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CUSTOM BIOLOGICAL INDICATORS

Stop trying to put a square peg into a round hole!

by Robert Bradley

Biological Indicators (BIs) have evolved quite a bit over the years. The continued development of new and improved biological indicators has continually made the practice of monitoring sterilization processes a fairly easy and inexpensive process. Even with the evolution of the biological indicator there still isn't always a BI for every situation. As new products, medical devices, and sterilization processes are created there isn't always a readily available BI that is adequate for monitoring these items or processes. What should you do if you have a situation where a standard BI just doesn't quite work? HAVE ONE MADE THAT DOES!!!

A person might say, "It doesn't matter what type of biological indicator I place in my load, it will tell me if I reach my SAL (Sterility Assurance Level). If the BI is killed that means I achieved my target SAL and as long as that happens I am happy." That argument will work great until you have a failure. Then what should be done? Time and time again, a customer will call and say "there is something wrong with your BI". Once all the details are presented, more often than not it is either improper use of the BI or the wrong BI all together. The reason there are so many different types of BIs out there is because not every BI is appropriate for every situation. Proper selection of BIs for your process is of the utmost importance.

Another customer might state, "I can just cut this BI into smaller pieces or fold it a few times and it will work for my application". You might think you can reconfigure a standard BI in a way that it will work but if you do that it will most definitely affect the performance of the BI. A biological indicator is a system composed of the inoculated substrate and the primary packaging. Modifying any of the components of that system will affect the performance of the BI. The two most likely characteristics that will be affected by modifying a BI are the population and resistance. This could mean that you are providing too little or too great of a challenge as to what was originally intended and you wouldn't be adequately monitoring your process. If the modification affected the BI in a way that it reduced the challenge you could completely inactivate the BI and your processed load could potentially be unsterile. If the modification affected the BI in a way that increased the challenge it could result in positive growth of the BI even though the sterilization cycle conditions should have been adequate to sterilize your load and completely inactivate the BI.

So let's say you are trying to process a product in a sterilization cycle that you're just not sure the BI you normally use can accurately monitor. What should you do? First call the BI manufacturer and see if there is a readily available alternative. You might be dealing with this for the first time but it is possible that the BI

manufacturer has dealt with this before and can provide you with an instant solution. If there isn't an available BI, the ideal scenario would be to use a custom BI that is specifically tailored to that application.
Many BI manufacturers offer specialized BIs for industrial use. Many of these industrial BIs start out as custom BIs that were specifically produced for one customer or another for applications that a standard BI just wasn't applicable for. Even with the development of a whole line of industrial BIs that are tailored to specialty applications, there is still occasionally a need for other custom biological indicators as new products, medical devices and sterilization processes are created.

Custom BIs vs. Standard BIs

There are times when it is necessary to develop a custom biological indicator because it is a more accurate representation of the load you are trying to sterilize. A prime example of this is the sterilization of vial closures or stoppers. There isn't a standard BI available that is similar enough to a stopper to be able to accurately monitor those types of sterilization loads. The various sizes, configurations and materials used in stopper manufacturing make them a challenge to sterilize. Over the years I have talked to many different customers who have tried to use traditional BIs to monitor the sterilization of stoppers. These customers tried many different ways to monitor the loads of stoppers from placing a traditional BI into the bag to trying to place BIs inside of the stopper collar and the end result was just not satisfactory. The traditional BI could be completely inactivated but the load wasn't sterile. When they placed BIs inside of the stopper collars often they wouldn't stay in there throughout the cycle and they subsequently would get lost in the bag. The search through the bag increased the likelihood of post-sterilization contamination.

The most logical thing to do is to turn the stoppers themselves into custom biological indicators. An inoculated stopper can monitor conditions that a traditional BI can't. When a large quantity of stoppers is placed into a sterilization bag, it is possible that some of the stoppers can be pressed together and shielded from the full effects of the sterilization cycle. By placing inoculated stoppers in the load, you can replicate that scenario and more accurately monitor the lethality of the cycle. How is a paper strip in a glassine envelope going to replicate that?

The other benefit of using the inoculated stoppers would be that you are using the same material for the BI as

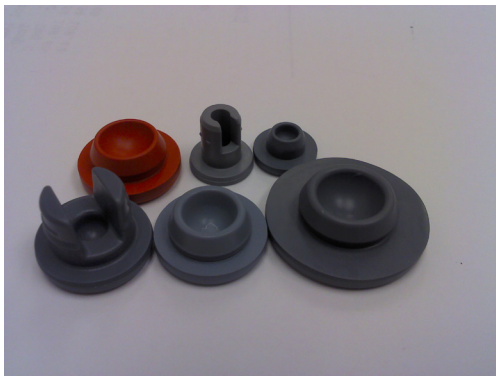

Figure #1: Stopper Variations

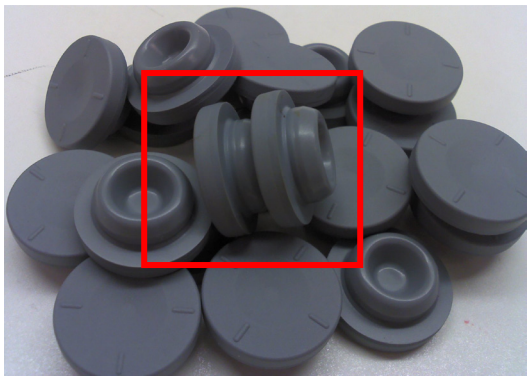

Figure #2: Stopper Shielding

the rest of the load so the thermal transfer will be the same. The heat transfer through the stopper material could be quite a bit different than through paper, plastic or glass. The table below shows how different the resistance of a particular batch of bacterial spores can be when inoculated on a stopper as compared to a traditional paper spore strips.

Stopper	Spore Batch #	Spore Strip D-value	Stopper D-value	% Difference
A	774S	1.4minutes	2.2minutes	+57%
B	774S	1.4minutes	1.8minutes	+29%
C	774S	1.4minutes	2.1minutes	+50%
D	774S	1.4minutes	2.2minutes	+57%
E	940S	1.6minutes	2.5minutes	+56%
F	964S	1.5minutes	2.4minutes	+60%
G	1021S	1.5minutes	2.2minutes	+47%
H	1045S	1.5minutes	2.0minutes	+33%

Table 1: Comparative D-values for Stoppers vs. Spore Strips

Each of the stoppers included in the table represent a different configuration; whether it is the material, size, shape or coating. Any or all of those items can have an impact on the performance of the stopper. As you can see there is a significant difference between the resistances of the spore batch on stoppers as compared to spore strips. Stoppers A-D were all tested using the same spore batch. The results of the testing on stoppers inoculated with spore batch #774S not only show how different the resistance of stoppers was compared to spore strips, but also how different the results can be from other types of stoppers.

Custom BIs vs. Direct Inoculation

As more and more medical devices are developed, there is an ever increasing need to develop BIs that can be used to monitor the processes used to sterilize these intricate devices. If traditional BIs won't work and these custom BIs aren't created, the only alternative is to directly inoculate the devices and that presents a whole new set of challenges. An existing customer approached us with a situation where they were trying to validate the sterilization of a very long, narrow lumen. No standard BI would fit in the narrow opening and the customer was not interested in direct inoculation. They were particularly interested in verifying that sterilization conditions were achieved throughout the entirety of the long lumen. In order to provide the customer with this information, a 48 inch polyester suture was inoculated at various specific locations along the length of the material. Once inserted into the lumen the inoculated area coincided with the most difficult area of the lumen to sterilize. After the sterilization cycle, the BI was removed and placed in a bottle of recovery media and monitored for growth. Sounds a lot easier than direct inoculation, doesn't it? While I have just presented one scenario, there are many more instances where the development of custom BIs is preferable to other alternatives.

The days of a single BI for all purposes are long gone. As we move forward and more intricate components/ devices and sterilization process are created, it will become increasingly important to ensure we are properly monitoring the sterilization of those items. In some instances, the best way to do this will be with a custom biological indicator.

About the Author

Robert Bradley is the Director of Laboratory Production for Mesa Labs' Omaha Manufacturing Facility. He started out with the company in March of 2003 as a Testing Coordinator. In that role he was involved with biological indicator production, research & development and contract studies. In 2004 he became the Laboratory Manager where he oversaw biological indicator production and contract studies. He served in that position until promotion into his current role in October of 2010.

Mr. Bradley holds a B.S. in Biology from Midland Lutheran College and a M.S. in Biology from the University of Nebraska at Omaha. He is a member of the Association for the Advancement of Medical Instrumentation (AAMI), the Parental Drug Association (PDA) and the American Society for Microbiology (ASM).