

# **Biological Indicators for Sterilization Processes**

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Jeanne Moldenhauer**

PDA  
Bethesda, MD, USA  
DHI Publishing, LLC  
River Grove, IL, USA

[www.pda.org/bookstore](http://www.pda.org/bookstore)

10 9 8 7 6 5 4 3 2 1

**ISBN: 1-933722-27-4**

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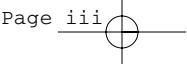


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2636 West Street  
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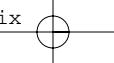
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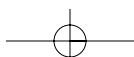
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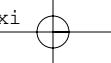
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## INTRODUCTION

The purpose of a sterilization process is to inactivate microorganisms; therefore, we need to verify that the sterilization process is effective in inactivating microorganisms. Even though sterilization processes are defined and monitored using physical parameters, the delivered lethality of the process is assessed by using a microbial challenge. Microorganisms are capable of sensing all the conditions that affect lethality and therefore the results that we obtain during a microbial challenge are an integration of all of these conditions, some of which we cannot measure or might be unaware of.

A biological indicator challenge system (BI), as defined in the Parenteral Drug Association Technical Report No. 1, is a “test system containing viable organisms of a pure, specified strain providing a defined resistance to a specified sterilization process”. It is important to note that BIs are defined as a system consisting not only of the sensing element, the microorganisms, but also of the carrier material onto or into which the spores are placed and the packaging used. Although there is some discussion as to whether we calibrate or characterize the resistance of a BI, it is important to use BIs for which the resistance to the particular sterilization process is known. Typically the organisms used in BIs possess a resistance to the inactivation process which is higher and in many instances highly exceeds the resistance of common bioburden organisms.

It is important to realize that we are dealing with biological entities to demonstrate the microbial killing power of an inactivation treatment. The response of the microorganisms to the inactivation treatment will be influenced by a variety of known and unknown factors and conditions to which the microorganisms are

subjected not only during the sterilization process but also before and after the sterilization process. All these factors must be tightly controlled since they affect the performance of the BIs and hence the results obtained.

In the first chapters of the book, the basic concepts necessary to the understanding of biological indicators are presented. The chapters include the history of biological validation and general principles, the kinetics of microbial inactivation and factors affecting resistance as well as a chapter dealing specifically with bacterial endospores since, due to their high resistance to most inactivation process, they are commonly used to challenge the process. The different perspectives on the use of BIs in the developments, validation and monitoring of sterilization processes in the U.S., Europe and Japan are presented as well as the various references and standards available worldwide.

The next chapters are dedicated to a discussion of biological indicators, or biological validation, used for specific sterilization or decontamination processes. These chapters present a guidance on the selection, use and interpretation of results and highlight the importance of using biological challenges that are appropriate for the particular microbial inactivation process.

Margarita Gómez  
Jeanne Moldenhauer  
October 2008

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## ABOUT THE EDITORS

**Margarita Gómez** is a microbiologist with M.S. and Ph.D. degrees in Food Science from the University of Minnesota. Her more than 20 year involvement with biological indicators began as a student in Dr. Pflug's laboratory at the University of Minnesota and has continued through work as a supplier of biological indicators and by providing training and consulting support in the validation of microbial-control processes. She recently joined Ocean Spray Cranberries Inc. as Quality Manager, Corporate Quality. Previously she was Manager of Technical Services at VPCI Inc., where she assisted clients on regulatory, compliance and technical issues in environmental monitoring, microbial control and risk analysis in the pharmaceutical industry.

Margarita has co-authored technical papers in the field of sterilization, among them the chapter on Principles of the Thermal Destruction of Microorganisms in Block's book on *Disinfection, Sterilization and Preservation*. She is a member of several technical associations and has been a lecturer for the University of Minnesota, CFPA, PDA, and ISPE organizations.

**Jeanne Moldenhauer**, Excellent Pharma Consulting, has more than 25 years experience in the pharmaceutical industry. She chairs the Environmental Monitoring/Microbiology Interest Group of PDA, serves on the Scientific Advisory Board of PDA, founded the Rapid Microbiology User's Group™, and is a member of ASQ and RAPS. She is the author of *Steam Sterilization: A Practitioner's Guide*; *Laboratory Validation: A Practitioner's Guide*; *Environmental Monitoring: A Comprehensive Handbook*; *Systems Based Inspections for Pharmaceutical Manufacturers*; and numerous other publications.

