ErtelAlsop

The First Name in Liquid Filtration™

MicroMedia®

DE Series
Depth Filter Media
Validation Guide

MMDEVG

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1. Introduction

1.1. Overview

Validation may generally be defined as, "Establishing documented evidence which provides a high degree of assurance that all specific processes used in the manufacture of a drug product will consistently produce a product meeting its pre-determined specifications and quality attributes" (quote from PDA/FDA Joint Conference on Sterilization Process Validation).

By extension, those elements, such as filters, used in the process must also meet these criteria. That is, they must consistently meet pre-determined specifications and quality attributes.

The purpose of this guide is to provide corroborating information about ErtelAlsop depth filter media used in pharmaceutical processing. The information was derived from tests performed by both independent testing laboratories as well as the ErtelAlsop QC Laboratory.

1.1.1. Quality Policy

The ErtelAlsop philosophy is continual improvement of all aspects of our company. Its objective is to meet or exceed customer requirements while supplying the fastest delivery available.

Our mission is to continue to foster superior innovations in aligning our customer needs with our empowered employees and management partnership. It is required that all employees participate within the Quality Policy.

1.1.2. Depth Filter Media Grades Covered by this Validation Guide

The following depth filter media grades are covered by this Validation Guide:
M-104P
M-404P
M-454P
M-504P
M-504TP
M-704P
M-854P
M-954P

1.2. Physical Characteristics

1.2.1. Appearance

The filter sheets/pads are dull white in color. They are rough on one side, and have a smooth screened appearance on the opposite side.

1.2.2. Composition

MicroMedia: DE Series depth filtration media is made with cellulose, diatomaceous earth filter aid, wet strength resins and cellulose copolymers.

1.2.3. Physical State

Filter Sheets/pads are manufactured in two shapes, round and rectangular, and are available in various sizes depending on user requirements.

ErtelAlsop Zeta-Pak® (Pak) depth filter cartridges, also known as depth filter modules, are available in several configurations and options. Paks are manufactured in 12 inch (30.5 cm) or (16 inch) (40.6 cm) diameter, and are assembled with a varying number of filter cells.

1.2.4. Technical Specifications

Depth Filter Media Grade	Retention Nominal Rating	Flow Rate* L/min/m^2 (Gal/min/ft^2)	Thickness mm (Inches)	Ash Content %
M-104P	10 µm	1029 (25)	4.1 (0.16)	20
M-404P	5.0 µm	514 (12.5)	4.1 (0.16)	36
M-454P	2.5 µm	309 (7.5)	4.1 (0.16)	43
M-504P	1.0 µm	154 (3.8)	4.1 (0.16)	50
M-504TP	0.8 µm	103 (2.5)	4.1 (0.16)	50
M-704P	0.45 µm	69 (1.7)	4.1 (0.16)	55
M-854P	0.3 µm	38 (0.9)	4.1 (0.16)	55
M-954P	0.25 µm	21 (0.5)	4.1 (0.16)	53

2. Validation Program

This validation program included the following tests:

2.1. Depth Filter Media

- Extractables
  - Total Extractables according to 21CFR 177.2260
  - Extractable Metals
  - Conductivity Shift
  - pH Shift
- Endotoxins
- (1→3)-β-D-Glucans
- Cytotoxicity
- USP Biological Reactivity Tests for Class VI Plastics

2.2. Plastic Components

- USP Biological Reactivity Tests for Class VI Plastics

3. Test Procedures and Results - Media

3.1. Extractables

3.1.1. Total Extractables according to 21CFR 177.2260

3.1.1.1. Procedure

Sample Preparation
Samples were prepared in accordance with 21CFR 177.2260.

Analysis
Samples were analyzed in accordance with 21CFR 177.2260, using the following solvents and temperatures.

Solvent	Temperature
Water	37°C
Water	63°C
Water	100°C
5% Acetic Acid	100°C
Hexane	68°C
8% Ethanol	78°C
50% Ethanol	78°C

3.1.1.2. Results

ErtelAlsop tested media grade is below the limits set forth and has met the requirements according to 21CFR 177.2260.

3.1.2. Extractable Metals

3.1.2.1. Procedure

Sample Preparation
Distilled water is pumped through the media at a flow rate of 500 l/m^2/hr. The first 50 L/m^2 of distilled water is flushed through the media and discarded.
An additional 10 L/m^2 is flushed through the media and saved for analysis.

Analysis
The resulting solutions were analyzed for the elements of interest by inductively coupled plasma optical emission spectroscopy (ICP-OES). The ICP-OES was calibrated with working standards prepared by serial dilution of purchased NIST-traceable stock standards. Yttrium was used as internal standard.

3.1.2.2. Results

Metal	Result (ppb)
Aluminum	17.5
Arsenic	<10
Calcium	6312
Chromium	<3
Copper	<3
Iron	4
Lead	<10
Magnesium	71
Nickel	<3
Potassium	51
Sodium	117

3.1.3. Conductivity Shift

3.1.3.1. Procedure

Sample Preparation
Distilled water is pumped through the media at a flow rate of 500 l/m^2/hr. Samples for measurement are taken at the following intervals:

Between 5-10L/m^2
After 50L/m^2
After 100L/m^2

Analysis
Conductivity is measured using a conductivity meter calibrated with NIST traceable standards.

3.1.3.2. Results

Starting Water (µS)	5 – 10 L/m^2 (µS)	After 50 L/m^2 (µS)	After 100 L/m^2 (µS)
109.6	310.5	57.2	44.8

3.1.4. pH Shift

3.1.4.1. Procedure

Sample Preparation
Distilled water is pumped through the media at a flow rate of 500 l/m^2/hr. Samples for measurement are taken at the following intervals:

Between 5-10L/m^2
After 50L/m^2
After 100L/m^2

Analysis
pH is measured using a pH meter calibrated with NIST traceable standards.

3.1.4.2. Results

Starting Water	5 – 10 L/m^2	After 50 L/m^2	After 100 L/m^2
5.8	7.8	9.0	9.4

3.2. Endotoxins

3.2.1. Procedure

Sample Preparation
Distilled water is pumped through the media at a flow rate of 500 l/m^2/hr. The first 50 L/m^2 of distilled water is flushed through the media and discarded.
An additional 10 L/m^2 is flushed through the media and saved for analysis.

Analysis
Samples were analyzed using the Kinetic Turbidimetric LAL method. The standard curve was constructed by plotting the log onset time against the log concentration of the standard endotoxin. The standard curve consists of six standard concentrations in duplicate. The regression analysis of the curve yielded a correlation coefficient of at least 0.980 and the mean measured concentration of positive controls was within 25% of the nominal concentration.

3.2.2. Results

All results were below the detection limit of 0.04 EU/mL

3.3. (1→3)-β-D-Glucans

3.3.1. Procedure

Sample Preparation
Distilled water is pumped through the media at a flow rate of 500 l/m^2/hr. The first 50 L/m^2 of distilled water is flushed through the media and discarded.
An additional 10 L/m^2 is flushed through the media and saved for analysis.

Analysis
The samples were analyzed using serial dilutions with LRW which ranged from 1:2 to 1:20 in duplicate, to find minimum, non-interfering dilutions. Positive product controls, a parallel series of sample dilutions fortified with a known amount of glucan standard, were tested in duplicate. The absolute value for the correlation coefficient for the calibration curve was greater than or equal to 0.980.

3.3.2. Results

(1→3)-β-D-Glucans (pg/mL)
886

3.4. Cytotoxicity

3.4.1. Procedure

Sample Preparation
Samples are prepared in accordance to USP 87

Analysis
Samples are analyzed in accordance to USP 87

3.4.2. Results

The test article met the USP 87 requirement.

3.5. USP Biological Reactivity Tests for Class VI Plastics

3.5.1. Procedure

Sample Preparation
Samples are prepared in accordance to USP 88

Analysis
Samples are analyzed in accordance to USP 88

3.5.2. Results

Systemic Injection	Intracutaneous	Intramuscular
Pass	Pass	Pass

4. Test Procedures and Results – Plastic Components

4.1. USP Biological Reactivity Tests for Class VI Plastics

4.1.1. Procedure

Sample Preparation
Samples are prepared in accordance to USP 88

Analysis
Samples are analyzed in accordance to USP 88

4.1.2. Results

4.1.2.1. Polypropylene Components

Systemic Injection	Intracutaneous	Intramuscular
Pass	Pass	Pass

4.1.2.1. Felt

Systemic Injection	Intracutaneous	Intramuscular
Pass	Pass	Pass

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