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PROTOCOL APPROVAL PAGE

PROTOCOL #	**PRC096898**	**REVISION:**	**A**	**DATE:**	**06/29/2020**
COMPLETION REPORT #	**PRC096899**	**MVP, ECP, DP or SPCR#**		**ECR0001689**	

TITLE:	**Gamma Sterilization Validation for Mimas Blade and Needle Products Due to Manufacturing Transfer**				
PROJECT NAME:	**Mimas**	**PROJECT LEADER:**	**Rafael Palma**		
Product Code:	See Scope Section	**Product Number:**	N/A	**Batch Number(s):**	**PRC096476**

PROTOCOL INFORMATION			
ORIGINATOR:	**Tim Achuff**	**PHONE NUMBER:**	
ORIGINATOR TITLE:	**Sterilization Sciences**	**SITE:**	**Cincinnati**

PRIORITY STATUS (Specify Document Due Date):	**N/A**

Protocol Document Type and Approval Governance				
Type:	**Protocol -Sterilization Validation**			
Organization Responsible - Governance	☐ **New Product Development** Pre-Launch/Stabilization (CP0258 or CP0150 if applicable)	☒ **Lifecycle Engineering** Post Stabilization (CP0150 if applicable)	☐ **External Manufacturing** (CP0231/CP0150)	☐ **Other**

APPROVAL LIST:

Function	Name	User I.D.	Signature/Date
ORIGINATOR	Tim Achuff	tachuff	eSig in EPICENTER
Franchise Sterilization Sciences	Ravi Patel	rpatel51	eSig in EPICENTER
Lifecycle Design Manager	Thomas No	tno	eSig in EPICENTER
Lifecycle Quality Engineer	Ihsan Samara	Isamara	eSig in EPICENTER

DISTRIBUTION LIST: N/A

NOTE: (Juarez Only): N/A

Revision	Change Description
A	Original Document

1.0 PURPOSE

1.1 To qualify the Megadyne EZ Clean Blade and Needle Products transferred to Independencia, Juarez for manufacturing, for Gamma sterilization as follows:

- the Steris Salt Lake City, UT facility, Processing for a gamma sterilization dose of 25kGy with a maximum exposure of 40 kGy

The successful completion of this protocol will qualify the Megadyne EZ Clean Blade and Needle device group for continued sterilization at the Steris, SLC sterilization facility.

Irradiation dose audit studies for this protocol shall be performed at Jabil, Albuquerque.

1.2 The following tests will be performed in accordance with the instructions in this protocol to qualify the Megadyne EZ Clean Blade and Needle Products for Gamma sterilization:

1.2.1 Bioburden Testing – To establish baseline bioburden data that is representative of the production manufacturing process (product and packaging) for guidance in establishing a verification dose.

1.2.2 Product Sterility Testing – The blade device shall be irradiated at the audit dose following the VDmax protocol, based on the recovered bioburden. The device will be removed from packaging, placed in liquid median and incubated whole.

1.2.3 Bacteriostasis and Fungistasis (B&F) Testing – To provide evidence that leachables (if any) do not adversely impact the validity of the sterility test method.

2.0 SCOPE

2.1 This protocol will be executed using 59, Product Code 0014 blade devices. The 0014 is 6.5in design which presents the largest size and surface area, and thus is the worst-case gamma-sterilized representative of the final production design and production manufacturing process for the products being transferred in Phase 1. Additional products in future phases shall be evaluated separately.

2.1.1 The Megadyne EZ Clean Blade and Needle devices are single-use electro surgical tools currently qualified for Gamma sterilization by cobalt-60 irradiator.

2.1.2 Each of the 0014 blade devices shall be packaged in a pouch that serves as the sterile barrier. A shelf box is used to contain the instructions for use, pouch, and product.

2.1.3 The 0014 blade devices shall be built and packaged in the final manufacturing facility on the production manufacturing equipment. The results of this protocol are applicable to all Megadyne EZ Clean Blade and Needle Products listed in section 2.3.

2.2 This protocol will test a minimum of 59, Product Code 0014 blade devices utilizing the bioburden-based audit dose to establish that the indigenous bioburden is not more resistant than the VDmax model bioburden.

2.3 The protocol applies to the following product codes in this family of products:

0012, 0012A, 0013, 0014, 0014A, 0018, 0018A

3.0 CRITERIA FOR SUCCESS

3.1 An average bioburden estimates of less than 1000 CFUs shall be determined for the 0014 blade device.

3.2 Product sterility samples exposed to the audit dose shall be incubated.

3.2.1 No more than one (1) positive sample for growth is acceptable and shall confirm the dose .

3.2.2 If two samples are positive, a confirmatory dose verification experiment at the same dose shall be performed. All samples shall be negative for growth.

3.2.3 Two or more positive samples from the initial experiment, or one or more samples from the confirmatory experiment are positive, the dose is not substantiated

3.3 The B&F testing shall exhibit growth within 5 days for *B. subtilis, C. albicans* and *A. brasiliensis* in SCDB. Current bioburden data have demonstrated no significant anaerobes and so FTM shall not be used. Growth between the control and test sample shall be comparable.

4.0 REFERENCE DOCUMENTS

4.1 ISO 11137:2006 – Part 1: Sterilization of Health Care Products – Radiation – Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process for Medical Devices

4.2 ISO 11137:2006 – Part 2: Sterilization of Health Care Products – Radiation – Part 2: Establishing the Sterilization Dose

4.3 ISO 11137:2006 – Part 3: Requirements for Development, Validation, and Routine Control of a Sterilization Process for Medical Device

4.4 AAMI/TIR-27 - Radiation Sterilization-Method VDmax

5.0 EQUIPMENT AND MATERIALS

5.1 Equipment and materials at Jabil, Albuquerque, NM (or similar gamma irradiator), are documented within their quality system and will not be documented within this protocol.

5.2 Equipment and materials at Nelson Laboratories are documented within the Nelson Laboratories quality system and will not be documented within this protocol.

6.0 RESPONSIBILITIES

6.1 Cincinnati Sterilization Sciences

6.1.1 Protocol coordination and analysis of the results.

6.2 Megadyne/Ethicon Juarez Team

6.2.1 Responsible to provide product samples which meet the requirements listed within this protocol.

6.3 Sterilization Contactor (Jabil, Albuquerque, NM or similar gamma irradiator)

6.3.1 Responsible for the execution of the fractional sterilization runs and any tests that are requested within this protocol.

6.4 Nelson Laboratories

6.4.1 Responsible for testing of requested samples

7.0 STRATEGIES AND ASSUMPTIONS

7.1 This validation is being conducted within the EES quality system on behalf of Megadyne as

enabled by the Inter Company Quality Agreement documented per Adaptiv document number 100571196. EES is performing the dose audit per WE0180 and ISO 11137-2 using Method VDmax substantiation of 25kGy from multiple production batches which is the same method used by Megadyne currently.

7.2 The successful completion of this protocol will qualify that a 25kGy sterilization dose shall result in a minimum sterility assurance level (SAL) of 10^{-6} for the Megadyne EZ Clean Blade and Needle Products that are manufactured by Ethicon in the Juarez facility.

7.3 Test samples for the audit dose, B&F, and bioburden studies will be built per the routine manufacturing production and will be representative of the final product design and packaging. No special processing is required for the product prior to packaging.

7.2.1 "NOT FOR HUMAN USE STICKERS" must not be placed directly on the devices as this is not part of routine production and not representative of the routinely manufactured devices.

7.4 Products only need to be manufactured up to packaging in the primary packaging. Once within this packaging, there is no potential for further bioburden contribution to the device via the manufacturing process and therefore, no further manufacturing steps are required or can proceed using non representative processes.

7.5 A batch will be defined as product produced in a continuous flow. A new batch is created by purging and cleaning the line before starting a new flow of devices. This will be adequate in representing variability in bioburden as a result of equipment, associates, line change-out, and the controlled manufacturing environment.

7.6 Additionally while products for this validation are not required to be functional because the functionality of the device does not impact the bioburden load or the potential bacteriostatic / fungistatic effects of the device, the products are required to be processed through all handling, in-process inspection and testing, assembly and packaging processes that would impact the microbial load on the device when it is routinely manufactured. **NOTE**: *see 7.2.1 above*

7.7 All products for this protocol will be built on the production equipment in the final production environment using the production procedure and techniques. This will assure that the bioburden on the device is representative of bioburden that will be present on the production device. Subassembly components and the component suppliers are to be those that will be utilized for routine manufacturing. This will assure bioburden contributed via the vendor is representative of routine manufacturing.

7.8 The batch must have manufacturing traceability.

8.0 TRAINING

8.1 Training for Jabil, Albuquerque, NM (or similar gamma irradiator) and Nelson Laboratories is covered under their quality system and will not be documented in this protocol. Training will be performed for those individuals who did not approve this protocol but were involved in the execution of the study.

9.0 PREREQUISITES

9.1 59 samples will be built per PRC096467A according to the requirements indicated in the strategies and assumptions section within this protocol. Samples shall be dispositioned in the following manner

9.1.1 Thirty (30) units in three batches of ten (10) each for bioburden
9.1.1.1 Batch 1: 10 devices
9.1.1.2 Batch 2: 10 devices
9.1.1.3 Batch 3: 10 devices

9.1.2 Twenty-nine (29) units from Batch 1, 2 or 3 for inoculated bioburden recovery, audit dose, and B&F testing.

10.0 PROCEDURE

10.1 Requested samples will need to be built per PRC096467A and forwarded to Cincinnati Sterilization Sciences.

10.2 Cincinnati Sterilization Sciences will label devices and allocate to the following studies:

10.2.1 Thirty (30) units in three (3) batches of ten (10) each for bioburden

10.2.2 Twenty-nine (29) units from Batch 1, 2 or 3 for inoculated bioburden recovery, audit dose, and B&F testing.

10.3 Bioburden Testing:

10.3.1 A total of thirty (30) products will be provided non-sterile and tested to determine bioburden. The products will come from three (3) batches, ten (10) products from each batch.

10.3.2 Indigenous bioburden levels are anticipated to be quite low; therefore, Nelson Labs shall perform a Bioburden Recovery validation performed by inoculation. This value shall be used for calculating the final bioburden.

10.3.2.1 Five (5) samples from one of the three batches shall be provided for the bioburden recovery validation.

10.3.2.2 Nelson Labs shall inoculate the devices with <100CFU of organisms and extract the bioburden using the same method as the bioburden samples.

10.3.3 The products will be forwarded to Nelson Laboratories to be tested at the following address. The product must at the very least be within its primary packaging. **Note:** Do not place “NOT FOR HUMAN USE” labels on the devices.

10.3.3.1 A Nelson Laboratories Sample Submission Form must be sent with the samples. This form will be generated by Ethicon Cincinnati Sterilization Sciences.

Log-in/Check-in
Nelson Laboratories
6280 Redwood Road
Salt Lake City, UT 84123
801-290-7500

10.3.4 Nelson Laboratories will use the product whole without disassembly for the bioburden extraction. No manipulation is required.

10.3.5 Nelson laboratories will extract the bioburden from the device using the following steps:

10.3.5.1 Equipment: 2" reciprocating (horizontal) shaker

10.3.5.2 Direction of container: Container cap end facing shaking direction

10.3.5.3 Shaking time: 10 minutes

10.3.5.4 Extraction Fluid: Sterile 0.1% peptone with 0.1% tween80/polysorbate 80

10.3.5.5 Test requirements: Aerobic and Fungal counts

10.3.5.6 Transfer method: Membrane Filtration

10.3.6 Transfer the culture to medium through membrane filtration. Assure a plating factor/detection limit of no greater than 3 CFU/device.

10.3.7 Test both for aerobic and fungal counts:

10.3.7.1 Aerobic – Trypticase Soy Agar – incubation time of 3-7 days and temperature of 30- 35°C

10.3.7.2 Fungi – Sabouraud Dextrose Agar – incubation time of 5-7 days and temperature at 20-25°C.

10.3.8 Calculate the bioburden average for each batch.

10.4 Audit Dose Testing:

10.4.1 The audit dose shall be chosen after the bioburden testing has been completed.

10.4.2 A total of 24 products from one of the three batches will be irradiated at the audit dose ±10%.

10.4.2.1 Ten (10) units shall be tested for sterility.

10.4.2.2 Three (3) additional samples shall be sent for B&F testing.

10.4.2.3 A redundant set of ten (10) products along with one (1) extra product shall be provided if confirmation testing is required or a sample becomes contaminated.

10.4.3 The samples will be forwarded to the Contract Irradiator:
Contract Irradiator: Jabil, Albuquerque, NM or similar gamma irradiator

10.4.4 Responsible to irradiate the twenty-four (24) products through the audit dose.

10.4.5 Immediately following the sterilization run, the sterilized samples will be shipped to Nelson Laboratories via overnight priority to be placed on test at the following address.

Log-in/Check-in Nelson
Laboratories
6280 Redwood Road
Salt Lake City, UT 84123
801-290-7500

10.4.6 Upon receipt of the products Nelson Laboratories shall place the devices on

test. The device is tested whole and requires no special manipulation.

10.4.6.1 Incubation conditions – Ten (10) devices

10.4.6.1.1 Ten (10) devices are to be placed in Soybean Casein Digest Broth (SCDB). Incubate for 14 days at 30-32°C

10.4.7 Observe for the evidence of growth for each sample.

10.4.8 If positive growth is observed in the sterility samples, an investigation shall be performed to determine if the growth is evidence of contamination or if the organisms are survivors.

10.4.8.1 If the growth is determined to be contamination, no further testing is required. Proceed to B&F

10.4.8.2 If the observed growth is evidence of surviving organisms or if the investigation is inconclusive, a second set of ten (10) units may be used for confirmation testing (in the event the number of positives is equal to 2).

10.4.8.3 Confirmatory sterility testing shall proceed in the same manner as for the initial audit does test

10.5 B&F Testing:

10.5.1 A total of three (3) products will be tested. The products can be from batch 1, 2, or 3. Samples used for the B&F study shall be samples that have already been exposed to the verification dose.

10.5.2 Immediately following the sterilization run the sterilized samples will be shipped to Nelson Laboratories via overnight priority to be placed on test at the following address.

10.5.3 Upon receipt of the devices at Nelson Laboratories the appropriate media volume will be calculated. This volume should be appropriate and be able to represent the media volume being used for the test of sterility.

Log-In/Check-In
Nelson Laboratories
6280 Redwood Road
Salt Lake City, UT 84123
801-290-7500

10.5.4 Nelson laboratories should place 3 devices in SCDB. Each container should be inoculated with <100 CFU of organisms. Control containers of SCDB shall also be inoculated with <100CFU of organisms. All containers shall be incubated at 28-32°C.

10.5.5 Nelson Labs shall inspect the containers for signs of growth. All containers must be positive for growth and the growth shall be comparable between the test container and the control container.

11.0 PRODUCT DISPOSITION

11.1 All testing for this study is destructive. Following testing Nelson Laboratories will dispose of any components that remain. Any unused samples may be returned to Cincinnati Sterilization Sciences.

11.2 Extra devices that were retained by Cincinnati Sterilization Sciences may be returned to the Mimas team or destroyed upon successful completion of all testing outlined in this protocol.

12.0 INVENTORY STRATEGY

12.1 N/A

13.0 COMPLETION ACTIVITIES

13.1 Cincinnati Sterilization sciences will analyze the data generated through the execution of this protocol's requirements.

13.2 Cincinnati Sterilization sciences will compile all data and generate a completion report for this protocol.

14.0 APPENDICES

14.1 N/A