Rapid Sterility Testing

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Editor

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PREFACE

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The current compendial sterility test methodology has been fully harmonized for Europe, Japan and the United States for many years (PF, 1999). In spite of having a fully harmonized test methodology the sterility test method as stated is flawed for its intended purpose. The dictionary definition of sterile is usually described as free from all viable microorganisms. As such, many who are unaware assume that the compendial test method, if acceptable, guarantees that there are no viable microorganisms present in the item being tested. Unfortunately, in reality the test methodology is only effective in detecting gross contamination in a batch of product. Two of the major issues with the test method were identified by Bryce in 1956 and include the following (Moldenhauer and Sutton, 2004):

- the test method is only able to detect those organisms that are able to grow under the conditions of the test

- the sample size for the test is so small that it only provides a gross estimate of the sterility of the product lot.

These same limitations stated in 1956 for the test are applicable to the conventional methods used today. Due to the flaws associated with the test method, other methods and controls are employed to aid in assuring the sterility of the product.

In the early 1980s Baxter Healthcare, Inc. implemented a program called parametric release. The program was based upon its extensive knowledge of its moist heat terminal sterilization processes. In fact, it understood these processes so well that when the specified acceptance criteria for the cycles is met, they could ensure that the product is sterile without performing a compendial sterility test. It was another 15 years before another company successfully obtained parametric release for its products.

With the current requirement for a 14-day incubation for the compendial sterility test, eliminating this requirement with the implementation of parametric release allowed for a substantial cost avoidance associated with storing the product during this time.

Companies that implemented parametric release for their terminally sterilized products then focused on how their aseptically processed products might achieve a shortened time to product release (as part of the sterility test). To date regulatory support has not been gained to support a program of parametric release for aseptically-filled products. This has resulted in many companies looking at rapid sterility testing methods to reduce the time to release for aseptically-filled products.

In this book you will find a detailed history of the sterility test methodology. Discussions are also provided for the regulatory requirements and allowances for gaining approval of rapid sterility test methods. Compendial requirements for validation and implementation of these methods in the United States and Europe are also discussed. Several different authors have provided information on the types of methods that can be considered for sterility testing. There are also chapters that discuss issues like the statistical methods used to validate these methods, especially since many of the new technologies are superior to the conventional methods. Last, there are

a substantial number of case studies describing how various companies have approached selecting, validating and implementing a new methodology for sterility testing at their site.

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