinges, articulations	Forceps, scissors
	Crevices, joints	Forceps
Conditions	Dimensions (range of medical device, e.g., instruments for micro implants or lower extremity)	Lengths, diameters
	Lumens and channels	Cannulations
	Capillary gaps	Function buttons, mechanisms, guiding
	mass	Small or large medical device
Storing	Tray	Metal, plastics
	Brackets	Metal, plastics
	Clamping	Tight, free

Table 12 Sterilization Validation Parameters

Parameters	Europe	US
Temperature	134-137°C	132-134°C
Exposure Time	3 min	3-4 min
Air Removal	Pre-Vacuum	Pre-Vacuum/ Gravity displacement
Steam Quality	Saturated Steam	Saturated Steam
Drying	10-30 mins	10-30 mins

9.1.2 TESTING AT LAB

9.1.3.1 INSPECTION OF TRAY

Samples were visually inspected and documented. All samples were found in good condition and observations were made.

9.1.3.2 Cleaning of tray

Tray was cleaned before test as per "Instruction for cleaning, sterilization, inspection and maintenance- OT-RG-1 Rev6." following general requirements.

For test cycle cleaning, first ultrasonic cleaning with 0.8% Enzol is performed, then manual precleaning and finally automated cleaning with 0.5% Neodisher Mediclean forte detergent is performed before sterilization steps.

9.1.3.3 Preparation of culture media

- Dehydrated culture media "Soyabean Casein Digest Medium (SCDM)" was prepared for the sterility test used for inoculated test items.
- Dehydrated culture media "Soyabean Casein Digest Agar (SCDA)" plates were prepared and used at various steps of test.

9.1.3.4 BI inoculation and placement

Samples were inoculated with spore suspension.

Samples were dried in LAF between 16 to 24 hours under operational LAF (Laminar Air Flow Unit).

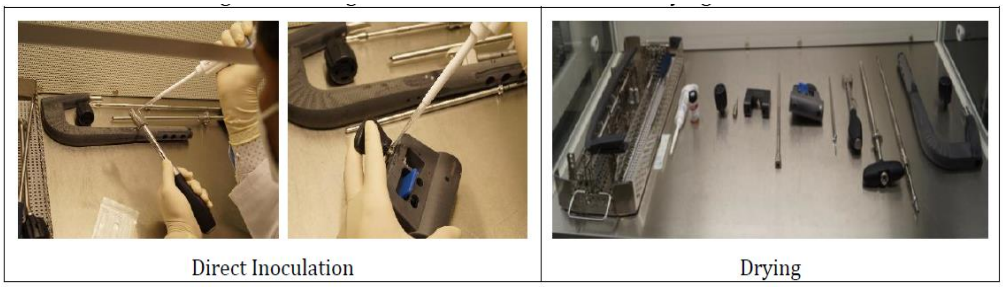


Figure 41 Biological Indicator inoculation and drying schematic

9.1.3.5 Biological Indicator (BIs)

Spore suspension presentation of BIs were used in this testing. Spore suspension was used for direct inoculation.

9.1.3.6 Sterility Test execution:

- Tray was double wrapped with sequential wrapping Envelop fold method and transferred to lower bottom of sterilizer.
- Tray was sterilized at 132°C for 1.5 min with Pre-vac (3x) pulses.
- After sterilization, tray was transferred to LAF immediately.
- Inoculated test instruments were transferred aseptically in Whirl Pak / Nasco Sterile Bags.
- Soyabean Casein Digest broth was poured inside the bags to submerge the test instrument.

- The bags were sealed and incubated. SCDM Negative control,
- Test device positive control (S.S. coupon), Environment control, Water Negative control, TSA (Tryptic Soya Agar/SCDA) Negative control and Environment Negative control were placed with test.
- All test / controls plates were incubated at 57.5°C for at least 48 hours. All Whirl Pak & Nasco bags were incubated at 57.5°C for at least 7 days.

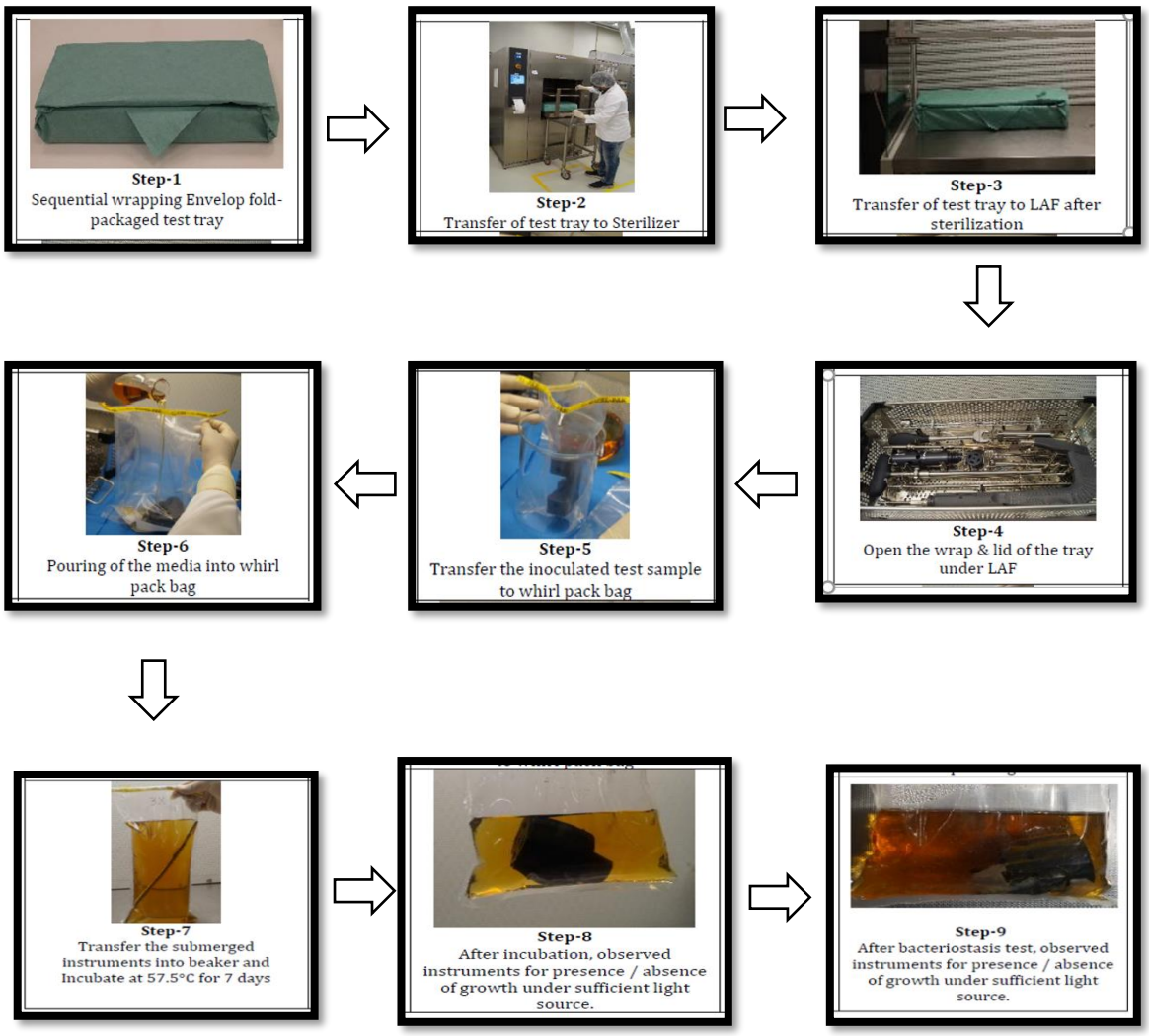
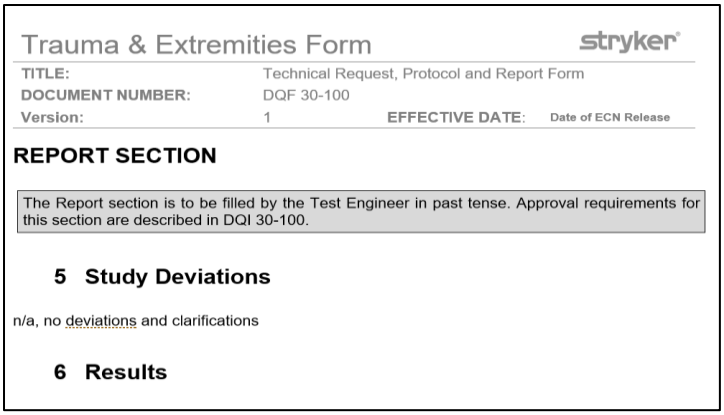


Figure 42 Overall Summary of Sterilization Validation

9.1.3 REPORT CREATION

Report is created where all the data is compiled in it i.e- Result, conclusion, Study Deviations if any.



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REPORT SECTION

The Report section is to be filled by the Test Engineer in past tense. Approval requirements for this section are described in DQI 30-100.

5 Study Deviations

n/a, no deviations and clarifications

6 Results

Figure 43 Report Section in Template

9.1.4 RELEASE IN ONEPLM

After verifying and validating the tray protocol document is released on onePLM.

9.2 RESIDUAL MOISTURE TEST

- Water Droplets leads to microbial growth.
- Total increase of weight Δh max. 0.2% is acceptable.
- There should be no visible moisture in or on containment device.
- Principle: In order to maintain their sterile barrier properties wrapping materials need to be sufficiently dried after sterilization.
- Several trials with different drying times may be performed to determine the times to fulfil the standards and to get a fully dried tray.
- Maximum drying time 30 min.

Results of visual inspection	Evaluation according ANSI/AAMI ST77
No visible moisture	pass
Visible moisture:	
• Few droplets, located at the bottom or within the edges, not creating a pathway for microorganisms	pass
• Droplets on the containing instruments or brackets	fail
• Droplets on the external surface of the tray	fail
• Sterilization paper wet	fail

Figure 44 Acceptance criteria for RMT

9.2.1 TEST REQUEST FROM PROJECT MANAGER

When design inputs for the new device are ready then product comes to get verified and validate in order to know that it will follow all sterility parameters according to standard regulations and will be customer safe.

Figure 45 Internal Template for Test Request

9.2.2 CREATION OF PROTOCOL

- Test protocol creation includes worse case device assessments and worse case tray/kit configuration.
- Discussion and decision if an adoption should be performed or if validation shall be required.
- Test execution/coordination and project related communication to external vendors.
- Residual moisture test method, parameters, quantity of test samples, are defined.

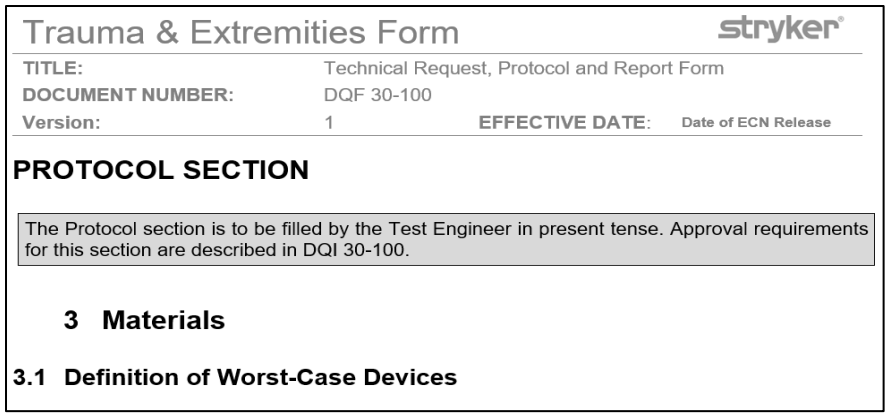


Figure 46 Protocol Template

9.2.3 TESTING AT LAB

9.2.3.1 Inspection of Tray

Tray was inspected and documented- The test sample “MMT Gamma 4 indication tray” consist of tray base, tray Insert & lid. Tray is loaded with instruments in it.

9.2.3.2 TEST PROCEDURE

- The test tray was conditioned to 23°C ± 2°C.
- The test tray was double wrap in sterilization paper (sequentially wrapped, envelope fold) according to the standard.
- The mass M0 & M1 of the test tray was weighed before each test cycle.
- For the sterilization process the test tray was put into a goods basket.
- Before starting a test cycle, the autoclave chamber was conditioned by performing one sterilization cycle with an empty chamber applying the same sterilization parameters as of test.
- Within 5 to 15 min after the pre-sterilization cycle the test item was put into the sterilization chamber.

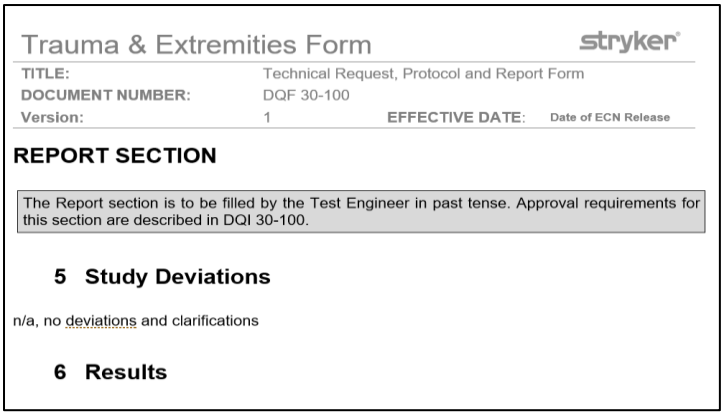
- The test item was positioned alone in the center/low position inside the sterilization chamber.
- In total, three independent sterilization cycles were performed at the below parameters

Table 13 Test Parameters and Set Values

Test Parameters	Set Values
Sterilization method:	Moist heat sterilization
Cycle type	Saturated steam with pulsed forced air removal
Sterilization temperature:	132°C
Exposure time:	4 min at 132°C
In-process drying time:	30 min
Stand in time:	0 min: Immediately after the end of the sterilization cycle (within 60 sec), shall be taken out the tray from chamber for cooling down.
Stand out time	5 min: cooling down with wire basket outside the autoclave at room temperature and determined the mass M2 60 min: cooling down with wire basket outside the autoclave at room temperature determined the mass M3.
Opening of sterility barrier	Conduct visual inspection of the tray for presence / absence of the residual moisture in and outside the tray, immediately after the determination of mass M3. The mass increase Δm shall be determined according to below, $\Delta m = \frac{m_{2/3} - m_1}{m_1} \times 100\%$

9.2.4 REPORT CREATION

Report is created where all the data is compiled in it i.e- Result, conclusion, Study Deviations if any.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REPORT SECTION

The Report section is to be filled by the Test Engineer in past tense. Approval requirements for this section are described in DQI 30-100.

5 Study Deviations

n/a, no deviations and clarifications

6 Results

Figure 47 Report Section in Template

9.2.5 RELEASE in OnePLM

After verifying and validating the tray protocol document is released on onePLM.

9.3 CLEANING VALIDATION

For any medical device, cleaning process is recommended by a device manufacturer and to assure users that a device can be cleaned successfully, device manufacturers focus on the following-

a. Device should be thorough cleaned with fully validated mechanical and/or manual processes.

b. Validation can be performed in health care facilities by using commonly available cleaning agents, equipment, and methods.

c. It should be performed in the that manner which are practical and feasible so they can also be performed by health care personnel.

d. It is recommended that a means should be defined by which users can verify the cleanliness of the device.

Two basic components of user verification of cleaning efficacy are

- Establishing reasonable benchmarks for the level of cleaning that can be achieved consistently for specific soil markers relevant to patient-used devices; and
- Developing rapid, easy-to-perform test methods that reliably demonstrate that the cleaning benchmarks that are achieved.

Note: The pre-cleaning for manual and automated reprocessing should be performed until the surfaces are visibly clean. The success of the cleaning efficacy depends heavily on this step of reprocessing. It shall be documented in the test report if multiple loops are required.

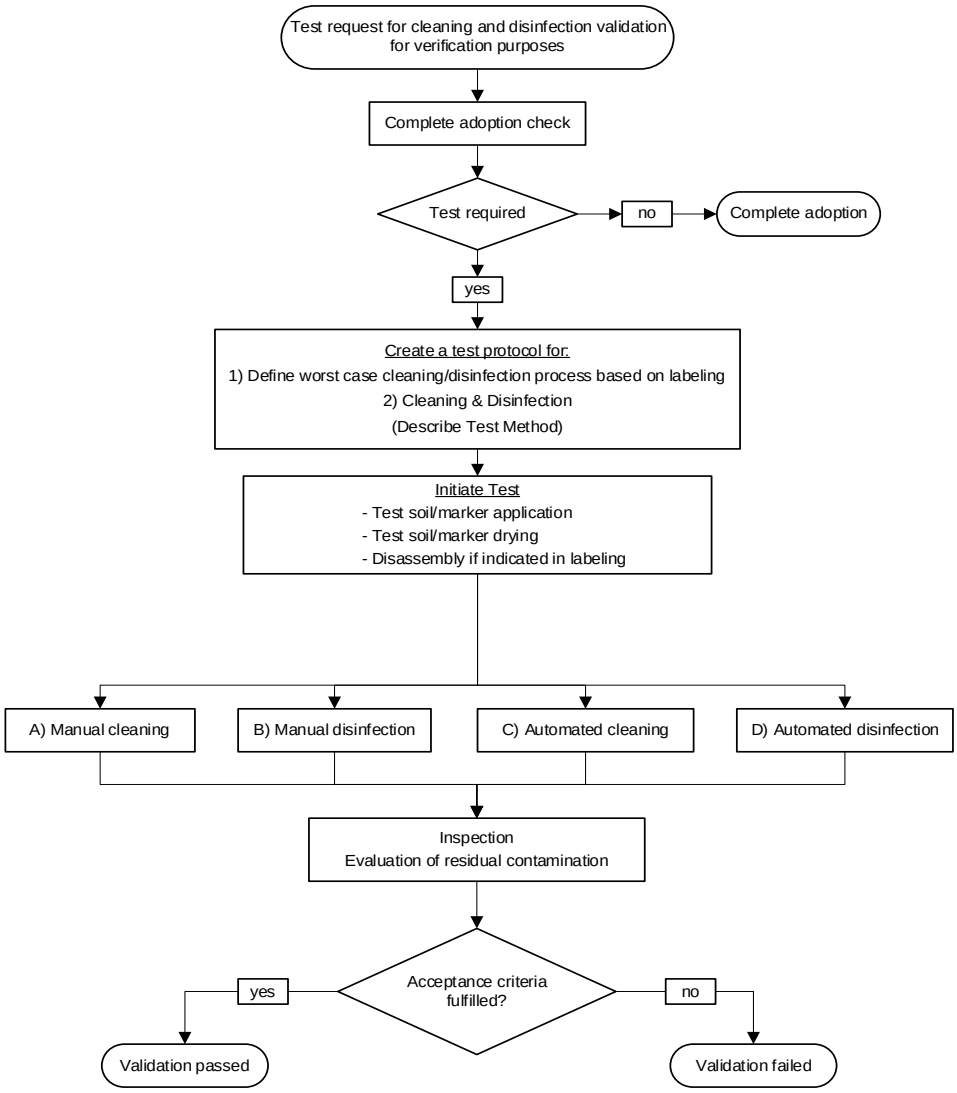

Figure 48 Process flow for Cleaning Validation

9.3.1 TEST REQUEST FROM THE PROJECT MANAGER

When design inputs for the new device are ready then product comes to get verified and validate in order to check that it will follow all cleaning parameters according to standard regulations and will be customer safe.


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Figure 49 Internal Template for Test Request

9.3.2 ADOPTION CHECK TO BE DONE WITH THE LEGACY PRODUCTS

If we have any existing product that is similar in the design, features as of the new product and is already validated then we can opt for adoption and not go for testing.

- Adoption check using the Cleaning Validation Device Assessment Form and adoption report.
- Adoption check using the Cleaning Validation Device Assessment Form.

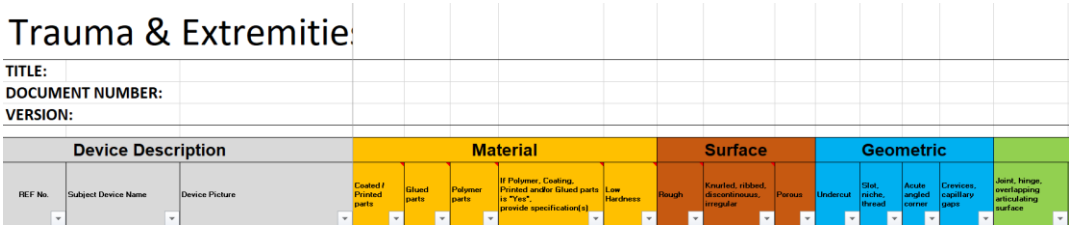


Figure 50 Feature assessment

The design features of the subject device shall be analyzed using the drawings and/or physical samples. The assessment shall be made according to the structure using the specific worksheet for Instruments and Implants or Trays and Tray Components, respectively.

For each identified feature (“Yes” for the presence of the feature is selected) either a reference shall be provided, or testing is required. The cleanability of each used polymer, coating, printing, and glue should be evaluated.

For some features, the respective dimensions should be provided to enable an easier comparison and worst-case selection for these features.

Table 14 Feature list to be evaluated

Group	Feature	Remark
Material	Coated / Printed parts	A coating is a covering that is applied to the surface of any objectThe purpose of applying the coating might be, functional, decorative or both.
	Glued parts	Devices glued or sealed with an adhesive.
	Polymer parts	Due to their surface structure some polymers (e.g., some silicone types) are considered as more difficult to clean.
	Low hardness, low resistance to wear	Over their lifecycle components with low hardness/ resistance to wear might display excessive dents, scratches or similar which affect the cleanability negatively.

Group	Feature	Remark
Surface	Rough	The higher the surface roughness the harder it is to clean. Visually / perceptibly detectable roughness, and/or roughness in drawing Rz > 50.
	Knurled, ribbed, discontinuous, irregular	Surface alterations / features with a specific pattern.
	Porous	N/A
Geometric	Undercut, Slot, niche, thread, Blind hole, Crevices, capillary gap	N/A
Design	Sharp cutting edges	N/A
	Cannulation, lumen or channel	The longer and narrower the cannulation is, the harder it is to clean. The respective ratio **may** also be considered. Additionally, the cannulation **may** be recessed and/or flexible, which typically increases the challenge to cleaning.
	Joint, hinge, overlapping articulating surface, (Ball) detents, securing/ closing mechanism	-
	Non-disassembled multiple components	Multiple components, which are not dismantled/ disassembled or opened for reprocessing, also including encasements, shrink tubes, coats sleeves
	(Ball) detents, securing/ closing mechanism	-
	Valves/ Taper locks	-
	Flexible elements	e.g., flexible reamer shafts, chains, wires and meshes

Informational score

Based on the selected "yes"- answers in the assessment sheet an informational score may be determined. The score is determined by adding the number of selected "Yes"-answers over all columns. This score is intended to support:

- the identification of worst-case/representative devices among a larger group of subject devices.
- sorting and organizing reference devices in an overview table.

Note: The score is not intended to be a decision factor whether a device shall be tested or not. The evaluation in each single column is the leading assessment.

Adoption report

The filled form shall be attached to a test report in order to justify any decision on either testing or referencing as well as the selection of representative or worst-case devices.

Note: Prior to freezing the design, respective cleaning/disinfection SME should review dimensions of the worst-case features of the devices in terms of cleanability and assess if any feature generates a new worst case as compared to reference devices. Feedback can be given to the design team to see if these features can be altered to improve the cleanability of the device.

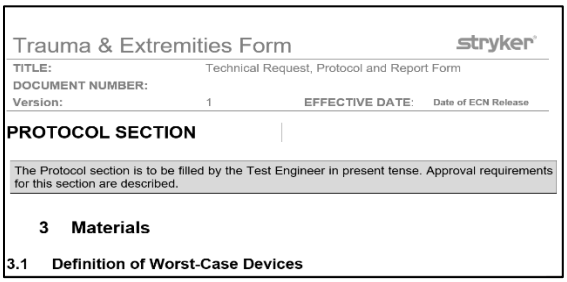
9.3.3 TEST REQUIRED

If the product is not the legacy product and does not exist, then testing is required in order to validate the new product.

9.3.4 CREATION OF TEST PROTOCOL

- Test protocol creation includes worse case device assessments and worse case tray/kit configuration.
- Discussion and decision if an adoption should be performed or if validation shall be required.
- Test execution/coordination and project related communication to external vendors.
- A protocol shall be established for verification purposes which describes the washing sequence in detail. Protocol shall be set up in accordance with the respective labelling documents (e.g., IFU/eIFU, T&E Cleaning, Sterilization, Inspection and Maintenance Instructions).

Note: The IFU is the leading document. Parameters shall be checked carefully prior to test start. The cleaning validation should be performed for the worst-case parameters stated in either the product specific IFU/eIFU and/or the T&E or CMF Cleaning, Sterilization, Inspection and Maintenance Instructions.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PROTOCOL SECTION

The Protocol section is to be filled by the Test Engineer in present tense. Approval requirements for this section are described.

3 Materials

3.1 Definition of Worst-Case Devices

Figure 51 Protocol Template

9.3.5 MARKERS AND TEST METHODS

For determination of the cleaning efficacy most test methods require a marker, which should be present in the test soil. FDA recommends that testing should include a representative inorganic and organic challenge that mimics actual in-use conditions. Furthermore, the guidelines recommend that the organic challenge should be representative of the types of soil to which devices are exposed during clinical use, such as serum, blood, secretions, etc. [AAMI TIR 12]. On the other hand, CEN and ISO published a list of national cleaning tests, in total 19 test methods [ISO 15883-5].

Test soils consisting of a microorganism marker solution alone (pure spore log reduction methods) shall not be used [FDA Guidance]. Test soils consisting of a solution of microorganisms combined with a medium (hybrid spore log reduction methods) is preferred. An overview of common and often mentioned test methods for determination of the cleaning efficacy is listed in Table below.

For trays and tray components tests done are-

- Microbiological test method
- Protein/BCA test method
- TOC test method

Note: When using a protein detection method for cleaning validation, the temperature during automatic cleaning (incl. thermal disinfection phase) should not be higher than 60°C

Table 15 Markers and test methods

Markers	Test method	Comment
Micro-organisms (e.g., bacterial spores)	Bioburden assessments [ISO 15883]	Laborious methods. More sensitive than protein and TOC-method.
Protein	Modified OPA-method [AAMI TIR 30]	Laborious, sensitive test method.

Markers	Test method	Comment
	Biuret/ BCA-Method (Biuret reaction) [AAMI TIR 30]	Laborious, sensitive test method. Semi-quantitative laborious method: a) Dabber-method: Discarding surface needed ≈ 10 cm2 b) Flushing-method: No determination of soil location possible.
	Ninhydrin	Rapid, less sensitive than OPA-method, not applicable to lumens [AAMI TIR 30]. Discarding (with dabber) test surface needed: 5-50 cm2
Carbon	TOC (total organic carbon)	Method for measurement of extraneous materials such as cleaning agents and protein materials [AAMI TIR 30].
Radio-actively-labelled test soil (e.g., heparinized sheep blood)	Radio nuclide method	Is very sensitive and provides excellent ability to monitor removal of the soil. However, it is not widely available [AAMI TIR 30].
Fluorescence screening test method according to recommendation of MDS	To support the decision for testing or adoption of test data from existing devices, a screening cleaning test using milk powder in combination with a fluorescent dye may be done. Furthermore, the method may be used to identify worst case spots/areas of devices under evaluation and to derive ideas for design improvement. The fluorescence method uses a contamination solution consisting of low-fat milk powder dissolved with sterile, physiological saline with Fluorescein Natrium.	
Carbohydrate	Consult with lab for appropriate test method	If carbohydrate is clinically relevant for the device being tested, it is acceptable
Hemoglobin	Consult with lab for appropriate test method	If hemoglobin is clinically relevant for the device being tested, it is acceptable
Endotoxin	Various	---

The test soil and soiled sites should be chosen according to the medical devices external communicating environment. Therefore, the environment of the medical device may be classified according to Table below and intended use:

9.3.6 TEST SOILS

A test soil shall be chosen which represents a worst-case challenge to the cleaning/disinfection process. Protein based soils should be used for medical devices entering sterile body cavities [AAMI TIR 30]. Additives may be added.

For trays and tray components, a low-level test soil is recommended (e.g., 30 g of low-fat milk powder dissolved in 750 ml physiological saline with 250 ml new-born calf serum added as used by Medical Device Services.

Table 16 Test soils simulating the medical device's environment

Communication environment	Test soil
Skin	hair, sebaceous, fat, …
Blood	sheep blood, bovine blood, …
Muscles	fibers
Bone, cement	sand

9.3.7 MEDICAL DEVICE CLEANLINESS

Before applying the test, soil and starting cleaning procedure the test device should be clean and decontaminated.

9.3.8 TEST SOIL/MARKERS APPLICATION

One of the following options should be selected.

Option 1: In case of full immersion/intense inoculation:

A full immersion of the device into the test soil should be considered as starting point. Stryker's Trauma & Extremities division performs this soil application due to given test reproducibility and worst-case considerations. All intended functional procedures (e.g., flexures, articulations) shall be conducted to soil the device to a worst-case condition.

In case of failure, consider a selective soil application as described in Option 2 (B).

Option 2: In case full immersion / intense inoculation of product is not performed:

A simulated use protocol shall be set up those mimics clinical handling according to the intended use and OP technique [AAMI TIR 30] Repetitive inoculation should be conducted, and the number of necessary repetitions should be carefully evaluated with external test labs or cleaning experts and must be justified.

The test soil/markers shall be applied on realistic Regions of Interest (ROI) which are considered as worst case in terms of cleanability and/or patient exposure. All intended functional procedures (e.g., flexures, articulations) shall be conducted to soil the device to a worst-case condition.

9.3.9 TEST SOIL/MARKERS DRYING

The soil should be dried after application to reflect worst case conditions. The drying time may depend on the test soil, test methods and the environmental conditions during drying.

60 min may represent a realistic minimum drying time for blood coagulation [AAMI TIR 30]. Ambient conditions are recommended as a reasonable drying environment. The medical device should be dried in an orientation considering worst case aspects (e.g., horizontal orientation represents worst case drying position for cannulated instruments).

Drying with a laminar flow to speed up the drying time (ca. 20 min) may apply.

9.3.10 AGENTS FOR CLEANING

For cleaning validation procedures, the agents listed in the respective labelling shall be used.

9.3.11 CLEANING EQUIPMENT (PRE-CLEANING AND MANUAL CLEANING)

For pre-cleaning and manual cleaning, appropriate cleaning equipment as listed in the respective labeling shall be used.

9.3.12 WASHER-DISINFECTOR

For automated cleaning, a washer-disinfector according to ISO 15883 shall be used.

9.3.13 VISUAL INSPECTION

After cleaning and prior to evaluation of the residual contamination, a visual inspection should be performed.

An un-magnified visual inspection under good light conditions is required. All parts of the devices should be checked for visible soil. No residual test soil shall be visible with unaided eye.

9.3.14 ACCEPTANCE CRITERIA FOR CLEANING VALIDATION

Table 17 Acceptance criteria for cleaning validation

Test	Acceptance criterion	Reference
Visual inspection	No residual test soil shall be visible with unaided eye	AAMI TIR 12
Bioburden	≥4-$\log_{10}$ for Simulated aging cleaning validation ≥3-log10 for field aging cleaning validation	AAMI TIR 30
Protein (Modified OPA-Method and BCA-Method)	<6.4 µg/cm2	AAMI TIR 30
Total Carbon Content (TOC)	<12 µg/cm2	N/A
Carbohydrate	<1.8 µg/cm2	AAMI TIR 30
Hemoglobin	<2.2 µg/cm2	AAMI TIR 30
Endotoxin	<2.2 EU/cm2	AAMI TIR 30
Radio – Nuclide Method [Company SMP]	n≤5 counts/s, considered as excellent. n<10 counts/s, considered as good.	AAMI TIR 30

Conduct the tests described in the test protocol and evaluate the results according to following acceptance criteria.

- **Microbiological method (bioburden)**

According to AAMI TIR 30 a bioburden reduction ≥ 3-log10 is a reasonable expectation. According to ASTM E2314, a bioburden reduction of 102 to 104 log10 can be produced by cleaning processes.

The history of T&E cleaning validations showed that for most non-aged devices a log reduction of ≥ 4-log10 is feasible. In order to have a safety margin between simulated aged devices to field aged devices the acceptance criteria are set as followed:

  - ≥ 4-log10 for devices excluding trays and devices in remediation process.
  - ≥ 3-log10 for field aging cleaning characterization, trays and for devices in remediation process.

- **Protein (modified OPA-Method and BCA-Method)**

Protein [AAMI TIR 30] : < 6.4 µg/ cm2

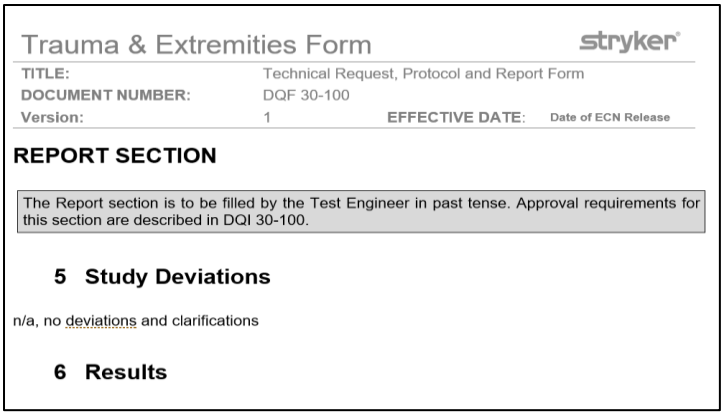
Note [AAMI TIR 30]: This acceptance criterion was evaluated on flexible endoscopes and is a reasonable starting point at present. For easily cleaned stainless steel surgical devices the benchmarks will no doubt differ from those for devices such as flexible endoscopes.

- **TOC**

No acceptance criterion is listed in the current standards. A limit of 12 µg/ cm2 should be considered. However, this value may depend heavily on the recovery rate of the test method.

9.3.15 REPORT CREATION

Report is created where all the data is compiled in it i.e- Result, conclusion, Study Deviations if any.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TITLE:	Technical Request, Protocol and Report Form		
DOCUMENT NUMBER:	DQF 30-100		
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REPORT SECTION

The Report section is to be filled by the Test Engineer in past tense. Approval requirements for this section are described in DQI 30-100.

5 Study Deviations

n/a, no deviations and clarifications

6 Results

Figure 52 Report Section in Template

9.3.16 RELEASE IN ONEPLM

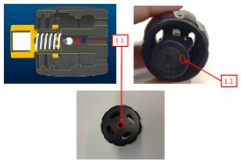
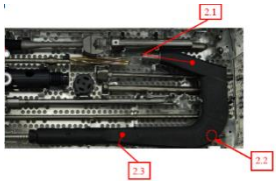
After verifying and validating the tray protocol document is released on onePLM.

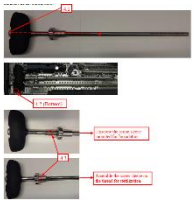
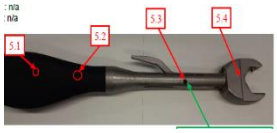
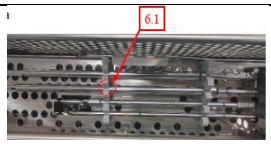
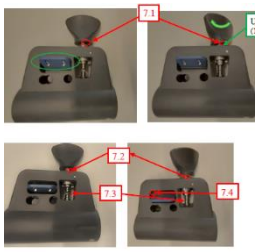
10.RESULTS

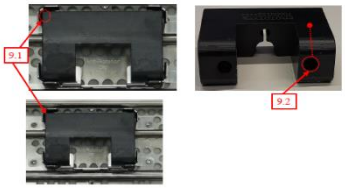
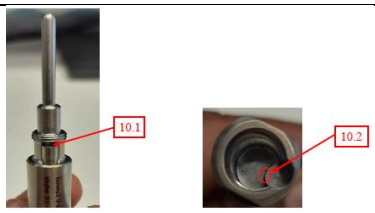
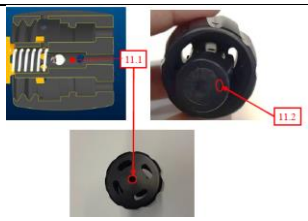
10.1 STERILIZATION VALIDATION

During incubation, test samples (instruments) were observed for presence / absence of growth. Refer the test results observation below table.

Table 18 Results of Sterilization Validation of Gamma4 Tray

Position	Name	Inoculated Sites	Images	Cycle 1	Cycle 2	Cycle 3
1.1 **1.2**	Targeting Sleeve	In the middle of the lumen In the gap		No Growth	No Growth	No Growth
2.1 **2.2** **2.3**	Plus Targeting Arm	In the middle of the lumen. On the Surface of Targeting Arm In the middle of the lumen		No Growth	No Growth	No Growth
3.1 **3.2**	Lag Screw Reamer	In the middle of the lumen Contact Surface between instrument shaft and clamping sleeve mechanism.		No Growth	Growth	No Growth

Position	Name	Inoculated Sites	Images	Cycle 1	Cycle 2	Cycle 3
4.1 **4.2** **4.3**	Leg Screwdriver	In the middle of the lumen On the Surface (Bottom, in the corner) On the Thread		Growth	Growth	No Growth
5.1 **5.2** **5.3** **5.4**	Opening Reamer Handle	On the surface of the silicon handle Contact surface instrument / Metal-Bracket In the gap of the mechanism In the gap of the mechanism		No Growth	No Growth	No Growth
6.1	Counterbore Drill, Long	Contact Surface between Instrument and PP bracket		No Growth	No Growth	No Growth
7.1 **7.2** **7.3** **7.4** **7.5**	Locking Adapter, Intermediate Nail	Gap between instrument knob /shaft (Adjusting Mechanism) Gap between instrument rod/shaft (adjusting mechanism) Between the closed gap of the upper and lower rod In the gap of chip corner. (joint; moving mechanism) In the gap of the locking pin		Growth	Growth	No Growth
8.1	Anti-Rotation Sleeve	In the middle of the Lumen (Front end)		No Growth	No Growth	No Growth

Position	Name	Inoculated Sites	Images	Cycle 1	Cycle 2	Cycle 3
9.1 **9.2**	Anti-Rotation Clip	Surface of the instrument at bottom In the blind hole		No Growth	No Growth	No Growth
10.1 **10.2**	Adapter Implant Extraction Set	In the Gap In the Blind hole of Instrument.		No Growth	No Growth	No Growth
11.1 **11.2**	Knob Mounted	In the middle of the lumen In the gap		No Growth	No Growth	No Growth
12.1	G3 Flexible Screwdriver	On the surface oriented to the silicon mat		No Growth	No Growth	No Growth

10.1.1 BACTERIOSTASIS TEST

After completion of incubation time, Bacteriostasis test was performed with test instruments, media, and whirl packs/ Nasco bags. < 100 cfu of ***Geobacillus stearothermophilus*** was transferred to test instruments media whirl packs/ Nasco bags and incubated again at 57.5 °C up to 7 days.

Deviations (if any): NA

Test Observation (If any):

For first cycle repeat test, sample location 4x (4.1, 4.2 & 4.3) Leg Screwdriver and 7x (7.1, 7.2, 7.3, 7.4 & 7.5) Locking Adapter, Intermediate Nail had shown typical growth.

A. Gram staining was performed from same sample media. ***Geobacillus stearothermophilus*** was observed as per microscopic observation i.e., Rod-shaped gram-positive organism with spores. So, the test observation confirmed **presence of *Geobacillus stearothermophilus*.**

B. 1 ml media of both samples were taken and plated using pour plates and spread plate method. The plates did not show any growth at incubation temperature 32.5°C but the plates incubated at 57.5°C had shown growth.

C. 1 ml media of both samples were taken and transferred in 10 ml fresh media and incubated at 32.5°C and 57.5°C. The media did not show any growth at incubation temperature 32.5°C but the media incubated at 57.5°C had shown growth. Growth was found settled at the bottom. Hence results are conclusive.

2. For second cycle repeat test, sample location 3x (3.1 & 3.2) Lag Screw Reamer, 4x (4.1, 4.2 & 4.3) Leg Screwdriver and 7x (7.1, 7.2, 7.3, 7.4 & 7.5) Locking Adapter, Intermediate Nail had shown typical growth (3rd day of incubation).

Below are the details of further confirmation tests to ascertain the results:

- Gram staining was performed from same sample media. ***Geobacillus stearothermophilus*** was observed as per microscopic observation i.e., Rod-shaped gram-positive organism with spore. So, the test observation confirmed **presence of *Geobacillus stearothermophilus*.**
- 1 ml media of all 3 samples were taken and plated using pour plates and spread plate method. The plates did not show any growth at incubation temperature 32.5°C but the plates incubated at 57.5°C had shown growth.
- 1 ml media of all 3 samples were taken and transferred in 10 ml fresh media and incubated at 32.5°C and 57.5°C. The media did not show any growth at incubation temperature 32.5°C but the media incubated at 57.5°C had shown growth. Growth was found settled at the bottom. Hence results are conclusive.

3. For third cycle repeat test, all test locations did not shown growth after completion of incubation period.

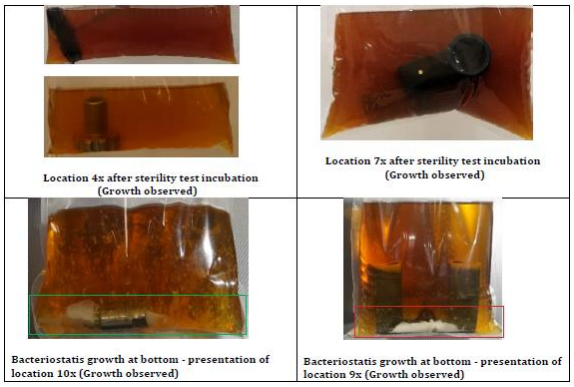


Figure 53 Results after incubation period – Growth

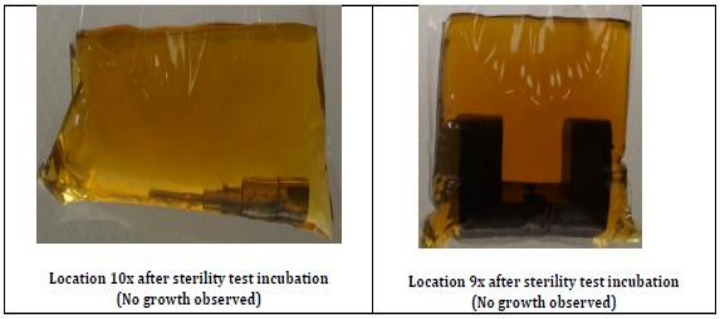


Figure 54 Results after incubation period – No Growth

- Three sterilization repeat tests were performed with the test tray and instruments. Refer below points for conclusion: 5.1. For first cycle repeat test, sample location 4x (4.1, 4.2 & 4.3) Leg Screwdriver and 7x (7.1, 7.2, 7.3, 7.4 & 7.5) Locking Adapter, Intermediate Nail did not meet test acceptance criteria.
- For second cycle repeat, sample location 3x (3.1 & 3.2) Lag Screw Reamer, 4x (4.1, 4.2 & 4.3) Leg Screwdriver and 7x (7.1, 7.2, 7.3, 7.4 & 7.5) Locking Adapter, Intermediate Nail did not meet test acceptance criteria.
- For third cycle repeat test, met the test acceptance criteria.
- Few additional test cycles we performed in which all instruments did not showed any growth and were passed.

10.2 RESIDUAL MOISTURE TEST

MMT Gamma 4 indication tray, the residual moisture testing (screening test) after double wrapping with Sterisheet and followed by moist heat (steam) sterilization. Test item was conditioned at 23°±2°C in lab during the test and was positioned alone in the center/low position inside the sterilizer. Tray weight was taken with and without wrap before sterilization, after 5 minutes of sterilization with wrap and after 60 minutes (cumulative) of sterilization with wrap. After 60 minutes wrap tray was open, and instruments were visually observed for presence / absence of residual moisture.

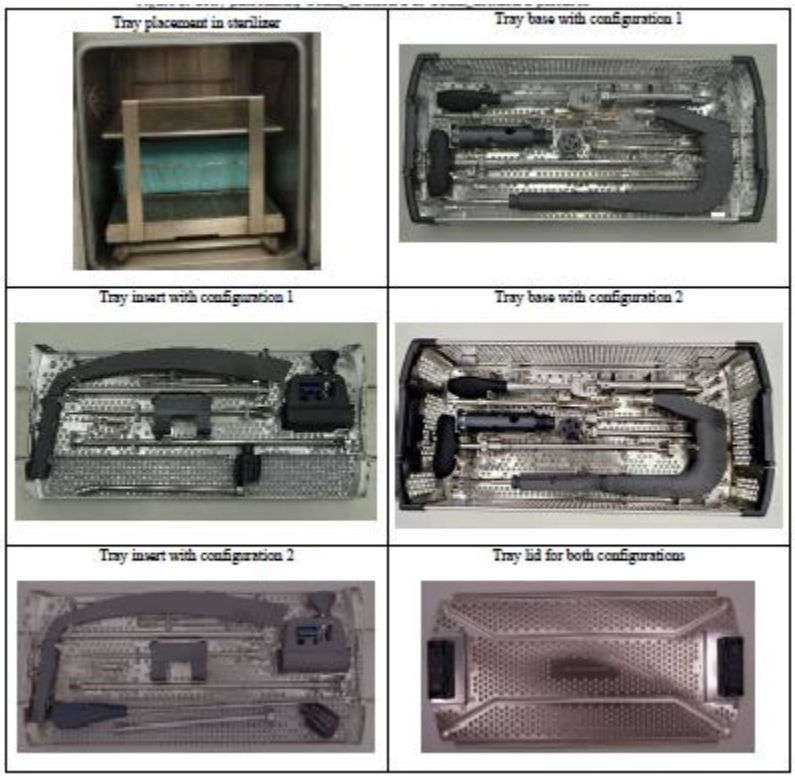


Figure 55 Tray Placement in Configuration 1&2

Results:

Note-: M0- Test sample initial weight without wrap. M1- Test sample weight before sterilization, M2- Test sample weight after 5 minutes of sterilization, M3- Test sample weight after cumulative 60 minute of sterilization.

Table 19 Results for Configuration 1

Configuration 1: Cycle repeat #	M0 (Kg)	M1 (Kg)	M2 (Kg)	M3 (Kg)	Relative mass change after 5 minutes of sterilization $\Delta m = \frac{m2 - m1}{m1} \times 100\%$	Relative mass change after cumulative 60 minutes of sterilization $\Delta m = \frac{m3 - m1}{m1} \times 100\%$	Moisture Results	
							Observation Moisture	Surface Presence
Cycle-1	9.829	10.018	10.011	10.012	-0.06 %	-0.05 %	1. Outer Wrap 2. Inside Tray 3. Inner wrap 4. Outside Tray 5. Instruments	No
Cycle-2	9.829	10.019	10.019	10.015	0.00%	-0.03%		
Cycle-3	9.829	10.020	10.020	10.016	0.00%	-0.03%		

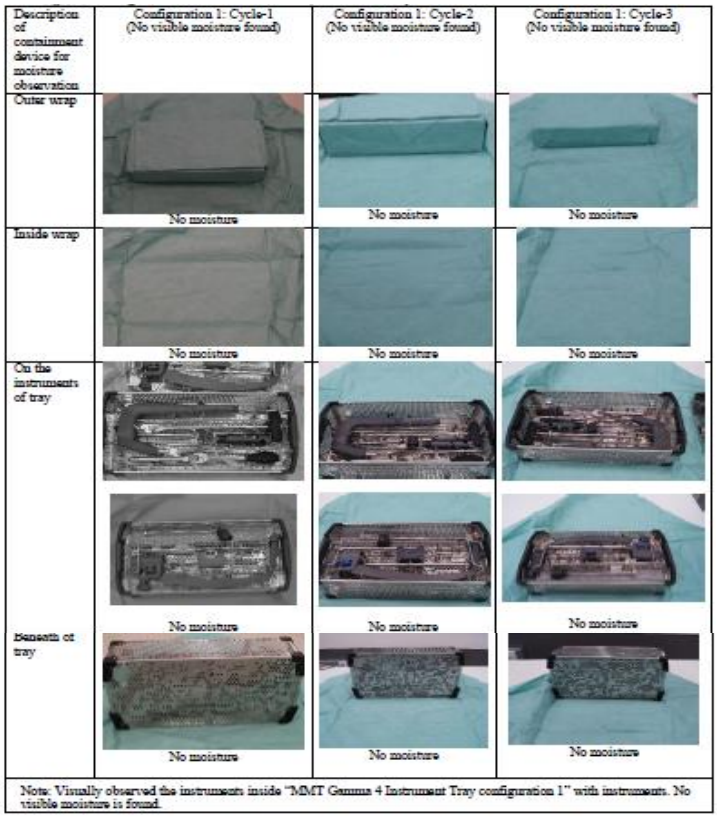


Figure 56 Result showing No Residual Moisture for Configuration 1

Table 20 Results for Configuration 2

Configuration 2: Cycle repeat #	**M0 (Kg)**	**M1 (Kg)**	**M2 (Kg)**	**M3 (Kg)**	**Relative mass change after 5 minutes of sterilization** $\Delta m = \frac{m2 - m1}{m1} \times 100\%$	**Relative mass change after cumulative 60 minutes of sterilization** $\Delta m = \frac{m3 - m1}{m1} \times 100\%$	**Moisture Results**	
							Observation Moisture	**Surface Presence**
Cycle-1	9.925	10.116	10.105	10.109	-0.10 %	-0.06 %	1. Outer Wrap 2. Inner wrap 3. Inside Tray 4. Outside Tray 5. Instruments	No
Cycle-2	9.925	10.117	10.113	10.111	0.03%	-0.05%		
Cycle-3	9.925	10.116	10.113	10.111	0.02%	-0.04%		

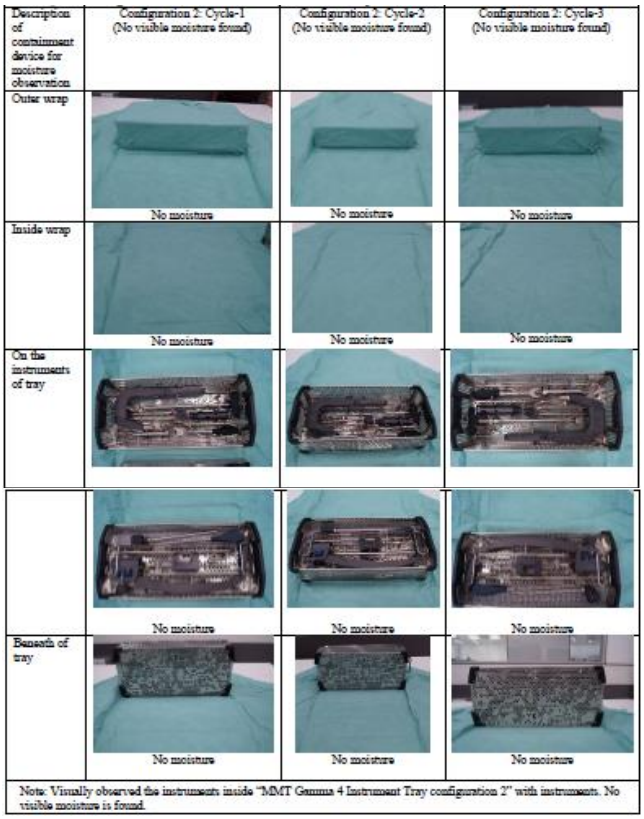


Figure 57 Result showing No Residual Moisture for Configuration 2

Acceptance Criteria

- Total increase of mass of maximal 0.2%.
- No visible moisture on containment device.

Test Observation:

- Total increase of mass of maximal was found less than 0.2% in all configurations.
- No visible moisture was found on containment device in all configurations.

10.3 CLEANING VALIDATION

A tray is a legacy product in Stryker on which all the cleaning tests were already performed. So, after comparing all the features with the existing trays gamma4 tray tests were adopted and no cleaning validations were performed on the tray.

11.CONCLUSION

Medical devices are boon to the mankind but can become bane if quality is compromised of medical devices. Quality plays a major role for any medical device company and to achieve its benchmark, they must go through numerous quality checks, processes, inspections, that involve various testing while if quality is not accounted it could affect humans in very hazardous manner.

In order to develop and release a device certain quality developmental procedures like design control (waterfall model) with many guidelines and standards are considered. Gamma4 Tray is a reusable tray which consists of various Instruments like Plus Targeting Arm, Lag Screw Reamer, Lag Screwdriver, Anti-Rotation Clip, and many more which is used for Hip fracture treatment. So, Gamma4 also went through developmental phase and then through quality check in which it was validated on all the aspects like sterilization, cleaning & disinfection and Residual Moisture Test.

Steam Sterilization protocols were executed, and the results confirmed that it is within the specifications and has qualified as per quality standards.

Similarly for **Cleaning validation** protocols were released as per Stryker procedures and when executed, they were conforming to the cleaning and disinfection specifications as stated in the Cleaning, Sterilization, and Maintenance Guide which is sent to our customers with the tray.

In addition to sterilization and cleaning, **Residual Moisture Testing** was also conducted as per the standards and the executed reports were reviewed which were deemed acceptable and they were within the specification as per standards.

All tests which were executed as the part of project have passed all the quality parameters according to the regulations and considering all standards. While in addition to this, in 2022, Gamma4 Tray is launched in the market helping customers to rebuild their lives.

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