Bacterial Aerosol Challenge of Tevadaptor®

Ensuring Sterility and Drug Safety

Nelson Laboratories, Salt Lake City, Utah, USA, June 2009

Summary

Drug sterility is of fundamental importance during any pharmaceutical procedure. Tevadaptor®, a closed drug reconstitution system developed by Teva Medical Ltd. to prevent the escape of hazardous drug species, was tested in order to ensure its ability to maintain sterility of pharmaceutical preparations. An aerosol challenge using Bacillus atrophaeus spores was applied. All 28 Tevadaptor® samples tested demonstrated **100% no growth** following the extreme bacterial aerosol challenge. All control samples were found to be contaminated. Thus Tevadaptor® was confirmed as a sterility-maintaining closed drug reconstitution system.

Introduction

According to NIOSH Publication No. 2004-165, a **closed system** is "a device which does not exchange unfiltered air or contaminants with the adjacent environment". A **Closed system drug-transfer** device is "a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapour concentrations outside the system."

The Tevadaptor® closed system and control devices were tested for conformance to these definitions.

All test samples were subjected to microbial aerosol challenge using Bacillus atrophaeus spores.

Objective

To ascertain the ability of the Tevadaptor® closed system to maintain sterility of the pharmaceutical preparations, through a bacterial aerosol challenge test.

Materials & Methods

Bacillus atrophaeus, was inoculated onto soybean casein digest agar (SCDA) plates and incubated. Challenge solutions were prepared by harvesting, filtration and heat shock. Two identical bacterial aerosolization tests were conducted, one for Tevadaptor® samples and one for controls. The challenge solution delivery rate was 20ml per hour, to a nebulizer attached to the aerosol exposure chamber.

Samples were exposed to the challenge for 60 minutes.

The aerosol levels were monitored with fallout samples consisting of five 2x2 inch pieces of gauze aseptically placed inside the chamber prior to the challenge. The gauze pieces were extracted, diluted and plated onto SCDA plates. All SCDA plates were incubated at 30-35°C for 24-48 hours and enumerated.

Colony counts from an Andersen sampler were converted to probable hit values using a validated spreadsheet. The mean particle size (MPS) of the aerosolized challenge was calculated.

1st Run - Control: Thirty sterile, empty syringes with plunger half drawn out, representing conventional technique. Following the challenge and prior to testing for the indicator organism, the exteriors of syringes were decontaminated. Samples were aseptically placed in an appropriate volume of soybean casein digest broth (SCDB) and tested for the indicator organism by flushing them with soybean casein digest broth (SCDB). The samples were then incubated for 7 days at 30-35°C. All samples were inspected for growth of the challenge organism.

2nd Run - Twenty eight sterile, TSB-filled (Tryptic Soy Broth) vials with mounted Tevadaptor® Vial Adaptor were tested for the indicator organism following the challenge. The exteriors were decontaminated and TSB samples aseptically withdrawn through the Vial Adaptor and flushed into an SCDB container, which was then incubated for 7 days at 30-35°C. All samples were inspected for growth of the challenge organism.

Results

Sample	Results	
	Run 1	Run 2
Test Samples	Growth (30/30)	No Growth (28/28)
Negative Samples	No Growth (2/2)	No Growth (2/2)
Positive Samples	N/A	Growth (2/2)
Compromised jar of SCDB	Growth (1/1)	Growth (1/1)
Media Monitor	No Growth (1/1)	N/A
Environmental Monitor	No Growth (1/1)	N/A
Growth Promotion	N/A	Growth (1/1)

In Run 1- All control samples failed the No Growth test.

In Run 2 **with Tevadaptor®** - All Tevadaptor® samples demonstrated 100% No Growth.

Tevadaptor® Samples tested from TEVA Medical LTD demonstrated 100% no growth following an extreme bacterial aerosol challenge.

Conclusion

Tevadaptor® ensures sterility maintaining of pharmaceutical preparations.

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