

Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT)



Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT) Team

Authors

The authors formed a multicompany consortium comprising more than 50 subject matter experts from 25 biopharmaceutical manufacturing companies and filter suppliers to consider the different aspects of implementing PUPSIT. The experts are experienced in sterile filtration and authors drew upon their collective experiences, current company practices, consultations with stakeholders and colleagues, and a review of current regulatory guidelines.

Steve Ensign, Eli Lilly and Company
Will Peterson, Merck Sharp & Dohme
Hal Baseman, ValSource
Dieter Bachmann, Johnson & Johnson
Stephanie Ferrante, Millipore Sigma
Jeff Gaerke, CAI
Maik Jornitz, G-CON Manufacturing Inc.
Tina Morris, Parenteral Drug Association
Thao Le Vinh, Glaxo Smithkline

Specieal Thanks To

Allan Elder, BioPhorum (retired) Jannika Kremer, BioPhorum Ali Wilson, BioPhorum

Points to Consider for Implementation of Pre-Use Post-Sterilization Integrity Testing (PUPSIT)

ISBN: 978-1-945584-18-3 © 2020 Parenteral Drug Association, Inc. All rights reserved.





www.pda.org/bookstore

Table of Contents

I.	INTRODUCTION AND SCOPE1
II.	GLOSSARY2
III.	BACKGROUND3
	Definition of a Sterilizing Grade Filter
	Overview of Filter Integrity Testing
	Selection of an Integrity Test Method5
IV.	UNDERSTANDING RISK DRIVERS FOR PUPSIT IMPLEMENTATION7 Patient Sterility Risk7
	Product Discard (Product Availability) Risk8
V.	INTEGRATION OF PUPSIT INTO THE MANUFACTURING OPERATION

	Considerations when Using Water or Buffer as the Wetting Fluid	.10		
	Considerations when Using the Process Solution as the Wetting Fluid	.13		
	Need for Redundant Filtration of the Process Stream.			
	PUPSIT Venting and Flushing Design Considerations	15		
	PUPSIT-Related Temperature Considerations	17		
	Considerations Related to Maintaining Sterility	18		
	Typical Steps in PUPSIT Operation	20		
	Change Control Considerations in Maintaining a			
	Robust PUPSIT Process	24		
VI.	CONCLUSION	25		
VII.	REFERENCES	26		
VIII. APPENDIX: TWO EXAMPLES OF PUPSIT IMPLEMENTATION27				

Example 1: Hard-Piped, Highly Automated System27 Example 2: Single-Use Manual System30

FIGURES AND TABLES INDEX

Figure 1	Points where Pre-Use and Post-Use Integrity Testing can be Performed3
Table 1	Suggested Integrity Test Method to Use for Systems with Different Filtration Areas6
Figure 2	Location of Filter Train9
Table 2	Advantages of Using Water or Buffer (Vehicle) as the Wetting Fluid11
Table 3	Disadvantages to Using Water or Buffer as the Wetting Fluid11
Figure 3	States of a Filter Assembly when Performing a Forward Flow Integrity Test12
Table 4	Advantages to Using the Process Fluid as the Wetting Fluid13
Table 5	Disadvantages to Using the Process Fluid as the Wetting Fluid13
Figure 4	Two Options for Venting/Flushing when Performing PUPSIT15
Figure 5	Backpressure Examples when Performing PUPSIT17
Figure 6	Schematic of Venting the Air Out of the System21
Figure 7	Schematic of Performing an Integrity Test22
Figure 8	Schematic of Performing an Air Blow for Drying23

Table A-1	Attributes for Two Examples of PUPSIT Implementation27
Figure A-1	Schematic of Filtration Operation for Example 127
Table A-2	Steps Associated with Example 128
Figure A-2	Venting Air Out of the System28
Figure A-3	Wetting the Filter Membrane28
Figure A-4	Performing the Integrity Test of the Filter (PUPSIT)29
Figure A-5	Performing Air Blow to Dry Filter Assembly29
Figure A-6	Performing the Integrity Test of the Vent Filters29
Figure A-7	Venting the Test Gas Out of the System30
Figure A-8	Schematic of Filtration Operation for Example 230
Table A-3	Steps Associated with Example 231
Figure A-9	Venting the Air Out of the System31
Figure A-10	Wetting the Filter Membrane31
Figure A-11	Performing the Integrity Test of the Filter (PUPSIT)32
Figure A-12	Performing the Integrity Test of the Vent Filter32
Figure A-13	Venting the Test Gas Out of the System32
	www.nda.org/boc

www.pda.org/bookstore



Bethesda Towers 4350 East West Highway Suite 600 Bethesda, MD 20814 USA Tel: +1 (301) 656-5900 Fax: +1 (301) 986-0296 E-mail: info@pda.org Web site: www.pda.org



The Gridiron Building One Pancras Square London N1C 4AG Tel: 06794795

www.pda.org/bookstore