RESEARCH

Challenges to Validation Of a Complex Nonsterile Medical Device Tray

Daniel Prince, Jozef Mastej, Isabel Hoverman, Raja Chatterjee, Diana Easton, and Daniela Behzad

About the Authors

Daniel Prince, PhD, is president of Gibraltar Laboratories, Inc. E-mail: danielprince@gibraltarlabsinc.com

Jozef Mastej is vice president of Gibraltar Laboratories, Inc. E-mail: jmastej@gibraltarlabsinc.com

Isabel Hoverman is a quality engineer at Orthofix. E-mail isabelhoverman@Orthofix.com

Raja Chatterjee is director of product quality at Orthofix. E-mail: rajachatterjee@Orthofix.com

Abstract

Validation by steam sterilization of reusable medical devices requires careful attention to many parameters that directly influence whether or not complete sterilization occurs. Complex implant/instrument tray systems have a variety of configurations and components. Geobacillus stearothermophilus *biological indicators (BIs) are used in overkill cycles to to simulate worst case conditions and are intended to provide substantial sterilization assurance. Survival of* G. stearothermophilus *spores was linked to steam access and size of load in the chamber. By a small and reproducible margin, it was determined that placement of the trays in a rigid container into minimally loaded chambers were more difficult to completely sterilize than maximally loaded chambers.*

Introduction

Reprocessing of medical device trays routinely is performed in hospitals or other centers based on instructions provided by the manufacturer. Validation of the tray systems is performed by the manufacturer and is registered by the U.S. Food and Drug Administration (FDA). Reprocessing involves the cleaning and steam sterilization of all of the components that are included in the tray system. Reprocessing allows the tray systems to be safely used many times without risk of infection to the patient. Millions of procedures are performed each year. For example, the number of hip and knee replacements performed in the United States yearly is currently over one million and is expected to surpass four million by the year 2030.[1]

Instructions for use (IFUs) and all of the data supporting them are shared with the FDA in a validation package intended to support the clearance of a 510K. The criterion for acceptance that is most often followed is published in ST79.[2] Before testing began, a detailed protocol was written that described the tray system in terms of the instruments present and type of container or wrap that is to be used when placing the tray into the steam sterilizer. Two systems are commonly employed: 510(K)-cleared hospital wrap and rigid container. Biological indicators (BIs) are positioned in the tray in the areas judged to be the most difficult to sterilize. All BIs must be killed after an exposure to 132°C for a two-minute half cycle. BI survival is determined by incubation in suitable bacteriological broth such as soybean casein digest broth at 55°C to 60°C for seven days. If no turbidity is observed, the IFU is written to require a full cycle four-minute exposure at 132°C which is taken to mean that a 12 log spore reduction will occur during routine sterilization. Alternatively, the validation may

be performed quantitatively wherein the actual number of surviving spores in the BI is enumerated directly from a four-minute full cycle exposure at 132°C.[3]

Methods

A family[4] of 14 implant/instrument trays was screened to select the tray system most difficult to sterilize by moist heat steam sterilization. Selection of the trays was based upon their density, complexity of medical devices (instruments/implants), the number of levels, configuration and weights. An FDA-cleared 510(K) Getinge USA Validated 275-liter Hospital Sized Pulsed Pre-vacuum (known as Dynamic-Air-Removal) Autoclave was used in this study.[5] The trays were subjected to heat penetration[6] evaluation and half- cycle qualification at 132°C for two minutes in both a minimally loaded and maximally loaded sterilization chamber. Upon selection, the validation tray was further exposed to two-minute half-cycles and four-minute full-cycles at 132°C. The validation tray consists of three levels containing 40 reusable instruments (Figures 1-3). Heat penetration item mapping of the tray system loaded in the steam sterilizer and determination of the sterilization chamber's cold spot was performed with NIST traceable thermocouples (Table 1). The validation tray was evaluated under both half[2] and full-cycle[3] exposure times, in both a minimally and maximally loaded chamber and as wrapped in hospital wrap or placed in a rigid container. Validation was based on three independent cycles. Biological verification of steam sterilization[7,8,9] was by sterility testing the BIs after sterilization in soybean casein digest broth for seven days at 55°C to 60°C as per USP.[10] Each instrument was fitted with *Geobacillus stearothermophilus* BI (ATCC # 7953, Lot # S83703; population 1.4 x 106 spores per 2 mm x 10 mm paper strip, D121-value 1.8 minutes, Z-value 9.2°C [based on 119°C, 121°C and 130°C exposures], NAMSA, REF/Product Code: STS-062). Verification of the BI population and identification with the Vitek Compact 2 was per USP.

Results

Positive BI results were obtained in two tray systems (Table 1). Heat penetration (Tables

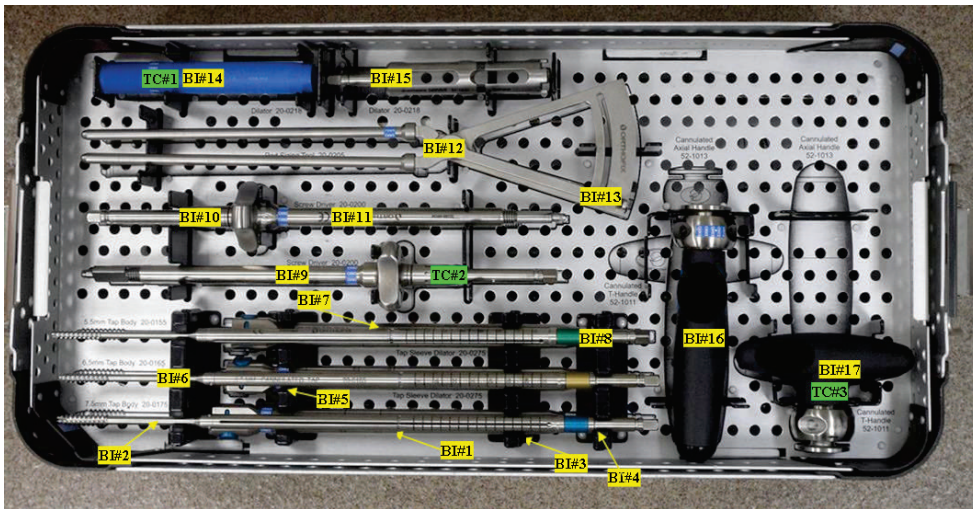


Figure 1. Upper Level of the Validation Tray

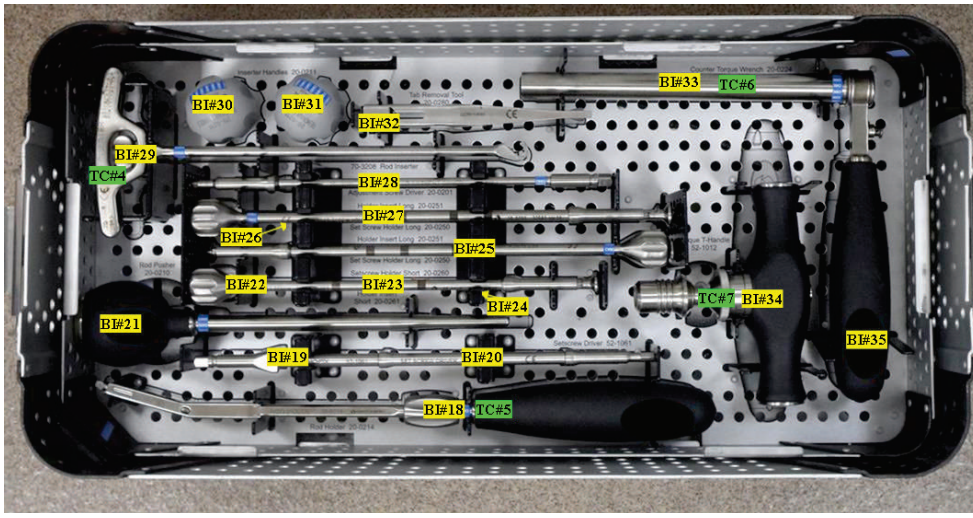


Figure 2. Middle Level of the Validation Tray

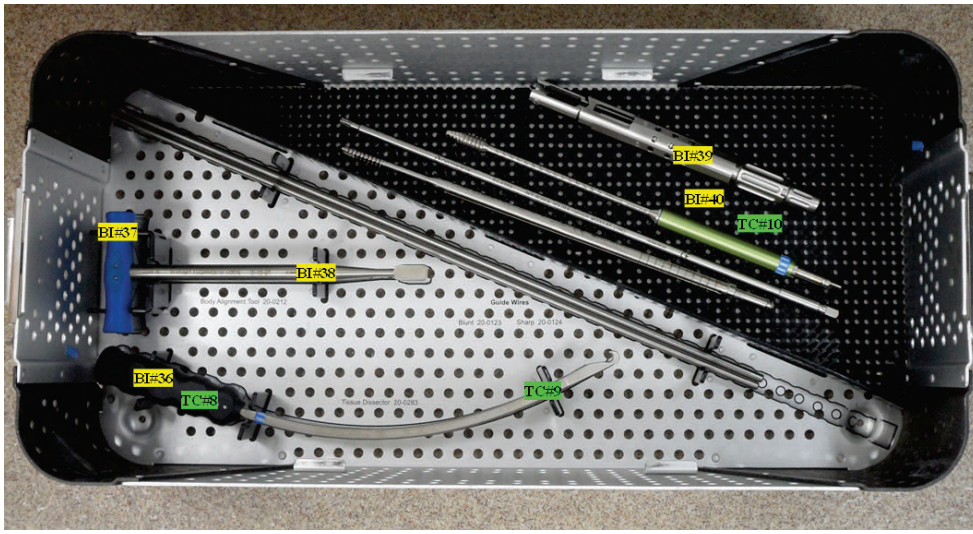
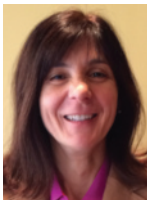


Figure 3. Bottom Level of the Validation Tray

About the Authors

Diana Easton is the vice president of quality and regulatory affairs at Orthofix. E-mail dianaeaston@Orthofix.com



Daniela Behzad is senior design assurance mechanical engineer for Orthofix. E-mail: dbehzad@orthofix.com

1-2) was equivalent for all 14 trays at 132 ± 2°C except in one location where the temperature was 127.1°C for the minimum load in Tray 1. Tray 1 also had the longest maximum load cycle time. Based on all of the evidence it was selected as the validation tray to represent the family for evaluation of placement inside a rigid container instead of wrapped in hospital wrap. Its density and weight was 0.018 lb/in3 and 23.5 lbs, respectively (Table 1). After incubation at 55°C, the same locations as in the screening study were again not completely sterilized in both maximum and minimum load configurations (Figure 4 a, b). The BI that was not sterilized was located in the middle of the three level tray system underneath a knob handle (Figure 2). When full-cycle four-minute exposure[3] sterilization was performed using hospital wrap, all locations were sterile as no survivors were detected (Figure 5) in both the minimum and maximum load configurations. When this study was repeated in a rigid container complete sterilization was accomplished in all three maximum loads and in two of the three minimum loads. Twelve spores were recovered from a single instrument when the above complete sterilization did not occur.

See Tables 1–2 and Figures 1–5.

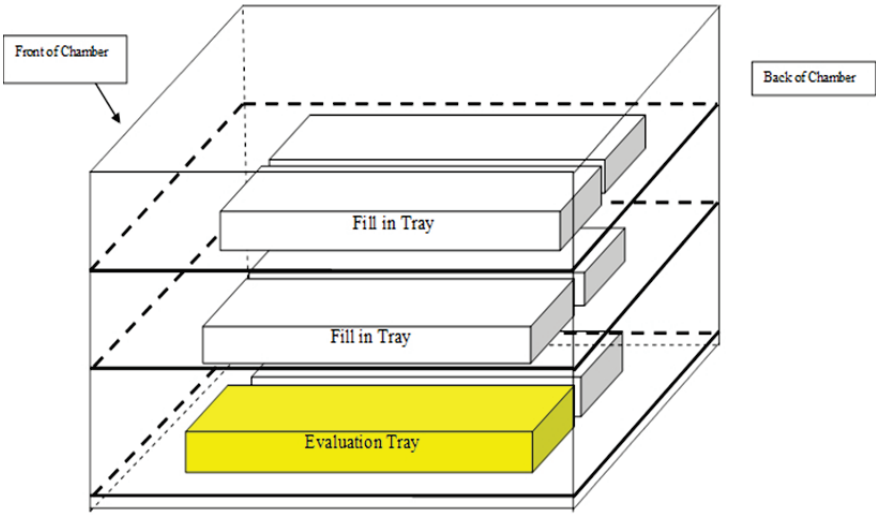


Figure 4a. Maximum Load. Validation tray was placed in chamber cold spot. The chamber volume is 275 liters. The Validation Tray was fully loaded and placed on the right side of the bottom shelf (chamber cold spot). Five additional fully loaded fill-in trays were also inside the chamber.

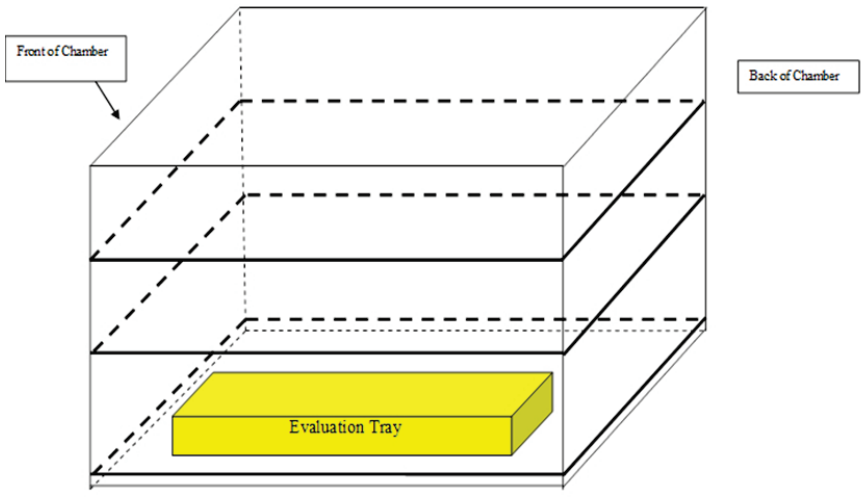


Figure 4b. Minimum Load. The validation tray was fully loaded placed on the right side of the bottom shelf chamber cold spot.

Discussion

Selection of the worst-case tray systems with respect to accomplishing validation of terminal moist heat sterilization is predicated on the use of biological indicators, heat penetration, and steam access. No one single parameter is sufficient to determine worst case. Critical parameters are tray design, instrument selection and location, density within the tray system, and tray system weight. Here we report how chamber load and rigid containers also are strong influencers of sterilization effectiveness. The significance of the findings is that equivalent results are obtained using rigid containers and hospital wrap under both maximum and minimum load condition because all 39 instruments that have patient contact were completely sterilized in 3/3 half-cycle sterilization runs using half-cycle qualification as per ST79[2] and full-cycle Fbio testing as per ANSI/AAMI/ISO 17665-1.

Fbio is a term used to describe the delivered lethality, measured in terms of actual kill of microorganisms on or in a BI challenge system. The Fbio value is calculated as DT x LR, where DT is the D value of the BI system at the reference temperature (T) and LR is the actual logarithmic reduction (log N0 – log NF) of the BI population achieved during the cycle.

The Half-Cycle Qualification is a qualification method that uses 50% of the exposure time to demonstrate sterilization cycle efficacy. The physical and biological lethality values achieved in the half-cycle exposure time are doubled to project the lethality that will be achieved by the full cycle. The

Tray	Wt (lbs)	Load Config.	Cycle Time (min.)	Temperature mapping [Avg.°C]										BI
				TC01	TC02	TC03	TC04	TC05	TC06	TC07	TC08	TC09	TC10	Result
1	23.5	Max	38.1	132.2	132.1	131.5	132.1	132.3	132.2	132.5	132.3	132.6	132.6	+
		Min	18.5	132.1	132	127.1	132	132.2	132.1	132.4	132.3	132.7	132.6	+
2	24	Max	35.2	132.3	132.1	132.3	132.1	132.3	132.2	132.5	132.3	132.7	132.7	-
		Min	19.4	132.2	132.2	132.4	132.2	132.3	132.3	132.5	132.3	132.8	132.8	-
3	20.8	Max	35	132.1	132.1	132.3	132.2	132.4	132.3	132.5	132.4	132.8	132.9	-
		Min	19.5	132.3	132.2	132.3	132.1	132.3	132.2	132.4	132.3	132.6	132.7	-
4	19.7	Max	34	132.2	132.1	132.3	132.1	132.3	132.2	132.5	132.3	132.8	132.8	-
		Min	18.2	132.3	132.1	132.3	132.1	132.3	132.2	132.5	132.3	132.7	132.7	-
5	8.5	Max	33.2	132.5	132.4	132.5	132.3	132.4	132.4	132.6	132.5	132.9	133	-
		Min	16	132.4	132.3	132.4	132.3	132.4	132.4	132.6	132.4	132.9	132.9	-
6	22	Max	34.5	132.2	132.1	132.2	132.1	132.3	132.3	132.6	132.4	132.9	132.9	-
		Min	18.3	132.1	132	132.2	132.1	132.3	132.3	132.6	132.4	132.9	132.9	-
7	26.75	Max	33.5	132.2	132.2	132.3	132	132.4	132.3	132.6	132.4	132.8	132.8	+
		Min	19.4	132.3	132.2	132.2	131.9	132.3	132.3	132.5	132.2	132.6	132.6	+
8	24.95	Max	33.1	132.4	132.3	132.4	132.3	132.4	132.4	132.5	132.4	132.9	133	-
		Min	18.2	132.3	132.2	132.3	132.2	132.4	132.3	132.3	132.3	132.8	132.8	-
9	22.8	Max	35.4	132.3	132.2	132.3	132.2	132.4	132.3	132.7	132.5	132.9	133	-
		Min	18.2	132.1	132.2	132.4	132.3	132.5	132.5	132.8	132.6	133	133.1	-
10	26	Max	33.3	132.2	132.1	132.3	132.2	132.1	132.4	132.7	132.6	133.1	133.2	-
		Min	19.2	132.1	132.2	132.4	132.3	131.5	132.5	132.6	132.5	132.9	133	-
11	14.35	Max	36	132.2	132.2	132.4	132.2	132.4	132.5	132.7	132.6	133	133.1	-
		Min	18.2	132.2	132.1	132.2	132.1	132.3	132.3	132.6	132.4	132.8	132.9	-
12	20.55	Max	33.3	132.1	132.2	132.4	132.3	132.4	131.7	132.6	132.6	132.9	132.9	-
		Min	17.5	132.3	132.3	132.4	132.2	132.5	132.4	132.7	132.5	132.9	132.9	-
13	30.6	Max	36.4	132.4	132.3	132.4	132.3	132.4	132.4	132.7	132.5	132.9	133	-
		Min	17	132.3	132.3	132.3	132.2	132.5	132.4	132.7	132.4	132.9	132.9	-
14	8.9	Max	32.5	132.2	132	132.2	132	132.4	132.4	132.6	132.5	132.9	132.9	-
		Min	17	132.3	131.3	132.3	132	132.5	132.5	132.7	132.5	133	133	-

Table 1. Fourteen tray systems were evaluated to select the validation tray. Tray 1 was selected as the validation tray.

TC #	Location	Rationale
Upper Section of the Tray (Figure 1)		
1	Dilator	Placed inside the lumen (cannulation) at the mid-point of the instrument; potentially difficult area to attain temperature, provide geometric coverage, worst-case position.
2	Multi-Axial Screw Driver on the bottom row	
3	Cannulated T-Handle	
Middle Section of the Tray (Figure 2)		
4	Rod Inserter	Wrapped around the instrument's handle; potentially difficult area to attain temperature, provide geometric coverage (top, left corner of the tray), worst-case position.
5	Rod Holder	Wrapped around next the instrument's handle; potentially difficult area to attain temperature, provide geometric coverage (bottom, middle of the tray), worst-case position.
6	Counter Torque Wrench	Placed inside the lumen (cannulation) at the mid-point of the instrument; potentially difficult area to attain temperature, provide geometric coverage, worst-case position.
7	Torque T-Handle	
Bottom Section of the Tray (Figure 3)		
8	Tissue Dissector	Wrapped around the instrument's handle on the left side; potentially difficult area to attain temperature, provide geometric coverage (bottom, left corner of the tray), worst-case position.
9	Tissue Dissector	Wrapped around the instrument's tip; potentially difficult area to attain temperature, provide geometric coverage (center of the tray), worst-case position.
10	Tabular Rod Reducer	Wrapped around the instrument in the middle; potentially difficult area to attain temperature, provide geometric coverage (top, right corner of the tray), worst-case position.
Within Chamber		
11	Inside the Chamber	Provide actual temperature of the chamber.
12	Inside the Chamber Drain	Provide actual temperature of the chamber drain.

Table 2. Thermocouple Placement in Validation Tray

validation tray was the most difficult to sterilize in this study by virtue of the fact that for one instrument not all BIs were killed under half-cycle conditions of two minutes at 132°C. Specifically, the most difficult to sterilize instrument was determined to be the inner cavity of a handle that has no patient contact. The handle fits on a tall support bar in the tray that has little access to steam.

Because not all spores were killed in the half-cycle qualification, verification testing also was performed under full-cycle conditions (i.e., four minutes at 132°C with quantitative enumeration of the surviving spores and calculation of the Fbio). The acceptance criterion for full cycle validation for Fbio must be ≥12. This was achieved in 3/3 runs when the chamber was maximally and minimally loaded. For the most difficult to sterilize instrument the Fbio was >12 in 2/3 runs. In the third run an Fbio of 9 was obtained.

The conclusion of this study was that different results can be obtained for the same instrument system based on whether it is sterilized when wrapped in hospital wrap or in a rigid container. Sterilization in rigid containers was more difficult to achieve in this study. This is due to limited steam access in some rigid container designs. It is also sometimes true that minimally loaded sterilization chambers accumulate less lethality (F0) then maximally loaded steriliza-

tion chambers. Consequently, complete sterilization may not occur in a minimum load. Therefore, validation protocols are recommended to include three challenges using both minimum and maximum chamber loads. ■

References

1. **HSS.** Growing Popularity of Hip and Knee Replacement Surgery Places Extra Burden on Critical Care Services. New York: June 5, 2012. Hospital for Special Surgery. Available at: www.hss.edu/newsroom_popularity-of-hip-knee-replacement-surgery-burden-critical-care-services.asp. Accessed June 19, 2014.
2. **ANSI/AAMI.** ST79:2010 & A1:2010 & A2: 2011 & A3:2012 (Consolidated text) – *Comprehensive guide to steam sterilization and sterility assurance in health care facilities*. Association for the Advancement of Medical Instrumentation. Arlington, VA.
3. **ANSI/AAMI/ISO** 17665-1:2006. Sterilization of health care products— Moist Heat—Part 1 Requirements for the Development, Validation and Routine Control Of Sterilization Process For Medical Devices. Annex D. Association for the Advancement of Medical Instrumentation. Arlington, VA.
4. **ISO/TS** 17665-3:2013. Sterilization Of Health Care Products— Moist heat— Part 3: Guidance on the Designation of a Medical Device to a Product Family And Processing Category for Steam Sterilization. Association for the Advancement of Medical Instrumentation. Arlington, VA.
5. **ANSI/AAMI** ST8-2013 Hospital Steam Sterilizers.
6. **ANSI/AAMI** ST77:2013 Containment Devices For Reusable Medical Device Sterilization.
7. **ANSI/AAMI/ISO** 11138-3:2006/(R) 2010— Sterilization Of Health Care Products – Biological Indicators – Part 3: Biological Indicators For Moist Heat Sterilization Processes.
8. **ANSI/AAMI/ISO** 18472:2006(R) 2010— Sterilization Of Health Care Products – Biological and chemical indicators – test equipment.
9. **ANSI/AAMI/ISO** 11138-1:2006/(R) 2010— Sterilization Of Health Care Products— Biological Indicators – Part 1: General Requirements.
10. **USP<55>** Biological Indicators-Resistance Performance Test.

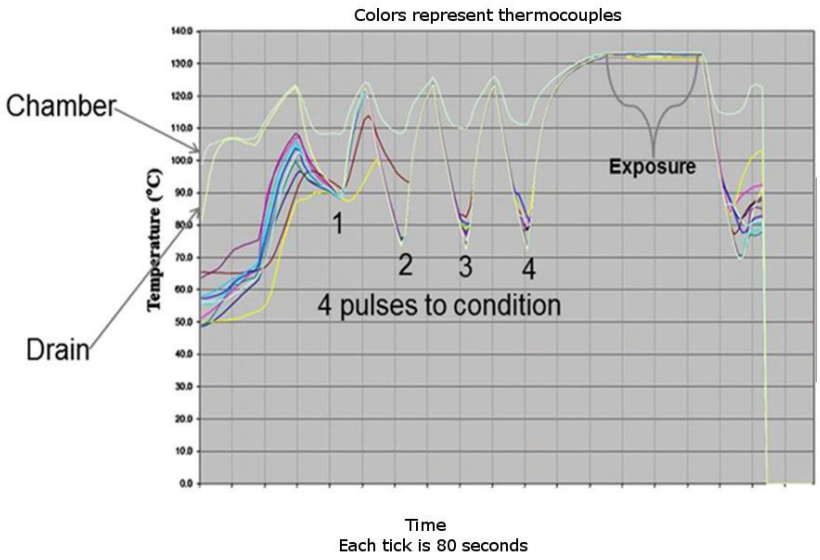


Figure 5. Full-cycle Pulse Pre-Vacuum Sterilization Process