Steam Sterilization Technologies and Challenges

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LEARNING OBJECTIVES

1. Discuss saturated steam sterilization and its different applications
2. Understand the requirements for cycle monitoring
3. Implement adequate, fast and reliable sterilized cycle release

Saturated steam sterilization cycle controls and monitoring indicators are continually challenged to determine whether current state delivers safe and effective sterilization cycles results. Historically, the first variable to be controlled in a cycle was the pressure (on manually operated gravity cycle sterilization equipment, known as the Chamberland autoclave, where the scale of pressures and equivalent temperatures of saturated steam for sterilization purposes[1] was used to determine that an equivalent temperature was present when pressure was obtained and controlled). Afterward, temperature control was implemented with the automation of the sterilization cycle, where exposure time would only start being counted when desired temperature was reached.

As technology evolved, cycle control variables with cycle phases were implemented, and cycle performance printouts became available for each cycle. This allowed for safer cycle performance interpretation and provided an additional tool for end users to determine whether a cycle was within the specifications. To determine a saturated steam sterilization cycle's lethality, microorganism spores were used, and their use continues today. Cycle lethality is demonstrated by its capacity to coagulate spores during exposure to saturated steam, thereby evidencing the presence of latent heat.

An increased demand for fast and accurate sterilization cycle release adds to the rigorous process of adopting new controls and quality indicator monitors.

Objective 1: Discuss saturated steam sterilization and its different applications

Saturated steam sterilization is used in a variety of industries. Each industry segment usually has an association or a group of subject matter experts (SMEs) from different companies and institutions who work together to improve cycle control, monitoring and load release. Most often, cross-functional research helps identify solutions implemented by a segment and allows its faster adoption in another segment. Unfortunately, the type of load that is processed is often overlooked or not given the priority it deserves.

Medical device manufacturers and pharmaceuticals industries have in common the standardization of the load being processed for terminal sterilization. The load is typically composed of identical products, and the loading configuration is always the same. The cycle configuration might differ, however, depending on the type of product being sterilized.[2]

In the pharmaceutical industry, it is common to see liquids being sterilized. The cycle configuration is similar to a gravitational cycle where steam is gradually injected into the chamber at the same time condensate is drained out—until the sterilization pressure is achieved and the sterilization temperature is within the required range. At the end of the cycle, the chamber is depressurized as the liquid temperature cools to maintain pressure just above the liquid's boiling point. The slow steam exhaust causes steam to condensate, and a significant amount of condensate will present at the end of the cycle; this is acceptable in liquid sterilization because the vials or flasks are hermetically or semi-hermetically closed, and the condensate will not compromise the sterile barrier or the sterilized product.[3]

Gravity and pre-vacuum cycle configurations are also used to sterilize medical devices. The main critical control relates to the change in pressure during conditioning and drying phases to prevent rupturing the sterile barrier or damaging the medical device. A common characteristic for saturated steam sterilizers used in the industry is the ability to configure all sterilization cycle parameters, so they reach the required sterility assurance level (SAL) of 10^{-6} (the probability of one spore surviving the sterilization process from an initial population of one million spores), to maintain product and sterile barrier integrity. This is necessary due to the different characteristics of the products being terminally sterilized. Full sterilization process validation and requalification must be performed at a pre-determined frequency or every time a change control requires it.

In healthcare settings, saturated steam sterilization is largely used to reprocess medical devices. Loading configurations vary for different devices being processed and use different sterile barriers and construction materials, specially metallics and non-metallics.[4] Cycle configuration parameters are not allowed to be changed by the user in healthcare settings; the only cycle control points allowed to be modified are sterilization time and temperature, if the minimal parameters are respected, and drying time. The principal of saturated steam sterilization is the same for all segments and settings, but how the equipment is loaded and how the cycle is configured differ significantly between industry and healthcare settings.

Objective 2: Understand the requirements for cycle monitoring

For saturated steam sterilization cycle monitoring, operator safety relies on the correct parameter information during the cycle to prevent risk of malfunction that can result in harm. It is also important to understand that a sterilization load can only be released if the registered evidence from the cycle monitoring shows that the SAL was reached.

In the mid-1950s, biological indicators (BI) were introduced to monitor sterilization cycle and provide real evidence of spore inactivation. *Bacillus stearothermophilus* was defined as the most heat-resistant spore to be used in BI monitoring of saturated steam cycles. It was after 1960 that sterilization was confirmed to be a probability process, not an absolute one, and a SAL of 10^{-6} was defined as a requirement for considering a product as sterile.[3] (See **Figure 1**)

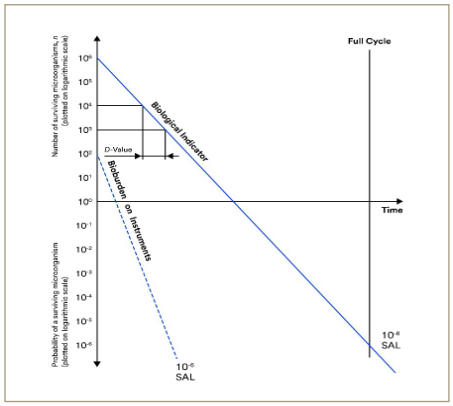

Figure 1: Logarithmic spore reduction. Overkill determined by a mathematical model.

After 1975, the adoption of BIs as a challenge device for sterilization cycles became the main reference for sterilization process validation. BI use saved the industry time, eliminated the need for product sterility sampling testing, and brought real evidence to demonstrate that a sterilization cycle reached the required SAL. Soon after, chemical indicators (CI) were adopted to monitor the sterilization cycle. The most common CI used today is the multi-parameter process indicator, where two or more parameters are monitor by the indicator.

A combination of physical indicators (temperature, pressure and time), equipment printouts, BIs or CIs are now used to support the assessment of sterilization cycle efficacy. The combined passing results of the CI with the negative growth of the BI—while also ensuring that physical parameters are within the specified range—provide

evidence that it is safe to release a load. If one of those provide an unsatisfactory result, the cycle should be considered "failed," and the load needs to be reprocessed.

As the industry evolved and needed to become more effective, attention was focused on improving the evidence of safe load release. Of the three indicators, only BIs offered an opportunity to improve the process and reduce the time to clear a sterilized load. The incubation time to determine spores' growth (through the ability to visually observe media turbidity as an indicator of spore growth) was seven days. The adoption of self-contained BIs (SCBIs) significantly reduced incubation time to 48 hours. SCBIs are fitted with the spores' strip and growth medium that contains a bromocresol purple pH indicator that changes color in the presence of spore growth. This allows users to visually observe—in 48 hours—the absence of spore growth by color change of the growth medium.

The automation of BI results was done by adding 4-methy-lumbelliferyl-alpha-D-glucoside to the growth medium; this converts to a fluorescent product in the presence of any active alpha-glucosidase enzyme. To detect a BI's fluorescent result at the end of a sterilization cycle, an incubator fitted with fluorescence-detecting sensors and processor program algorithms is required. This incubator, together with the SCBI, created a breakout technology known as a rapid readout BI (RRBI), which provides a fast, self-interpretating BI growth result that has been demonstrated to be equivalent to or exceed the growth positive response of a seven-day incubation procedure.[5]

In parallel to the BI technology development, another group of SMEs began studying the adoption of parametric release to eliminate the time required for BI readout results. The mathematical approached to determine the sterilization cycle lethality, also known as F_0 (zero), is based on the saturated steam sterilization cycle parameters and BI logarithmic inactivation required during cycle validation. This serves as the basis for parametric release.

Saturated steam sterilization parametric release uses the table temperature and pressure of saturated steam in moist heat sterilization[6] to compare the measured temperature value with the theoretical steam temperature for a given pressure. If the temperatures are equivalent, it is assumed that moist heat is present and the lethality calculations, F_0, are valid. (See **Figure 2**)

$$F_0 = \sum 10^{\frac{T-Tr}{Z}}$$

T = measured temperature
Tr = referenced temperature
Z = reciprocal of the slope of the thermal death curve for the target spore

Figure 2: F_0 formula

Parametric release became an option for the medical device and pharmaceutical industries to accelerate clearance of a terminally sterilized load because it doesn't rely on a BI readout to determine whether the load was sterilized.[7] Unfortunately, the concept of not having BIs for every single load has been interpreted by some as a cost-cutting measure, which is an inaccurate assumption. Parametric release requires the monitoring of multiple cycle variables, which must be validated with BIs to demonstrate the validity of the calculations used for lethality. The load must be accessed and standardized, and any changes to the process, product, loading or equipment require requalification runs to demonstrate that the load still meets the previous validated specifications.

Figure 3: Example of a standardized load used in the industry

Once a sterilization cycle is complete, parameters are then analyzed by a quality control team to determine whether all sterilization parameters were within the validated range, and a parametric release certificate is generated. If any parameters are out of specification, the load must be reprocessed because sterility testing is not allowed when parametric release is adopted.

In hospitals, the adoption of parametric release poses a higher challenge than what is seen for the medical device and pharmaceutical industries. This is largely because of the medical device and pharmaceutical industries' need to standardize sterilization loads, which is nearly impossible for hospitals to accomplish due to their need to meet various instrumentation needs for different procedures. (See **Figure 4**) Also, hospitals have access to SCBIs with super rapid readout (SRR), which basically have the same technology as the 48-hour varieties but with incubators that can provide a readout in 24 minutes.

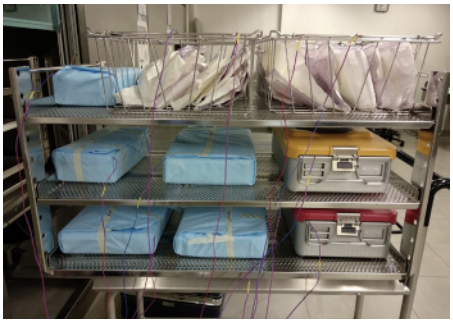

Figure 4: Example of a hospital load configuration with different medical devices and sterile barriers

Recent research provides additional evidence that pressure and temperature parametric values are not sufficient to demonstrate the presence of saturated steam required for spore inactivation with latent heat. The findings are related to steam quality supplied to the equipment and present on the load, which are not monitored by the sterilizer. Steam quality is affected by the load, meaning that saturation will change depending on the sterile barrier, device construction material and weight.

The absence of non-condensable gases (NCG) should also be assessed to determine steam quality. NCG currently is only monitored when the sterilizer is installed and can be verified annually. NCG is undetectable by pressure and temperature sensors, and because its presence will impact the sterilization efficiency, additional cycle quality monitors are required[8,9] *Note: NCG is the most critical component of steam quality. Its presence causes wet packs and needs to be monitored.*

Steam saturation is another critical component. Typically, the steam supply is configured and validated during installation to deliver the correct steam saturation to the sterilizer. Mechanical components in the steam line will have diminished performance following a period of use, and if preventive maintenance does not follow the replacement schedule, steam saturation will be altered (again, because it cannot be measured by the sterilizer's temperature and pressure sensors). If steam is delivered with more saturation, it will have less energy and require more time to inactivate spores. Another condition, super-heated steam, can be caused by mechanical component failure. When admitted into the sterilizer chamber, it will not inactive spores due the absence of latent heat. SAL and super-heated steam can also be caused by the load, especially in hospitals, and neither can be detected by equipment.[1,3,10,11]

Objective 3: Implement adequate, fast and reliable sterilized cycle release

Today, there is heightened pressure to improve the supply chain, and because sterilization is a major component, actions to reduce sterilization time are more prevalent. Industries that already adopted parametric release may be seeking alternatives to reduce time. A new idea is to implement real time release (RTR), whereby sterilization loads are cleared immediately upon cycle completion. The procedure for its implementation is still under discussion by industry SMEs, and attention must be given to current parametric release inefficiency to accurately measure steam quality.

The recently released universal SCBI brings an important solution to RTR, including measuring steam quality for every load. This new BI maintains the same 24-minute readout time for previous hospital SRRs, except the same SCBI can now be used in multiple cycle configurations: gravitational and dynamic air removal, with temperatures ranging from 121°C to 135°C. The universal SCBI, placed inside a process challenge device (PCD), is capable of effectively detecting the presence of NCG and the correct steam saturation, and then providing final readout in 24 minutes. This characteristic, when added to parametric measurements of temperature and pressure, will be the foundation of the future RTR.

Another key factor regarding future discussions and actions aimed at providing fast and accurate sterilized load release is the proper assessment of the products being sterilized and the sterile barrier being used. It is common to see equipment performance evidence used to justify a new device or configuration, especially in relation to steam quality; however, the load to be processed is often overlooked. Not looking into what is processed could influence the targeted cycle outcome.

Sterilizer manufacturers develop and validate their cycle control parameters using loading configurations that have only mass as a configuration criterion. Medical device manufacturers validate the sterilization section of their instructions for use (IFU) using only their device in most cases because there is no requirement for how to prepare a test load. When medical devices from different manufacturers are placed on sterilization carts in a hospital, they create a different sterilization condition than what was previously validated by the manufacturers, and the cycle outcome may show different results than what were previously seen.

Conclusion

Saturated steam sterilization is a common principle; however, its cycle monitoring and load releases should not be viewed as processes that can be applied to all institutions and settings. Each segment has its own requirements, which need to be assessed individually.

Steam quality is a critical requirement. Because it cannot be monitored by current equipment or cycle parameter measurements, different results from equipment printouts and BIs can be expected. Therefore, safe load release requires that every load be monitored with BIs, and loads should only be released if cycle parametric values are within the specified range and when BI results are negative for spore growth.

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