

## STERILITY ASSURANCE:

# It is Less about the Time, More about the Kill

What you need to know about biological indicators

by Sailaja Chandrapati, PhD

A range of monitoring devices is currently available to monitor the steam sterilization process. Each of these monitoring devices measures different parameters and performs different functions. To effectively reduce risks for patients and your facility, it is important that you know exactly when and how to use them. (Risk reduction, as you know, is key to improving the bottom line in any business.)

Recently, there has been some confusion among healthcare professionals about the response of biological indicators (BIs) in steam sterilization cycles. One common question is: Why do BI spores die during the first half of the sterilization cycle?

As you will learn in this article, this is just one of several safety margins built into the process of sterilization. When it comes to monitoring the sterilization process, it's not simply about measuring the cycle exposure time; it's about measuring the ability to deliver sufficient lethality to kill highly resistant organisms within the BI.

### Rigorous infection prevention is more important than ever

Statistics from the Centers for Disease Control and Prevention (CDC) show that an estimated 1.7 million health-care-associated infections (HAIs) occurred in 2002 and were associated with approximately 99,000 deaths.<sup>1</sup> This loss of life is roughly equivalent to a fully loaded Boeing 747-400 going down every other day for one year. According to the CDC, HAIs are now the sixth leading cause of death in the United States, killing almost twice as many people as breast cancer and HIV/AIDS combined.<sup>2</sup>

Approximately one in 10 hospitalized patients will acquire an infection after admission. The CDC estimates the annual cost of dealing with these infections to be \$6.7 billion, further contributing to the mounting costs of healthcare within the United States.<sup>3</sup>

### Measuring the Effectiveness of Sterilization: What monitoring devices can (and cannot) tell you

Sterilization is intended to minimize the risk of surgical site infection by destroying all microorganisms on a surgical instrument.

Today, three universally accepted methods are used to measure the effectiveness of the sterilization process: physical monitors, chemical indicators (CIs) and biological indicators (BIs). These devices perform specific roles, and each has its advantages and limitations.

As you consider the options, it is important that you understand the device, its intended use and its limitations. What is it designed to measure? What is it capable of telling you?

### Sterilization Monitoring Tools

- ▶ Physical monitors
- ▶ Chemical indicators
- ▶ Biological indicators

*Physical (mechanical) monitoring* involves observing gauges and computer printouts to verify that sterilization parameters (cycle time, temperature and pressure) are met.

*Chemical indicators* respond to physical and chemical conditions in a chamber. CIs can be made with different formats and chemistries and their responses to the sterilization process can differ depending on design. To illustrate the differences, two classes of CIs used for internal pack monitoring are described below:

- ▶ Class 5 integrating indicators are designed to react to all critical variables (time, temperature and the presence of steam). In order to comply with ISO 11140-1:2005, they must have Stated Values that correlate to a BI at **three** time/temperature relationships.<sup>4</sup>
- ▶ Class 6 emulating indicators are also designed to react to all critical variables. They are often called cycle specific indicators as each cycle would require a different Class 6 CI. Class 6 indicators have **one** Stated Value for time and temperature for the specific cycle it's designed to monitor. There is no requirement for three Stated Values as there is for Class 5 Integrating Indicators. Additionally, their response is not required to correlate to a BI throughout the temperature range.<sup>4</sup>

A *biological indicator* (BI) is a "test system containing viable microorganisms providing a defined resistance to a specified sterilization process."<sup>4</sup> Given that they contain living organisms, AAMI ST79, Section (10.5.3.1) states that "biological indicators are the only sterilization process monitoring device that provides a direct measure of the lethality of the process."<sup>5</sup>

The theory behind the BI is that if your process is effective enough to kill a large population of highly resistant spores, it will also kill a lower number of less

resistant organisms on the medical devices. Because it detects the killing of microbial spores, a BI is capable of yielding information that is more valuable than any other sterilization monitor.

After exposure to the sterilization process, BIs must be incubated to determine if any spores survived. For this reason, results are not immediately available. However, advances in BI technologies have led to Rapid Readout BIs, which provide the end user with actionable results within 1 to 3 hours.<sup>6</sup>

**Understanding SAL**

Sterility is defined as being free from all living organisms.<sup>7</sup> Since it is not practical to test every device for the absence of microorganisms, the concept of sterility is assumed to be a statistical probability. The sterility assurance level (SAL) defines the probability of a non-sterile unit for a validated sterilization process. For example, when the SAL is 10<sup>-6</sup>, it means that there is one chance in a million that a device is not sterile.

Biological indicators are used to develop and validate processes, and therefore estimate SAL. A negative BI result indicates that sufficient lethality has been achieved to kill a large population of highly resistant spores whose resistance is far greater than the routine microbial bioburden on reprocessed medical devices.

**Table 1. A Sampling of Organizations Recommending the Routine Use and Frequent Monitoring of Sterilization Effectiveness with Biological Indicators**

Organization	Recommendation
Centers for Disease Control and Prevention (CDC) <sup>9</sup>	"Inadequate sterilization of surgical instruments has resulted in SSI outbreaks. The importance of routinely monitoring the quality of sterilization procedures has been established. Microbial monitoring of steam autoclave performance is necessary and can be accomplished by use of a biological indicator."
Association for the Advancement of Medical Instrumentation (AAMI) <sup>5</sup>	"Biological indicator test packs also should be used routinely in sterilization loads at least weekly, but preferably every day the sterilizer is in use." "Additionally, BIs within PCDs should be used to monitor every load containing implants. Biological indicators within a PCD may be used as part of the criteria for release of non-implant loads."
Association of periOperative Nurses (AORN) <sup>10</sup>	"In an emergency, when flash sterilization of an implant is unavoidable, a rapid-action BI with a Class 5 chemical integrating indicator (or enzyme only indicator) should be run with the load." "Steam sterilizers: <i>Geobacillus stearothermophilus</i> biological indicators should be used for routine sterilizer efficacy monitoring ... Routine sterilizer efficacy monitoring should be done weekly, preferably daily, as follows: each load containing an implantable device should be monitored with a BI and quarantined until the results of the BI testing are available, and ..."

**BIs: The Industry Gold Standard**

BIs have gained the status of a tried-and-trusted measure of spore lethality. They are universally accepted by key opinion leaders and professional organizations as the "Gold Standard" for identifying sterilization process failures.<sup>6</sup>

As referenced in the 2008 CDC *Guideline for Disinfection and Sterilization in Healthcare Facilities*, "biological indicators are recognized by most authorities as being closest to the ideal monitors of the sterilization process,"<sup>8</sup> and "biological indicators are the only process indicators that directly monitor the lethality of a given sterilization process."<sup>8</sup>

Various organizations recommend the routine use and frequent monitoring of sterilization effectiveness with biological indicators. (Table 1.)

**A Design to Kill with Multiple Margins of Safety**

Margins of safety exist all around us—in buildings and bridges, in healthcare, even in finance and transportation. Margins of safety are designed into the sterilization process, as well. They include BI spores

that exceed the bioburden and SAL, which is built into the sterilization process. Additional lethality is also provided by the sterilizer during the come-up time.

**Margin of Safety: BI Spores that Exceed the Bioburden**

Studies have shown that used medical devices, when adequately cleaned, are contaminated with a relatively low bioburden of organisms, typically less than 1,000 organisms.<sup>11</sup>

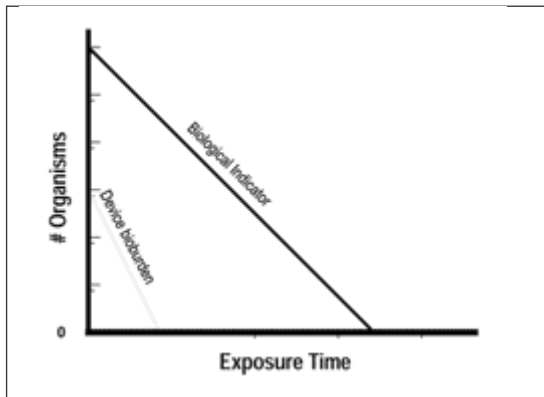
Given that the BI spores chosen for sterilization validation are more resistant and present in greater numbers than the bioburden typically contaminating a medical device, a negative BI result indicates that the process delivered sufficient lethality. This is the safety margin inherent to the BI.

The concept is represented on Graph 1 on page 42, where we see how typical device bioburden are killed with the line starting at a lower initial population. The spores in the BI, represented by the top line, have a higher initial population at time = 0 and are more difficult to kill.

**Margin of Safety: SAL Built into the Sterilization Process**

Both sterilizer and medical device manufacturers use BIs for validating sterilization cycles. That is because BIs are designed to

**Graph 1: Rationale for Use of Biological Indicators**



provide a challenge to the sterilization process, which exceeds the challenge of the natural bioburden in or on products. (CIs are not used for validating these types of cycles because they do not provide a direct measure of lethality.)

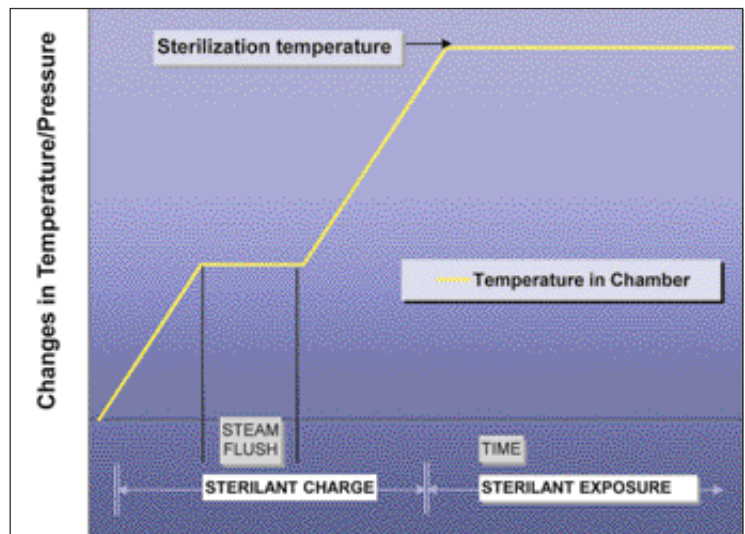
These manufacturers rely on the concept of SAL (see box) to validate the sterilization cycle. The typical procedure is to find out the time required to kill a million spores, and then double it. This is called the overkill or half-cycle method and provides another margin of safety.

Typically, this validation is achieved by completing three consecutive successful half cycles (cycles shortened to half the normal time) in order to qualify the proposed exposure time for routine sterilization processing of medical devices. Success is defined by the inactivation of all BIs after incubation for the three half-cycles tested. For example, if there are no positive BIs in three test cycles of 2 minutes exposure at 270°F (132°C), then a routine exposure time of 4 minutes at the same temperature would be an adequate sterilization process for the medical devices.

### Hospital Sterilizer Come-up Time

Additional lethality in a sterilization process can be obtained during the come-up time or the preconditioning phase of the sterilizer (Graph 2). As steam is injected and the temperature in the chamber (and consequently the load) continues to rise, so does the “kill” effect of the process. A come-up time can vary from 1-20 minutes for gravity cycles and 4-20 minutes for vacuum-assisted cycles. In some instances, in cycles where critical parameters such as air removal and steam quality are optimal, the lethality imparted during this part of the process may be sufficient to inactivate the BI.

**Graph 2: Come-up Time in a Gravity Cycle Sterilization Chamber**



**Figure 1: Margins of Safety Exist Everywhere**

### Margins of Safety Impart Confidence

The Federal Aviation Administration requires that an aircraft, like a Boeing 747, must be capable of coming to a full stop within no more than 60 percent of the landing distance available. The certification standard provides a 40 percent margin of safety to allow for pilot landing techniques and less than ideal runway conditions.<sup>12</sup>

Just like you can feel confident of having a safe landing the next time you fly, you can be confident that a negative BI indicates that sufficient lethality has been delivered to your steam sterilization process.



### It is Less about Time and More about Kill

Recent studies comparing the survival of spores in BIs to the response of ink-based CIs in cycles with varying exposure times have shown

that BIs are inactivated before the CIs indicated a pass condition.<sup>13</sup> Considering the safety margin principles above, it is obvious that when a BI is inactivated, sufficient lethality to kill one million spores has been delivered.

Furthermore, if a more resistant BI were needed, a BI could be designed to survive for longer time periods. But this is not necessary given the margins of safety principles described above.

Rest assured that BI inactivation during the early phases of the sterilization cycle does not mean that it offers less assurance. On the contrary, it indicates that sufficient lethality has been delivered.

## Know When to Use Your Monitoring Devices

With ever-increasing demands for faster instrument turnaround, it can be tempting to count on CIs for sterilization results. To reliably verify the performance of the load, however, you need a BI.

Studies involving side-by-side comparison of different types of monitors have repeatedly demonstrated the superiority of BIs in being able to detect failures that were often missed by other monitors.<sup>14,15,16</sup>

Additionally, the 2008 CDC guideline states, “chemical indicators should be used in conjunction with biological indicators, but based on current studies, should not replace them because they indicate sterilization at marginal sterilization time and because only a biological indicator consisting of resistant spores can measure the microbial killing power of the sterilization process.”<sup>14</sup>

Dr. Rutala, co-author of the 2008 CDC guideline, noted at the 2008 Association of Professionals in Infection Prevention (APIC) Meeting that Class 6 indicators “... are not a substitute for biological indicators.” He added, “No professional organization has recommended the use of Class 6 emulating indicators as a substitute for biological indicators and there are no data that demonstrate that it mimics a BI at suboptimal sterilization times.”<sup>17</sup>

Based on these insights, here is a good rule of thumb:

- ▶ Trust your BI for load control: Only a BI can detect actual killing of microbial spores inside a sterilizer. This is why load control remains the most reliable level of testing you can use.
- ▶ Trust your CI for pack control: CIs are ideal for internal monitoring of packs, trays, etc. CIs help detect “local” problems that can occur due to human error or mechanical malfunctions and can single out packs that were not exposed to sufficient sterilization conditions.

Remember, the objective of a sterilization process is to deliver sufficient lethality to destroy or kill the bioburden on the medical devices. This is not measured by physical monitors or

the end-point change of a CI indicator. A BI, however, inherently provides the margin of safety you need for sterility assurance.

In summary, BI inactivation during the early phases of the sterilization cycle does not mean that it offers less assurance. On the contrary, it indicates that sufficient lethality has been delivered.†

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