MICROBIOLOGY IN PHARMACEUTICAL MANUFACTURING

SECOND EDITION

REVISED AND EXPANDED

Richard Prince

Editor

VOLUME 2

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INTRODUCTION

In the 1980s, we witnessed the beginning of the AIDS pandemic. It remains out of control in parts of the developing world. In the first decade of this century, we saw indicators of an avian influenza pandemic possibly one day ravaging humanity. What will happen in the next decade or two? What impact will climactic variability, whether "natural" or human-derived — have on microorganisms that cohabit our planet? Will it subtly change microbial ecosystems in a manner that will impinge upon eukaryotic ecosystems, including our own? Will the march of biotechnology soon lead to the plausible use of "designer genomes" that will benefit humans? And, if so, how will the community of microorganisms respond? I would guess in a way that reestablishes some degree of inter-species stability to neutralize the impact of human intervention. Regardless, we seem fated to continue to engineer new industrial approaches — including the recent, remarkable advances in creating synthetic microorganisms — intended to either safeguard our species from the ever-present danger of microorganisms or to leverage microorganisms themselves for some other useful benefit to humanity. We humans are endowed with a purpose. We now have the molecular biological methods to change the natural world to serve our purpose. A basic respect for microorganisms and the field of microbiology is thus in order!

The pharmaceutical industry exists to discover, develop, manufacture and distribute diagnostic and therapeutic products (drug; biologics) that will protect and advance human health. Some of these drugs (antibiotics) are designed to kill pathogenic microorganisms, some are designed to prevent disease in the first place

(vaccines) while yet others are intended to improve some type of biological performance. All drugs, biologics and allied products must be manufactured properly so that they themselves are not the carriers of disease and death. Microbes seemingly lurk everywhere. So, our task as an industry is to design, develop and implement quality systems that will be used in a manufacturing setting to help ensure that product batches are consistently made to all predefined quality attributes and specifications. But quality of course is more than just meeting specifications; it is attitudinal. Quality (as a discipline, as a field) is about — or should be about — identifying new, more sophisticated ways to maintaining and augmenting our assurance of the quality of the products that are commercially distributed. This is not an easy task given the scale and variability expressed in microbiological systems as well as the variability experienced in the systems used to manufacture, test and distribute such products. And even if we could outwit microorganisms (through technology, in particular) in our ability to consistently provide safe and efficacious products of highest possible quality, it can become somewhat moot given the uneven compliance practices of humans to dispense and administer such products at home. Microbes are like slippery eels that we seek to temporarily grab but we can't in fact hold on to for very long. We try to control them, even to conquer them, but for every new drug or biologic that satisfies an unmet clinical need, there is, as well, the steady sting of microbial mutation, of microbial resistance, and of primitive, prokaryotic defiance. Microbes, then, are friend and foe, a formidable intellectual and enduring professional challenge for the scientist, the ethicist and the philosopher.

In the first edition of this book, published in 2001, the reader was advised to think of microbiology in a comprehensive and systematic way. That book was very well received and argued the need for a second edition, which is hereby presented. If there is a message in this edition, it is this: Our health is a function of many variables, some within our control (e.g., living practices) and some beyond (e.g., our genetic make-up), and our ability to maintain or improve our health rests upon our humility to appreciate the fragility and variability of life, the difficulty in changing our ways, and the insidious, invisible, ubiquitous role played by microorganisms. We must be vigilant, but we must also be sensible in the things that we can do to meaningfully improve our quality of life. Our noble pursuit is to try and raise the bar on human longevity and wellness. Somewhere in that quest, we intersect with microorganisms, charged with their own ancient, ambivalent mission. We will need to summon all of our creative talents and wisdom to strike the proper balance between the conflicting human traits of hegemony and humility.

The second edition is largely modeled on the first edition. Many of the authors who contributed chapters in the first edition have updated their respective chapters for this edition. Some authors appear for the first time in this text. All of them are subject-matter experts in their respective fields, they are found throughout the regulated world, and all of them provide content that will be of practical benefit to the pharmaceutical and biologics industry, and all of its allied fields.

Volume 1 covers Chapters 1–14

- Phylogeny
- Epidemiology
- Taxonomy
- Industrial Microbiological Primer
- Parenteral Facility Engineering
- Process Capability and Product Specifications
- Control Strategies during Product Development
- Risk Assessment in Production Operations
- Designing and Validating a Contamination Control Program
- Control Strategies for Biological Processes
- Sterilization Process Validation
- Sterilizing Filtration of Liquids
- Cleaning Validation
- Water Microbiology.

Volume 2 covers Chapters 15–30

- Science of Particulates
- Environmental Monitoring
- Disinfectants and Other Chemical Germicides
- Training of Aseptic Processing Personnel
- Comparison of Global Compendial Methods
- Rapid Microbiological Technologies and Methods (two chapters)
- Bacterial Endotoxins Testing
- Microbial Limits Testing
- Stability Program
- Handling and Management of Deviations
- Modern Quality Systems
- Regulatory Stewardship: Global Regulatory Dossier
- Internet and Microbiology
- Expert Opinion on Aseptic Processing.

The goal of this book is to provide updated and expanded microbiological information for the benefit of a global audience of stakeholders. It is sincerely hoped that each reader will find some content that will aid in formulating keener questions as well as finding smarter solutions, in a way that brings credit to all.

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