## Editorial

# Biological Indicators for a Liquid Chemical Sterilizer: A Solution to the Instrument Reprocessing Problem?

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In this issue of *Infection Control and Hospital Epidemiology*, Dr. Raymond Kralovic reports the results of an intricate series of laboratory studies to determine the feasibility of using filter paper strips impregnated with bacterial spores ("biological indicators" [BIs]) to monitor liquid chemical sterilization cycles in a proprietary reprocessing system (hereafter referred to as the "Steris Process" [SP].[1] The SP was reviewed in detail in a 1992 Product Commentary in this journal." It is an enclosed tabletop unit with an automated processor controlling circulation of a mixture containing peracetic acid [PA] (a 34% concentrate of PA is diluted to 0.2% within the machine just prior to each cycle) and "inerts" (buffers, corrosion inhibitors, and detergents) at 50°C to 56°C for 12 minutes. The germicidal exposure is followed by four rinses of filtered water claimed by the company to be sterile. Company literature also claims that the process is equal in efficacy to steam or ethylene oxide sterilization, is more effective than glutaraldehyde at reaching contaminated surfaces, and "...is the first liquid chemical sterilization system to have passed FDA review for use specifically for the sterilization of immersible medical, surgical, and dental instruments," including rigid scopes and cameras, microsurgical instruments, flexible scopes and forceps, "general hard goods," and "future instrument technology." The spore strip BIs used in the report are commercially available and are designed and intended for use specifically in the monitoring of steam autoclave or dry heat and ethylene oxide sterilization cycles.

Unfortunately, the data and conclusions presented in the article give rise to more questions than they answer. The conclusion that BIs designed to monitor either steam autoclave or ethylene oxide sterilization cycles can be taken from their containers and exposed directly to a fluid environment to monitor the efficacy of liquid chemical sterilization cycles is not warranted by the data presented. Perhaps the spore/filter paper strips could be used in the laboratory in some fashion to evaluate or improve the system, but questions regarding possible PA residuals, recovery of PA-injured spores, the appropriateness of spore test species, and spore wash-off need more intensive study. Although it was demonstrated that *some* spores remained on the filter paper strips during the cycle, the singular observation that from 400 to 73,000 were removed eliminates any notion that this technique is suitable for routine monitoring of cycles in healthcare settings.

Furthermore, the fact that the BI is placed openly in the swirling milieu of the system indicates that it is not in a location fundamental to the basic concept of BI use. Interestingly, a recent report describes a BI failure in the SP system when a spore strip was challenged inadvertently by using a strip holder different from the type recommended by the company.[3] The holder contributing to the failure had jaws with flat surfaces, and in the 12-minute exposure cycle, the PA failed to penetrate the filter paper held

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*Bond WW. Biological indicators for a liquid chemical sterilizer: a solution to the instrument reprocessing problem?* Infect Control Hosp Epidemiol *1993;14:309-312.*

https://doi.org/10.1086/646748 Published online by Cambridge University Press

between the mated surfaces.

For a full understanding of some of the unique aspects of the SP as well as the implications of Dr. Kralovic's article, it is necessary to review briefly some of the basic concepts and terminology of disinfection and sterilization procedures and the design and biological monitoring of these procedures. It is also important for the users of medical instruments and certain germicidal chemicals to recognize that they may be regulated by two governmental agencies in the United States. Detailed discussions of these topics can be found elsewhere.[4,5]

The Environmental Protection Agency (EPA) registers and regulates germicidal chemicals of all types and requires that certain standard microbicidal potency ("efficacy" in EPA terms) data be submitted by manufacturers. The Food and Drug Administration (FDA) regulates medical devices and considers liquid chemical germicides used to reprocess medical instruments as accessories to the instruments. Data in addition to those required for EPA registration may be required before such a liquid chemical germicide product can be marketed. Since 1982 and until just recently, the EPA did not independently confirm the data submitted by manufacturers. Historically, the FDA also has not confirmed these data. The EPA requires that a registered product include its "EPA registration number" on the product label. The FDA, in contrast, does not allow manufacturers to create any impression, on the product label or in advertising, that compliance with FDA premarket regulations is suggestion or proof of product efficacy.

The terms *sterilization* and *disinfection* often are misinterpreted and misused, especially when liquid chemical germicides are employed to reprocess medical instruments. Sterilization is defined as a procedure effected by physical, chemical, or radiation agents that results in the inactivation of all microorganisms including highly resistant bacterial spores. It is an absolute term: an item is either sterile or it is not. From an operational standpoint, however, designers of sterilization cycles define sterility in terms of the probability that even one member of a given microbial population or "bioburden" (typically, $10^6$ bacterial spores) will survive on an item subjected to a given sterilization cycle. In the medical device industry, the term used to describe this probability is *sterility assurance level* (SAL). The SAL for most medical devices is $10^{-6}$. In designing some sterilization processes, a conservative and widely used rationale is to assume that the bioburden on each item being sterilized is composed of bacterial spores. Therefore, it is reasonable to assume that if high numbers of spores are killed, then all other microorganisms of lesser resistance have likewise been killed. Disinfection is defined as a generally less lethal process than sterilization and usually is accomplished using liquid chemical germicides. For reasons discussed below, disinfection procedures cannot be monitored biologically.

Biological indicators are standardized preparations of bacterial spores known to be comparatively resistant to the physical or chemical agent being monitored. Specifically designed BIs are used to monitor moist or dry heat, gas, or radiation sterilization processes. For routine monitoring of a sterilization cycle, the appropriate type of BIs are placed inside a test pack in a standard load in a sterilizer and then retrieved after the cycle and sent for culture to verify that all spores were killed. The BIs are placed in the most difficult to sterilize location(s) in the load. The sole design and purpose of the BIs are to verify that the germicidal agent penetrated through the standard packaging and loading configurations of the sterilization vessel. BIs do not offer proof that each individual item within the packaging is sterile; this aspect is addressed early in the cycle design phase by intensive physical and microbiological characterization of the sterilizing agent and the individual items themselves. Fundamentally, any BI test result is meaningless at best and misleading or inaccurate at worst if the BI is suspended in open areas within the sterilization vessel or if it is placed on the outside of an individual package within the load.

For the following reasons, there is no precedent in the scientific literature for the biological monitoring of liquid chemical sterilization cycles. Items in a liquid chemical sterilization cycle cannot be wrapped because this would prevent necessary penetration of the germicidal agent and contact with the individual units in the load. Items most commonly reprocessed using liquid chemical germicides are those that are not only heat sensitive, but so physically complex that characterizations of bioburden and consistent penetration of liquid (and even gaseous) chemical germicides to all internal surfaces cannot be assured.[6,7] In these instances, a BI is neither representative of the bioburden nor can it be placed in the most occluded location of the load. Furthermore, a BI (eg, a spore strip) would have to be unpackaged in order to be exposed to the liquid chemical germicide, and this would compromise the BI's integrity. If any spores were released from the strip during a process failure, this would add to the bioburden in the system. All of these features were demonstrated in the article presented in this issue.

Because Dr. Kralovic refers to EPA registration criteria in his article and relates a number of his methodologies and conclusions to them, consideration of these data in this editorial is important. The company data submitted to EPA are unique in a

https://doi.org/10.1086/646748 Published online by Cambridge University Press

number of respects.[8] The Association of Official Analytical Chemists (AOAC) Sporicidal Test, on which some of these data are based, was conducted in a highly modified manner.

First, the test units (porcelain pennicylinders and loops of suture material inoculated with bacterial spores) were exposed in the SP machine with full fluid circulation including four rinse cycles. In the standard AOAC method, the pennicylinder or suture loop is placed within a test tube containing the disinfectant being evaluated; the test tube then is held immobile in a water bath for the test cycle. One of the criticisms of this standard method, which does not involve a constant flow of liquid such as that seen in the SP machine, is that some portion of the spore inoculum is washed off; this concern is even more applicable to the dynamic environment of the SP machine.

Second, the temperature of the SP test could have been anywhere between 50°C and 56°C. Even a small increase in temperature can have a dramatic effect in increasing the activity of a chemical germicide, and also, the more powerful the chemical, the more substantial the increase in activity. PA is a very powerful germicide, even in very low concentrations. In the standard AOAC test, the temperature of the test exposure is controlled in a water bath with much less temperature variation than in the SP method.

Third, the suture loop material used in the SP tests was dacron instead of the standard silk thread.[9] There are no data comparing the retention or resistance of spores in silk versus dacron suture loops.

Fourth, the "wash-off control" data were qualitative rather than quantitative. This means that the tests were capable of detecting "wash-off' of the inoculum *only* if the entire inoculum was removed. One of 60 carriers in the test series was negative, suggesting that all the spores were "washed off' of this test unit by the SP process (minus PA).

Fifth, it also was unclear whether appropriate neutralizers (as required by the standard test methods) were used in the recovery tests. In addition to being a very potent sporicide, even in very low concentrations, PA also has the reputation for not being inactivated readily in the presence of organic material. Inoculating broth with an uninjured bacterial spore inoculum and concluding that there is no residual chemical remaining on a filter paper strip that could inhibit an injured spore from germinating is insufficient evidence to conclude that no neutralizer is necessary in tests as critical as these.'

Sixth, there seems to have been no search conducted for a spore that may be more resistant to PA than the standard test species. BIs, whether used to design or to monitor sterilization cycles, are chosen from among those known to have the highest resistance to the agent.

Finally, similar modified methodology was used in the AOAC carrier tests for bactericidal, tuberculocidal, fungicidal, and virucidal activity of the PA/SP system; no details were given for the "wash-off controls" in these tests. It could be expected, however, that the retention of inoculum in each of the tests would vary with the type of organism and the carrier substrate.

Dr. Kralovic presents an argument in this article that spore strip BIs can be used to monitor the SP sterilization cycle,[10] but a number of questions remain:

1) Should users of the SP continue to use BIs to monitor their systems? Certainly, this is their option, but the practice should be done with the full knowledge that none of the BI systems available today are cleared as required by FDA for marketing and use in this manner.

2) If the SP system cannot be monitored biologically, is there assurance of sterilization of medical instruments as claimed? The SP system has been reviewed by FDA and is cleared for marketing. The assumption is made that all company claims were part of the review process, yet there are no independent, peer-reviewed, and published challenges or confirmations of the company data or claims. Company literature has nonspecific disclaimers referring users to instructions of other manufacturers and also stating, in effect, that the SP method will achieve sterilization only when instruments have been totally precleaned and are totally accessible to the germicide. Healthcare workers should be aware that some of the currently recommended and used methods of instrument access and cleaning, particularly inside the channels and valves of flexible fiberoptic endoscopes, may not be as effective as once believed.[6,7,11-13]

3) Do certain classes of medical instruments, specifically the optic portions of flexible fiberoptic and rigid endoscopes, need to be sterilized to be safe for patient use? The apparent consensus is that high-level disinfection, if meticulously and consistently done, gives a high degree of patient safety; this appears to be the current standard of care worldwide.[14-18] Some medical specialty organizations have expressed the opinion that sterilization is the standard for all endoscopes; clearly, this goal is desirable, but at present, it may not be possible to implement or even achieve in all circumstances.

## CONCLUSION

Biological monitoring of liquid chemical sterilization processes using exposed filter paper spore strip BIs designed for penetrating germicidal agents such as steam or chemical gas does not appear feasible at this time. BIs could be useful, however, in research

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settings and carefully controlled laboratory studies centered around liquid chemical germicide process development or improvement. Furthermore, the most common uses for this type of automated reprocessing system involve complex, heat-sensitive medical instruments with components that are difficult, if not impossible, to clean. It seems only logical that the instrument problems must be addressed first.[12] Pitting such a medical instrument against any type of liquid chemical germicide system, however powerful, is not a fair challenge. Therefore, it would also seem logical for the manufacturers of chemical germicides and reprocessing systems to join with the infection control community in influencing governmental agencies to act accordingly under their existing regulatory authorities. Medical instrument manufacturers need to proceed immediately with device redesign where necessary and to provide in a timely manner clear, valid, data-based instruction for all aspects of access and cleaning for each individual instrument design. Until such action and information is forthcoming, there will continue to be claims, counter-claims, diversions of responsibility, confusion, and uncertainty. *Caveat emptor* or *caveat venditor?*

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