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Edited by Rosamund M. Baird, Norman A. Hodges and Stephen P. Denyer, **Handbook of Microbiological Quality Control, Pharmaceuticals and Medical Devices**

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Although this book is intended as a complete reference source in its own right, it is a companion book to the *Guide to Microbiological Control in Pharmaceutical Devices* (eds. S. Denyer & R. Baird 1990) shortly to be published in its second edition. The editors state that it is their intention to provide detailed practical information in this the Handbook, to accompany the methodology of the techniques advocated in the *Guide* and hence the publications should be used concomitantly. This book contains fourteen chapters covering the topics of Microbiological Practices, Culture Media Used in Pharmaceutical Microbiology, Sampling, Enumeration of Micro-organisms, Identification of Micro-organisms, Pharmacopoeal Methods for the Detection of Specified Micro-organisms, Microbiology Laboratory Methods in Support of the Sterility Assurance System, Endotoxin Testing, Microbiological Assay of Antibiotics in Pharmaceutical Preparations, Disinfection and Cleansing, Microbiological Hazard Analysis and Audit and a final chapter of case studies and worked examples.

The emphasis on risk assessment in the first chapter entitled *Safe Microbiological Practices*, is noteworthy. Detailed reference is made to current relevant legislation with a good discussion of the major acts governing handling of micro-organisms and the specific advisory groups and bodies in the United Kingdom. Although not currently relevant to microorganisms used in pharmacopoeal tests there is appropriate reference to the recently introduced legislation concerned with all aspects of handling genetically modified microorganisms. Chapter 2 reviews culture media used in pharmaceutical microbiology. An interesting discussion concerning resuscitation media for recovering injured cells with reference to a number of agents more widely used in food microbiology rather than pharmaceutical microbiology is provided. I found the section of particular interest since no reference is made to the likely presence of damaged organisms in either the sterility test or the preservative efficacy test in the current edition of the BP organisms.

Quality assurance underpins the chapter on sampling with a clear recognition of the additional problems posed by sampling for microbiological contamination. New quality concepts for sampling methodology are reviewed such as hazard analysis and control of critical points (HAACP) with appropriate reference to the implications of such approaches for sampling methodology. There is an excellent discussion on the limitations associated with current pharmacopoeal sterility tests due to the probability of passing contaminated batches. Guidance on tests for specific products is included in this section with useful notes for heat-sterilised products, aseptically made products and samples intended for endotoxin testing. Particular attention is given to the problem of bioburden sampling for medical devices with appropriate reference to the regulatory guidelines for new products. Chapter 4 reviews the enumeration of microorganisms and details the issues that must be addressed in terms of sample preparation and sample pretreatment requirements. The actual counting methods have changed little over the years – a fact readily acknowledged by the authors. The major advances over the past 10 years or so have been the advances in technology which have facilitated the development of a range of sophisticated automatic and "rapid" techniques but these are mentioned separately in Chapter 7. The techniques of pour-plating, membrane filtration, spread plating, Miles and Misra plating and most probable number are concisely presented. Turbidometric methods are discussed separately since the typical cell suspension concentrations will be of the order of 10^6 to 10^9 ml^{-1} for this technique.

Methods for identification of microorganisms are outlined in Chapter 5. The organisms most commonly found as contaminants of medicines and devices are all bacteria, yeasts and moulds; viruses are not normally considered as contaminants. The cultural and microscopic features of bacteria and moulds, which may assist in their identification, are tabulated and discussed. Biochemical tests used in schemes for bacterial identification are summarised. Common problems associated with staff training, correct assignment of Gram staining reactions and atypical aggregation patterns are briefly discussed. Methods for detection of specific microorganisms are presented in Chapter 6. An overview of the tests recommended by the European Pharmacopoeia (1997) is also provided in this section. A commendable feature of this chapter is the use of colour plates to illustrate the detection of various species. Chapter 7

details rapid methods for the enumeration and identification of microorganisms, building on the concepts introduced in Chapter 4 and it is difficult to see why these chapters were not presented in sequence. New technologies based on ATP bioluminescence, impedance and chemiluminescence are reviewed. The merits and demerits of current identification methods are briefly discussed and there is an interesting section devoted to future trends in identification largely concerning the utility of nucleic acid probes in this area.

Chapter 8 discusses the Sterility Assurance System and is further sub-divided into sections concerning sterility testing, bioburden testing, biological monitoring and environmental monitoring. While an informative chapter there is a degree of repetition particularly in the areas of sampling and methodology. Since the topic under discussion is rather general perhaps this is unavoidable and there is little new information presented in this chapter. Perhaps the same criticism could be levelled at Chapter 9, which reviews Endotoxin Testing but this is possibly due to the necessity to present a large amount of material in an abridged manner.

Chapter 10 details antimicrobial preservative efficacy testing with a good overview of the necessity for, and limitations of such tests. Practical guidelines concerning selection of counting methods, operator competence, selection and maintenance of test organisms, as well as growth, standardisation and storage of test inocula are outlined. The problems associated with container material compatibility with the preservative are addressed as are testing of anhydrous products. Performance criteria for preservative efficacy in the different pharmacopoeias are clearly explained. Useful suggestions for additional test organisms and cultural conditions are also included. Chapter 11 reviews the microbiological assay of antibiotics and this chapter is presented in a narrative fashion, detailing the two main assay methods with appropriate reference to the factors dictating assay performance and reliability of results.

Chapter 12 covers the topics of disinfection and cleansing. A notable inclusion here is the section on cleaning, disinfection and sterilisation of isolators since such information is sparse in the literature. Additionally the section on Clean-In-Place (CIP) and Sterilisation-In-Place (SIP) systems is a welcome inclusion in this chapter. Nor is the importance of validation of cleaning methods neglected with good attention given to the requirements for data and document collection, analytical methods, sampling methods and acceptance criteria. Brief monographs on the major disinfectant groups are also included. Chapter 13, microbiological hazard audit is very much written from the regulatory perspective. The preparation and management and follow-up of an audit are outlined. Typical procedures for audit of the microbiological laboratory and for audit of the manufacturing process are detailed. The last chapter presents a number of worked examples on topics such as calculation of viable counts and preservative efficacy test data, calculation of air change data. Case studies detailing the necessity for environmental monitoring in non-sterile manufacturing areas and audit of culture media manufacture are presented from a regulatory perspective. Such material might have been integrated more usefully into the relevant chapters but this is not to detract from the wealth of valuable and practical information detailed in this handbook, which will prove a useful reference to microbiologists in industry and academia.

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