ErtelAlsop

The First Name in Liquid Filtration™

MicroCap Pro™

Single Use Disposable Filter Capsules Validation Guide

VGMCP-1/19 Rev A

Contents

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 MicroCap Pro for use in pharmaceutical processing. The information was derived from tests performed by both independent testing laboratories as well as the ErtelAlsop QC Laboratory.

1.2. Quality Policy

The ErtelAlsop philosophy is continuous 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.

2. Determination of Water Flow Characteristics

2.1. Introduction

The purpose of this test was to determine the differential pressure across the range of ErtelAlsop filter media in all three sizes of MicroCap Pro capsules. The outcomes prove linear scalability of the capsule design.

2.2. Summary

The filter media grades selected for this test were single layer M103P and double layer M954P which represent the highest and lowest water permeability in the ErtelAlsop media range. Each media type was run in multiple large, medium, and small capsules to capture a large array of data.

Filtered water was pumped through the capsules in the forward flow direction, after the capsules were fitted in an ErtelAlsop Chassis used as the test station. Flux started at 750 L/m2·h for 10 minutes, then flow was increased. Pressure readings were taken automatically from pressure transducers installed on the inlet and outlet of the test assembly, as flux was increased 50-100 L/m2·h, and allowed to settle. Each test was repeated three times per capsule and results were corrected to a standard of 20 °C.

2.3. Results

Figure 1:

Water Flow Characteristic Results of Media Grade M103P

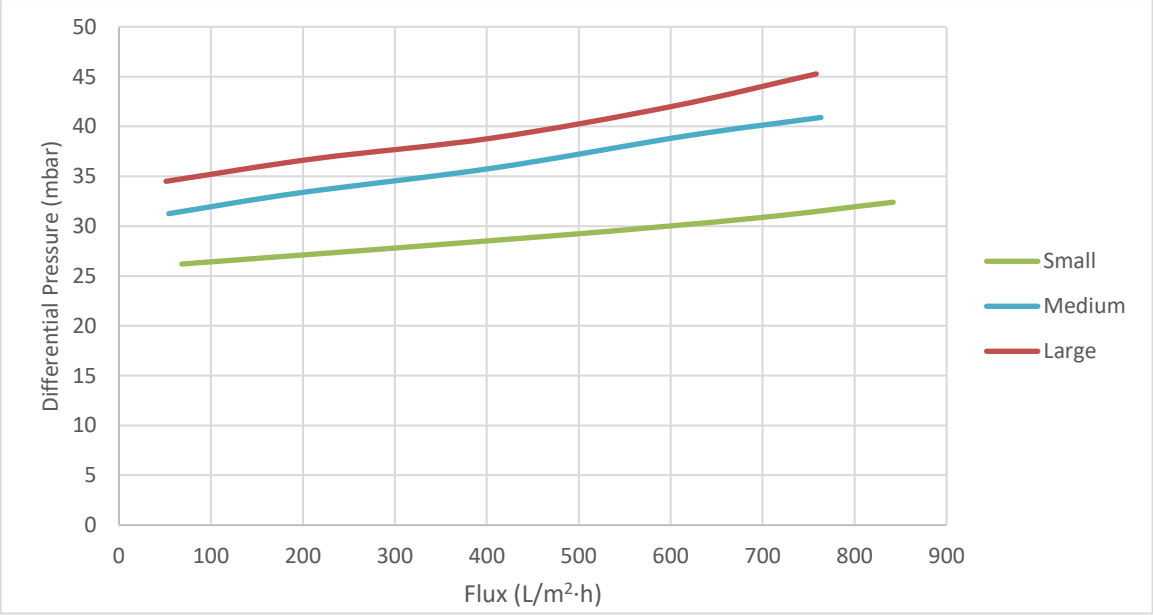


Figure 2:

Water Flow Characteristic Results of Media Grade M954P Double Layer Configuration

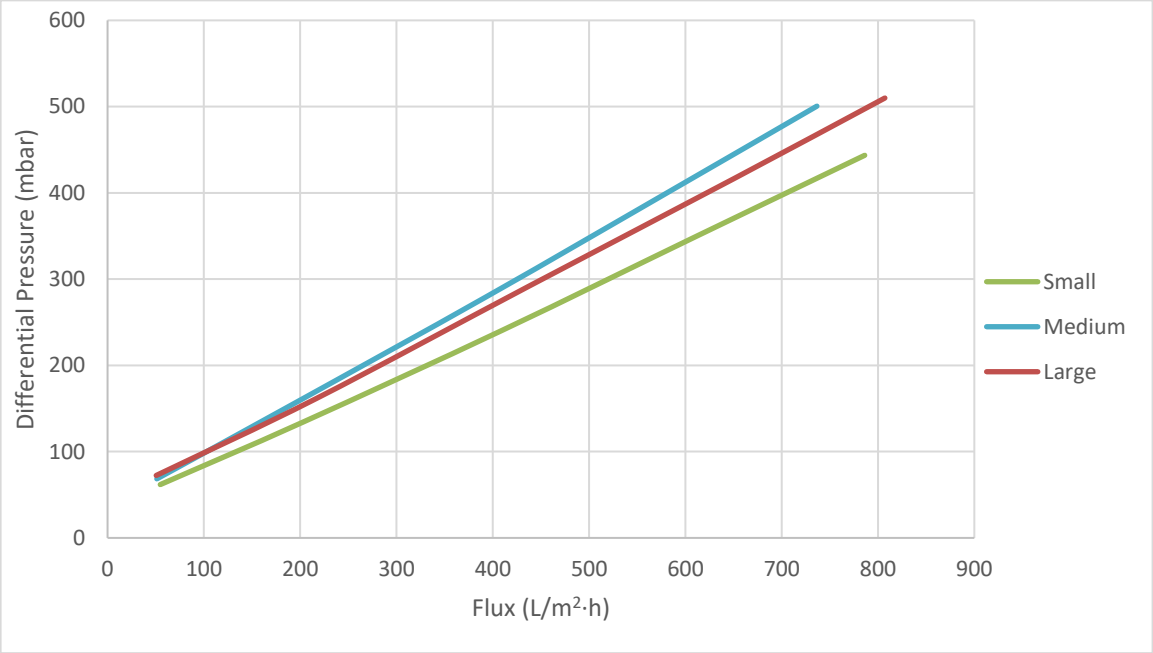
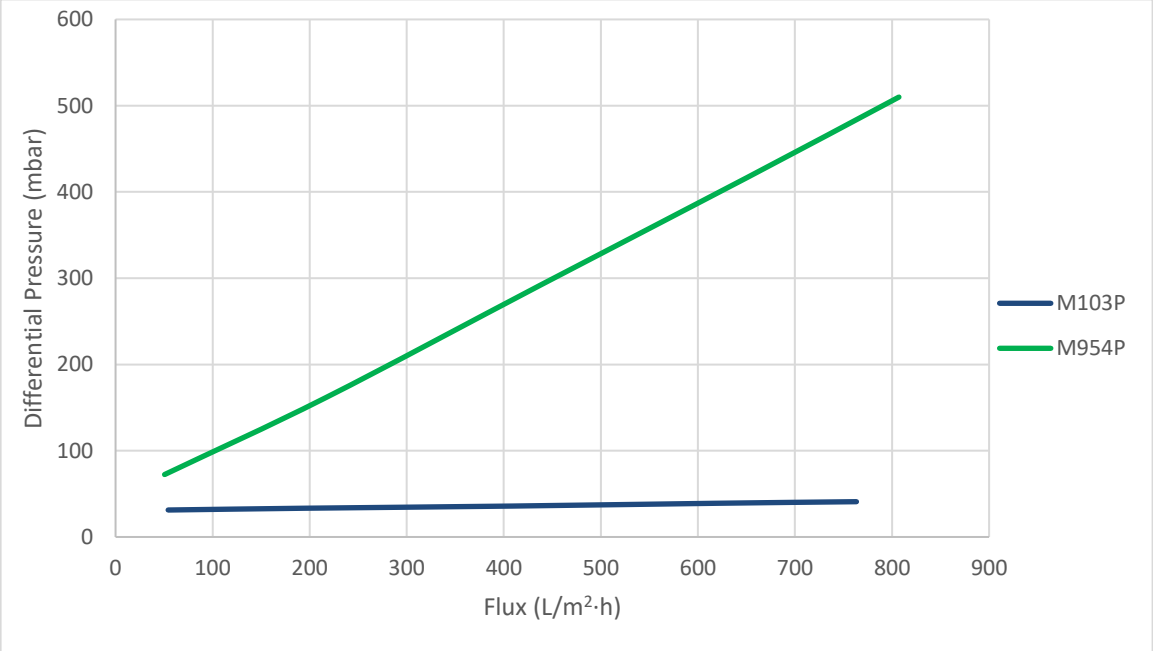


Figure 3:

Average Water Flow Characteristic Results of Both Media Grades



2.4. Conclusions

The results above demonstrate that the water flow characteristic of ErtelAlsop filter media used in all MicroCap Pro capsules is consistent when using the same grade, regardless of capsule size. This demonstrates consistent linear scalability from small to large capsule sizes. This is beneficial as end users can expect reliable results from lab scale through full volume manufacturing.

3. Determination of Capsule Weight and Fluid Hold-Up Volume

3.1. Introduction

The purpose of these tests was to establish the Capsule Weight of MicroCap capsules with various grades of wetted filter media in them, after an appropriate blow-down with pressurized air. The difference between the dry and wet capsules was calculated as the Fluid Hold-up Volume.

3.2. Summary

The filter media grades selected for this test were single layer M103P and double layer M954P which represent the highest and lowest water permeability in the ErtelAlsop media range. Each media type was run in multiple large, medium, and small capsules to capture a large array of data.

Dry capsules were first weighed on an electronic scale with a resolution of 0.01 kg to determine the dry weight. Filtered water was then pumped through the capsules at 800 $L/m^2 \cdot h$ for 15 minutes to saturate the media. This was followed by an air blowdown with the outlet open to drain. Pressure on the inlet and outlet were monitored to ensure there was no bypass of the media. After a suitable amount of time had passed the capsule was again weighed on the same scale to measure the wet weight. Fluid hold-up was then calculated as the wet weight minus the dry weight.

3.3. Results

Table 1: Average Capsule Weights and Hold-up Volumes

Media Grade	Capsule Size	Serial Number	Dry Weight (kg)	Wet Weight (kg)	Fluid Hold-up (kg)
M103P	Small	180430001	4.67	6.30	1.63
M103P	Small	180430002	4.67	6.30	1.63
M103P	Small	180430003	4.63	6.26	1.63
M103P	Medium	180430006	5.76	8.71	2.95
M103P	Medium	180430007	5.76	8.71	2.95
M103P	Medium	180430008	5.76	8.71	2.95
M103P	Large	180430014	6.89	10.66	3.76
M103P	Large	180430028	6.94	10.75	3.81
M103P	Large	180430029	7.12	10.93	3.81
M954P/M954P	Small	180430004	6.03	8.89	2.86
M954P/M954P	Small	180430005	6.08	8.80	2.72
M954P/M954P	Small	180430011	6.03	8.94	2.90
M954P/M954P	Medium	180430009	8.12	13.11	4.99
M954P/M954P	Medium	180430010	8.12	13.11	4.99
M954P/M954P	Medium	180430027	8.12	12.38	4.26
M954P/M954P	Large	180430012	10.21	16.56	6.35
M954P/M954P	Large	180430013	10.30	16.92	6.62
M954P/M954P	Large	180430030	10.34	16.56	6.21

3.4. Conclusion

The capsule weights dry and after being wetted with a suitable blow-down, are presented in the table above. The two grades tested represent the lightest and heaviest combination of media that ErtelAlsop offers and thus it can be expected that all other grades in any configuration will fall in this range. The results can assist to determine the approximate weight of a MicroCap Pro system and indicate a typical fluid hold-up volume.

4. Resistance to Autoclave Conditions

4.1. Introduction

The purpose of these tests was to determine the effects of exposure to harsh autoclave cycles on the MicroCap Pro capsule. The results serve to demonstrate the ability of the capsules to withstand autoclaving while maintaining structural integrity of both the internal structure, including the filter media and the capsule shell.

4.2. Summary

The filter media grades selected for this test were single layer M103P and double layer M954P which represent the highest and lowest water permeability in the ErtelAlsop media range. Each media type was run in multiple large, medium, and small capsules to capture a large array of data.

The structural integrity of the capsule was tested using the pressure decay method. Each capsule was subjected to two to three autoclave cycles.

Filtered water was pumped through the filter capsules at a flux of 800 $L/m^2 \cdot h$ for 5 minutes. Air pressure was then applied on the inlet side to assess the structural integrity of the capsules and their internals by monitoring the pressure decay. If after stabilization the pressure decay was less than 10% in one-minute test time then the capsule was deemed integral. The capsules were then autoclaved in cycles of one hour at 125 °C using the default program of fractionated pre-vacuum draw of 3 x -500 mbar. After each cycle the flush and pressure decay tests were performed again.

A typical process at a customer site may not involve wetting the sheets prior to the first autoclave cycle, therefore some tests omitted the flush before the first autoclave cycle. Wetting the media before the first cycle represents a worst-case scenario, which is why that scenario was also included.

4.3. Results

Table 2: Resistance to Autoclave Testing Results

Capsule Size	Media Grade	Sample Number	Serial Number	Pressure Decay Test After Flush Cycle # (Pass/Fail)			
				0	1	2	3
Small	M103P	1	180508016	Pass	Pass	Pass	Pass
Small	M103P	2	180508017	Pass	Pass	Pass	N/A
Small	M954P/M954P	1	180508018	Pass	Pass	Pass	Pass
Small	M954P/M954P	2	180508019	Pass	Pass	Pass	N/A
Medium	M103P	1	180508020	Pass	Pass	Pass	N/A
Medium	M103P	2	180508021	N/A	Pass	Pass	Pass
Medium	M954P/M954P	1	180508022	Pass	Pass	Pass	N/A
Medium	M954P/M954P	2	180508023	N/A	Pass	Pass	Pass
Large	M103P	1	180508024	Pass	Pass	Pass	N/A
Large	M103P	2	180508025	N/A	Pass	Pass	Pass
Large	M954P/M954P	1	180508026	Pass	Pass	Pass	N/A
Large	M954P/M954P	2	180508027	N/A	Pass	Pass	Pass

4.4. Conclusion

MicroCap Pro depth filters have demonstrated the capability to withstand at least two autoclave cycles at 125 °C. Both the internal structure and the capsule shell maintained structural integrity and operating safety margin throughout repeated testing. These results support the claim on each MicroCap Pro capsule label of withstanding autoclave conditions at 125 °C for up to one hour.

5. Burst Testing

5.1. Introduction

The purpose of these tests was to demonstrate that MicroCap Pro depth filter capsules can withstand the maximum specified operating pressures of 3.5 bar/50.8 psi at 25 °C and 1.0 bar/14.5 psi at 60 °C, while maintaining structural integrity and operating safety, with an appropriate safety margin.

5.2. Summary

The filter media grades selected for this test were single layer M103P and double layer M954P which represent the highest and lowest water permeability in the ErtelAlsop media range. Each media type was run in multiple large, medium, and small capsules to capture a large array of data.

Prior to burst testing all capsules were pre-treated with two autoclave cycles at 125 °C. To simulate a production environment, the capsules were then fitted into an ErtelAlsop chassis. The chassis was placed into a water bath at 25 °C or 60 °C for three hours to ensure the entire system was at the desired temperature. The capsule was then completely filled with water until all air had evacuated followed by closing the valves and increasing the pressure gradually. Once the capsule burst the pressure was recorded.

5.3. Results

Table 3: Burst Pressure

Capsule Size	Part Number	Serial Number	Media Grade	Temperature (°C)	Burst Pressure (bar/psi)
Small	F9S9CAP3S6	180924045	M954P/M954P	25	12.7/183
Small	M103PCAP3S6	180924039	M103P	25	12.8/185
Medium	F9S9CAP5S6	180924064	M954P/M954P	25	10.0/145
Medium	M103PCAP5S6	180924044	M103P	25	12.4/180
Large	F9S9CAP7S6	180924057	M954P/M954P	25	9.0/130
Large	M103PCAP7S6	180924051	M103P	25	8.6/125
Small	F9S9CAP3S6	180924061	M954P/M954P	60	7.3/106
Small	M103PCAP3S6	180924050	M103P	60	7.6/110
Medium	F9S9CAP5S6	180924059	M954P/M954P	60	7.3/106
Medium	M103PCAP5S6	180924043	M103P	60	7.2/105
Large	F9S9CAP7S6	180924060	M954P/M954P	60	6.9/100
Large	M103PCAP7S6	180924063	M103P	60	7.2/104

5.4. Conclusion

MicroCap Pro depth filters have proven the ability to withstand the maximum specified operating conditions at both low and high temperatures with a considerable safety margin. The capsules demonstrated this even after being autoclaved for two cycles at 125 °C. The average recorded burst pressure at 25 °C was 10.6 bar (153.3 psi), exceeding the maximum operating pressure of 3.5 bar (50.8 psi). The average recorded burst pressure at 60 °C was 7.2 bar (105.0 psi), exceeding the maximum operating pressure of 1.0 bar (14.5 psi).

6. Creep-Rupture Testing

6.1. Introduction

The purpose of this test was to demonstrate that ErtelAlsop depth filter capsules keep structural integrity and operating safety when under pressure for long periods of time. Testing was performed at 25 °C and at 60 °C with all three size capsules. All capsules were exposed to two autoclave cycles at 125 °C before testing commenced.

6.2. Summary

The filter media grade selected for this test were single layer M103P and double layer M954P which represent the highest and lowest water permeability in the ErtelAlsop media range. Each media type was run in multiple large, medium, and small capsules to capture a large array of data.

Prior to testing the capsules were pre-treated with two autoclave cycles at 125 °C for one hour. Capsules were fitted into stainless steel chassis just like they would be at customer sites and connected to the appropriate test rig devices to maintain set pressures within the capsule. The chassis were then submerged into water tanks at 25 °C and 60 °C and allowed to equilibrate for three hours. The tank temperature was maintained and the pressure was monitored until capsule failure occurred, at which point the time and failure mode were recorded.

6.3. Results

Figure 4:

Creep-Rupture Test Results for MicroCap Pro Capsules at 25 °C

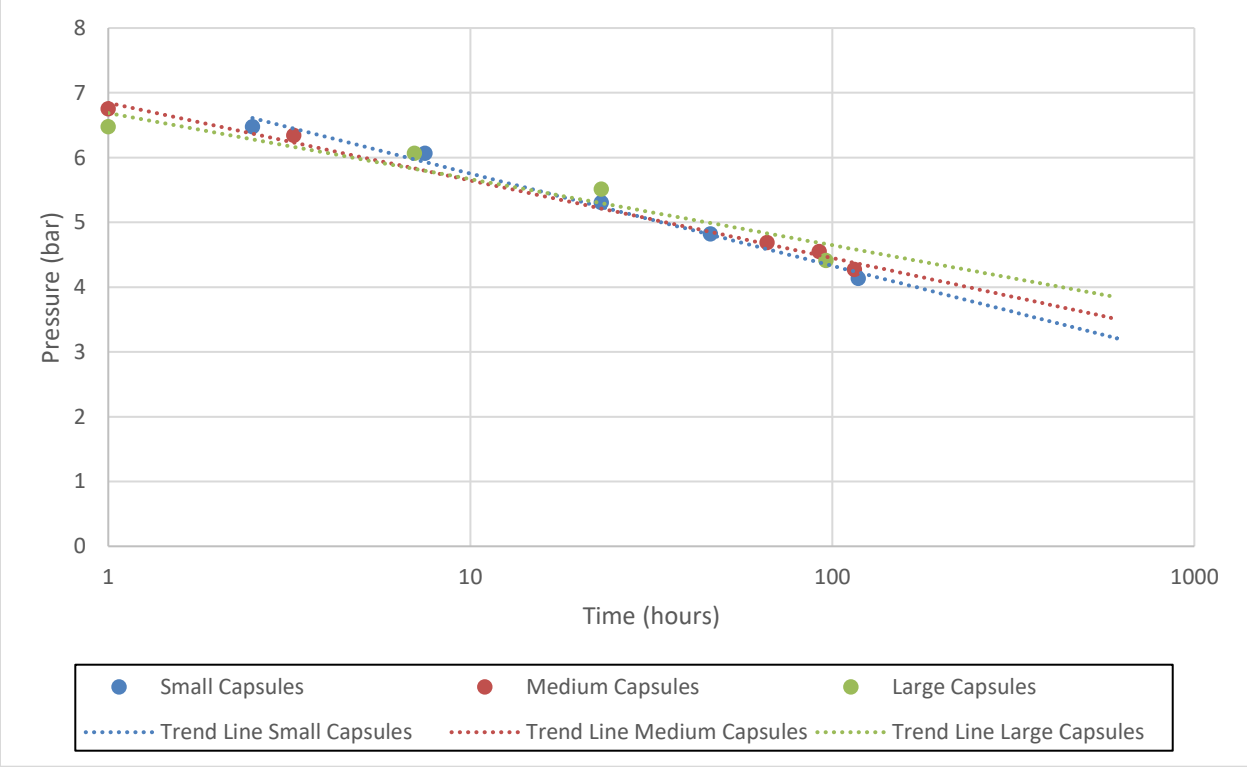
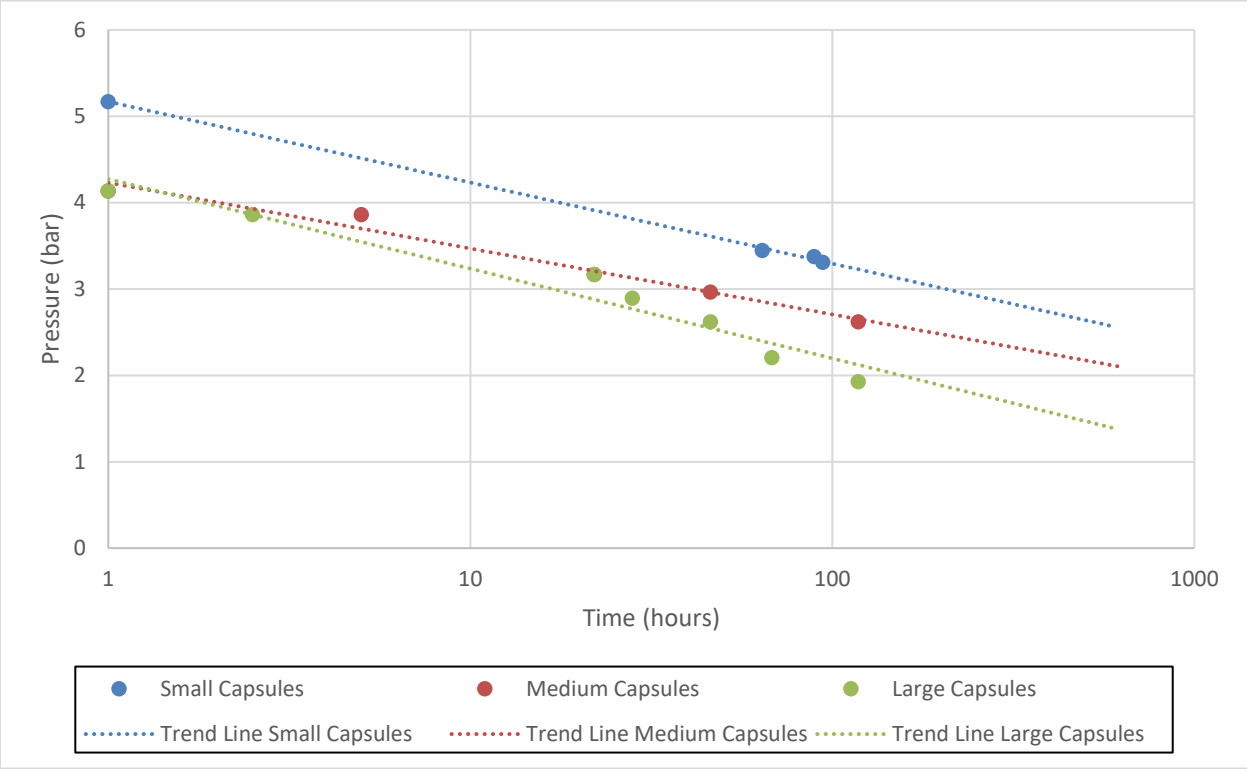


Figure 5:

Creep-Rupture Test Results for MicroCap Pro Capsules at 60 °C



6.4. Conclusion

MicroCap Pro depth filter capsules have been designed for continuous use in a single cycle for up to 10 hours at both 3.5 bar (50.8 psi) at 25 °C and 1.0 bar (14.5 psi) at 60 °C. When the trend lines from the creep-rupture data are extrapolated for all capsule sizes it can be safely assumed that they will maintain a constant maximum pressure in excess of 100hours, well beyond the design limit of 10 hours. This exhibits the robust safety margins that have been incorporated into the design and operation of the capsules.

7. Extractables Testing

7.1. Introduction

The purpose of these tests is to quantify and characterize the material that can be extracted from the capsule body of a MicroCap Pro depth filter capsule using water. Water was used for extraction, as it is considered a model solvent for most aqueous applications.

Extractables data for the various grades of ErtelAlsop Pharmaceutical Grade Depth Filtration Media can be found in the specific ErtelAlsop Media Validation Guides.

7.2. Summary

MicroCap Pro capsule body moldings were selected at random for testing. Samples were soaked in a fixed amount of distilled water at room temperature for 1 hour before being submitted for extraction tests.

TOC Analysis

The resulting solution was analyzed by a third party for Total Organic Carbon using a TOC analyzer.

Metals Analysis

The resulting solution was analyzed for specific metals using ICP-OES analysis.

7.3. Results

7.3.1. Total Organic Carbon

Results of the TOC extraction testing are as follows:

Total Organic Carbon (mg/L)
1.7

7.3.2. ICP-OES Analysis

Results of the ICP-OES extraction testing are as follows:

Iron (ppb)	Aluminum (ppb)	Calcium (ppb)	Magnesium (ppb)
4	2	155	11

7.4. Conclusion

TOC extractable content was found to be very low. An initial flush of the capsule is recommended to reduce the amount of TOC in the final solution.

ICP-OES extractable content was found to be very low. An initial flush of the capsule is recommended to reduce the amount of extractable content in the final solution.

8. USP Biological Reactivity Tests

8.1. Introduction

The purpose of these tests, is to evaluate the biological reactivity of the capsule body, and the internal molded parts.

Biological Reactivity data for the various grades of ErtelAlsop Pharmaceutical Grade Depth Filtration Media can be found in the specific ErtelAlsop Media Validation Guides.

8.2. Summary

Sample preparation and testing was performed in accordance with the appropriate USP Guidelines, as follows:

USP Biological Reactivity Tests, in vivo, for Class IV Plastics: USP<88>

- USP Systematic Toxicity Study in the Mouse
- USP Intracutaneous Toxicity Study in the Rabbit
- USP Implantation Study in the Rabbit

USP Cytotoxicity -Elution Test – MEM Extract USP 40 <87> rev 05/2017

8.3. Results

8.3.1. USP Biological Reactivity Tests, in vivo, for Class IV Plastics: USP<88>

Capsule Body

Systematic Injection:	Pass
Intracutaneous:	Pass
Intramuscular:	Pass

Internal Molded Parts

Systematic Injection:	Pass
Intracutaneous:	Pass
Intramuscular:	Pass

8.3.2. USP Cytotoxicity – Elution Test – MEM Extract USP 40 <87> rev 05/2017

Capsule Body

The test article has met the standard.

Internal Molded Parts

The test article has met the standard

8.4. Conclusion

The Capsule Body and the Internal molded parts meet the requirement of USP Biological Reactivity Tests, in vivo, for Class IV Plastics: USP<88>, and USP Cytotoxicity -Elution Test – MEM Extract USP 40 <87> rev 05/2017.

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