PALL BioPharmaceuticals

Validation Guide

USTR 2057

Validation of special purpose 'Fluorodyne' II grade DFL filter cartridges

*Filtration. Separation. Solution.*SM

CONTENTS

Part 1. Overview

1. Introduction

'Fluorodyne' II DFL 'P'-grade filters have been fully validated for sterilising liquid applications in the Pharmaceutical industry. Results of the validation study are published in Pall publication 'Validation guide for Pall 0.2µm Fluorodyne II membrane cartridges', reference USTR1548.

A new variant of **Fluorodyne** II DFL 'P'-grade filters has been developed for specific automated steam-in-place processes and offers enhanced strength compared to the standard product. The part number for a 25cm filter for the special purpose product is ABGY1DFL7PH4. The only difference in the variant is the composition of the material used to manufacture the filter core. The core for the general purpose product is manufactured using polypropylene and that for the special purpose product is made from polypropylene with the addition of glass reinforcement to provide a higher strength material.

The published validation guide for **Fluorodyne** II DFL grade filters is equally applicable to the special purpose filters. The new core only affects the performance of the filter by increasing the overall strength of the filter construction. The other properties of the filter remain unchanged.

Additional laboratory tests have been performed to confirm that special purpose **Fluorodyne** II DFL filters (part number ABGY1DFL7PH4) provide

- **Equivalent performance to the general purpose product regarding bacterial removal efficiency, resistance to cumulative steam sterilisation and biological safety.**
- **Resistance to transient differential pressure of up to 3bar immediately after steaming at 142°C.**

These tests are summarised in this report.

2. Bacterial challenge tests with *Brevundimonas diminuta* (ATCC 19146)

Filter samples (part number ABGY1DFL7PH4) from a typical batch were selected at random and subjected to a microbial challenge test using an aqueous suspension of *Brevundimonas diminuta* (ATCC 19146). In all cases, the challenge level used was > $1x10^7$ colony forming unit per cm^2 of filter membrane area.

Before and after the challenge test the filters were integrity tested using the Forward Flow method. The procedures used have been described in detail in the validation guide for the standard product (see reference above).

The microbial challenge results are shown in Table 1. The higher of the two Forward Flow values are presented. All of the filters passed the Forward Flow test and gave sterile effluent when challenged with *B. diminuta*.

Table 1. Microbial challenge results for ABGY1DFL7PH4

Pall filter serial number	Forward Flow* value (ml/min)	Sterile effluent	Titre reduction
ID1199011	11.0	Yes	> 1.8×10^{11}
ID1199022	10.7	Yes	> 2.0×10^{11}
ID1199047	10.2	Yes	> 1.7×10^{11}
ID1199097	9.2	Yes	> 1.6×10^{11}
ID1199101	10.0	Yes	> 2.0×10^{11}
ID1199015	11.3	Yes	> 2.3×10^{11}
ID1199035	10.7	Yes	> 1.2×10^{11}
ID1199044	10.6	Yes	> 1.7×10^{11}
ID1199056	10.9	Yes	> 1.9×10^{11}
ID1199080	11.4	Yes	> 1.8×10^{11}
ID1199088	10.7	Yes	> 1.7×10^{11}

* *Forward Flow parameters: Filters water wetted, air test pressure 2760 mbar, maximum allowable limit 12.0 ml/min.*

3. Resistance to cumulative steam sterilisation

Filter samples (part number ABGY1DFL7PH4) from a typical batch were selected at random and subjected to 20 one-hour steam in place cycles at 142°C. Between each steam cycle the filters were cooled with dry compressed air for 30 minutes. After every five cycles filter integrity was checked using the Forward Flow test method.

The results are shown in Table 2. All of the filters retained integrity after exposure to 20 one-hour steam cycles at 142°C. These data demonstrate that special purpose **Fluorodyne** II filters can withstand exposure to cumulative steam cycles.

Table 2. Forward Flow measurements during repeat in-line steam sterilisation cycles for ABGY1DFL7PH4 filters

Pall filter serial number	Forward Flow*(ml/min) after steaming at 142°C for the following number of one hour cycles:				
	0	5	10	15	20
ID1199016	9.8	8.7	8.5	8.5	7.8
ID1199020	8.3	9.6	9.6	9.6	9.6
ID1199052	10.4	9.8	9.3	9.3	9.1
ID1199064	8.3	11.1	11.4	11.4	11.3
ID1199083	9.8	9.6	9.7	9.7	9.4

* *Forward Flow parameters: Filters water wetted, air test pressure 2760 mbar, maximum allowable limit 12.0 ml/min.*

4. Collapse tests

Filter samples (part number ABGY1DFL7PH4) from a typical batch were selected at random and subjected to collapse tests. The tests were performed as follows. Each filter to be tested was flushed with water and then steamed at 142°C for 30 minutes. On completion of the steaming period the filter assembly was vented to remove the steam and air was immediately introduced on the upstream side of the hot filter at a pressure of 3 barg. Under these conditions the hot filters were therefore exposed to a differential pressure of 3 bar. After each cycle the filter core was inspected for damage.

The above sequence was repeated for up to five cycles.

The results are shown in Table 3. None of the filters tested (part number ABGY1DFL7PH4) were found to collapse after 5 cycles of exposure to high differential pressures at high temperature.

Table 3. Results of collapse tests for ABGY1DFL7PH4 filters

Pall filter serial number	Status of filter ΔP cores after the following number of high DP / high temperature cycles:				
	1	2	3	4	5
ID1199013	OK	OK	OK	OK	OK
ID1199061	OK	OK	OK	OK	OK
ID1199099	OK	OK	OK	OK	OK

5. Biological Safety

The biological safety of general purpose **Fluorodyne** II grade DFL filters has been confirmed and the results are reported in the validation guide for that product, ref. USTR 1548. As the core of the special purpose version contains a different material, a typical sample of the core used in this product (part number ABGY1DFL7PH4) has also been tested. The tests were performed in accordance with the Biological Reactivity Tests in vivo for Class VI - 121°C Plastics as described in the current *United States Pharmacopeia*. The tests were conducted by Gibraltar Laboratories Inc., Fairfield, New Jersey.

The test report attached confirms that the material used to manufacture the core used in special purpose **Fluorodyne** II grade DFL filters (part number ABGY1DFL7PH4) meets the requirements of the USP for Class VI -121°C Plastics (*in vivo*).

GIBRALTAR LABORATORIES, INC.

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122 FAIRFIELD RD., FAIRFIELD, NJ 07004-2405 • PHONE: (973) 227-6882 • FAX: (973) 227-0812
13504-C SOUTHPOINT BLVD., CHARLOTTE, NC 28273-5763 • PHONE: (704) 588-7288 • FAX: (704) 588-6158
e-mail: danielprince@gibraltarlabsinc.com • internet: http://www.gibraltarlabsinc.com

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LABORATORY REPORT

FINAL REPORT

Sponsor: (0850)
Pall Corporation
25 Harbor Park Drive
Port Washington, NY, 11050
Attn: Janet Mathus
Purchase Order #: P434807

GBL Ref.: 1399- 196- 7202
GBL Sample No.: 10888/1.30
Lot #1:
Lot #2: None
Lot #3: None
Date Received: 08/26/99
Date Tested: 08/31/99
Date Completed: 09/10/99

USP 23 CLASS VI on Glass Filled Polypropylene Core
Interim Report Activity:

Description:
One clear plastic bag containing Glass Filled Polypropylene Core approximately 9 1/4" in size.
Bag labeled: 10" AB Core; Material: Fiberfil; J60/20/Natural

1. Purpose
To determine the reaction of normal animal tissues and living animals to the presence of extracts and/or portions of the test material.

2. Test System
2.1 New Zealand albino rabbits, either sex, 2.62 to 3.59 kg.
Two for intracutaneous injection, two for implantation.

2.2 Swiss Webster albino mice, either sex 22.1 to 30.0 grams.
Five test and control (intravenous and intraperitoneal injection).

3. Method: Test Material Preparation and Extraction
3.1 2.3 grams were extracted in 11.5 mL of the following solvents:
(X) USP Sodium Chloride for Injection (Saline)
(X) 5% Ethanol in Sodium Chloride (ETOH/Saline)
(X) Cottonseed Oil (CSO)
(X) Polyethylene glycol 400 (PEG)

3.2 Extraction Conditions
( ) 50C for 72 hours
( ) 70C for 24 hours
(X) 121C for one hour

3.3 Dosing Procedures
(X) IC Injection - three day observation period
(X) Systemic Injection (IV and IP) - three day observation period
(X) Intramuscular Implantation - seven day observation period

Respectfully Submitted,
GIBRALTAR LABORATORIES, INC.

Date Written: 09/16/99
Approved By:
Analyst: 41 J. Chris Knutsen, Ph.D. or Daniel L. Prince, Ph.D.
Protocol #: None

AUDIT 9/16/99 GBL

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13504-C SOUTHPOINT BLVD., CHARLOTTE, NC 28273-6763 • PHONE: (704) 588-7288 • FAX: (704) 588-6156
e-mail: danielprince@gibraltarlabsinc.com • internet: http://www.gibraltarlabsinc.com

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LABORATORY REPORT

4. Results: See Tables 1 to 3.

Table 1: Intracutaneous Irritation

Extract	Average Test Score	Average Control Score	Difference
Saline	(0.00)	(0.00)	(0.00)
ETOH/Saline	(0.00)	(0.00)	(0.00)
CSO	(3.75)	(2.92)	(0.83)
PEG 400	(0.00)	(0.00)	(0.00)

Table 2: Systemic Toxicity

	(Test Group)		(Control Group)		
Extract	Death	Morbidity	Death	Morbidity	Difference
Saline	0/5	0/5	0/5	0/5	0/5
ETOH/Saline	0/5	0/5	0/5	0/5	0/5
CSO	0/5	0/5	0/5	0/5	0/5
PEG 400	0/5	0/5	0/5	0/5	0/5

Table 3: Intramuscular Implantation

Sample Size	Average Test Score	Average Control Score	Difference
1 x 10 mm	(0.00)	(0.00)	(0.00)

5. Conclusion: The material conformed to the requirements of this test.

PALL BioPharmaceuticals

Europa House, Havant Street
Portsmouth PO1 3PD, United Kingdom

Telephone: +44 (0) 23 9230 3303
Fax: +44 (0) 23 9230 2506
e-mail: UltrafineUK@pall.com
World Wide Web site: http://www.pall.com

Visit us on the web at www.pall.com

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