



Life Sciences

## Validation Guide

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USTR 2918

# Activated Carbon Filters Incorporating Seitz® AKS Filter Media (Grade AKSJ)



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## 1. Introduction

Seitz AKS filter media grade AKSJ contains a special type of activated carbon which is widely used in the Japanese pharmaceutical market.

This document contains validation data applicable to Pall activated carbon filters incorporating Seitz AKS filter media (grade AKSJ) and should be read in conjunction with Pall publication USTR2491: 'Validation Guide for Activated Carbon AKS Depth Filter Media'.

This report contains a summary of tests carried out and results obtained by Pall. The data in this report are typical measured values, the correctness and reproducibility of which are controlled on a regular basis. The document has been compiled for the users of Seitz AKS filter media grade AKSJ as a basis and support for their own validation procedures.

The validation program includes:

- Extractables Testing
- Conductivity and pH
- Total Organic Carbon
- Extractable Cations
- Total Extractables
- Endotoxin Levels
- Biological Reactivity

## 2. General Characteristics Of Seitz AKS Filter Media Grade AKSJ

Seitz AKS filter media grade AKSJ is manufactured under special production conditions that guarantee the highest purity possible. These conditions include:

- Specific cleaning and disinfection of the manufacturing line
- Use of reverse-osmosis water for final rinsing of the filter media according to the specifications

## 3. Typical Properties

**Table 1**

*Typical properties*

<b>Seitz AKS Filter Media Grade</b>	<b>Weight Per Unit Area (g/m<sup>2</sup>)</b>	<b>Thickness (mm)</b>	<b>Ash Content (%)</b>	<b>Adsorption Substance A<sup>1</sup> (mg/m<sup>2</sup>)</b>
AKSJ	1350	4.7	1	200

<sup>1</sup>Representing molecules between 200 – 400 Da

## 4. Leachables and Extractables

### 4.1 Methods

In the adsorption process of pharmaceutical products, it is essential that the product composition is unaffected by leachables released from the activated carbon filters. An appropriate rinsing procedure after sterilization was therefore used to remove any leachables substances. The most common rinsing medium is Water For Injection (WFI). Additionally, in many processes organic solvents are used to dilute the products. Therefore, in addition to WFI, 40% ethanol was chosen as a second extraction medium, representing other organic solvents. For the extraction curves discussed in the following section, a filter with an effective filter area of 670 cm<sup>2</sup> was used. The flow rate was adjusted to 500 LMH (L/m<sup>2</sup>/hr).

Samples for the determination of

- Conductivity
- pH
- TOC
- Cations (Al, Ca, Mg, Fe, Ni, Cu, Cr, As)

were taken at rinsing volumes of:

- 5 - 10 L/m<sup>2</sup>
- After 50 L/m<sup>2</sup>
- After 100 L/m<sup>2</sup>

### 4.2 Conductivity and pH Values in WFI

#### 4.2.1 Method

Conductivity and pH values were measured using calibrated conductivity and a pH meter.

#### 4.2.2 Results

**Table 2**

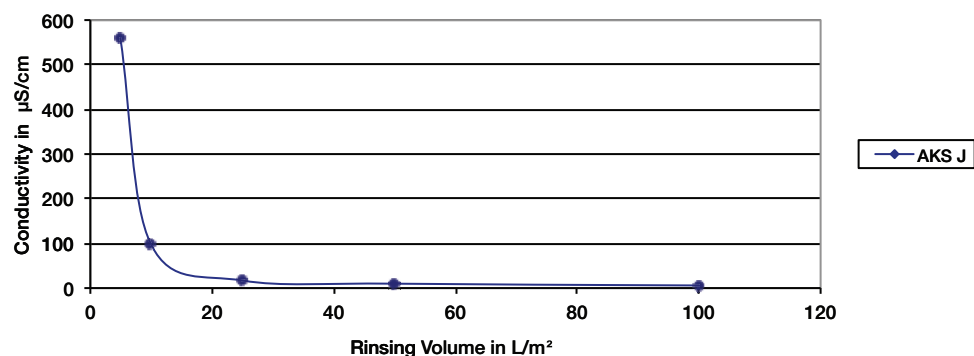
*Conductivity shift and pH value in WFI*

	Conductivity shift in $\mu\text{S}/\text{cm}$			pH Value		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	97	10	6	5.1	5.0	5.2

*Control WFI Sample: pH value 5.5, conductivity < 1 s/cm, TOC < 500 ppb*

**Figure 1**

*Conductivity in  $\mu\text{S}/\text{cm}$  after Rinsing with WFI*



### 4.3 Total Organic Carbon in WFI

#### 4.3.1 Method

TOC in WFI is the parameter characterizing organic extractables and potential leachables from the filters.

#### 4.3.2 Results

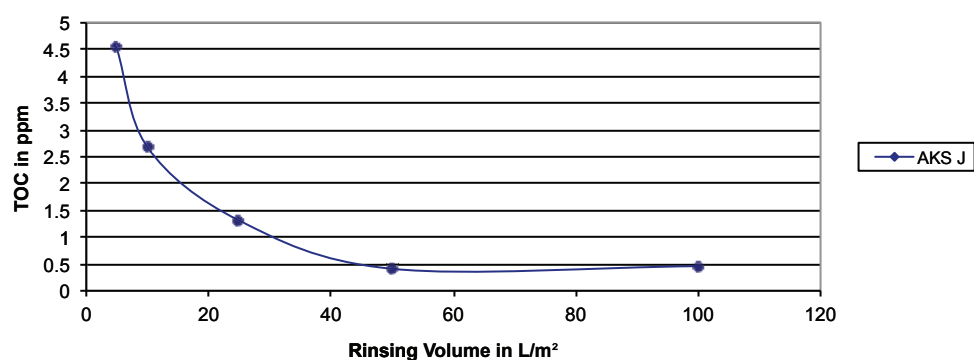
**Table 3**

*TOC in WFI*

	TOC ppm		
	Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100
AKSJ	2.7	< 0.5	< 0.5

**Figure 2**

*TOC after Rinsing with WFI*



#### 4.3.3 Conclusion

After a rinsing volume of 100 L/m<sup>2</sup>, the TOC in WFI is below 5 ppm for Seitz AKS filter media grade AKSJ.

### 4.4 Extractable Cations

#### 4.4.1 Method

Cations (Al, Ca, Mg, Fe, Ni, Cu, Cr) extracted in ethanol and WFI were determined by AAS (atomic adsorption spectroscopy) by flame or graphite tube technique.

#### 4.4.2 Results

**Table 4**

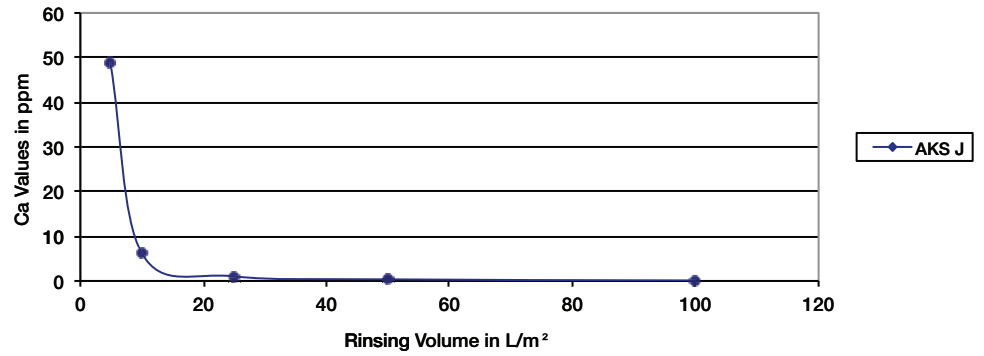
*Al in ppb*

	Al (ppb) in WFI			Al (ppb) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	<5	<5	<5	10.35	<5	<5

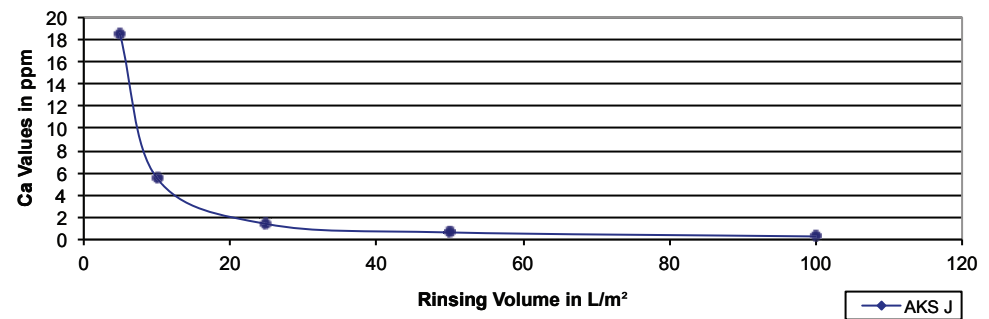
**Table 5**  
Ca in ppm

	Ca (ppm) in WFI			Ca (ppm) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	6.17	0.36	0.11	5.53	0.64	0.28

**Figure 3**  
Ca Values in ppm after Rinsing with WFI



**Figure 4**  
Ca Values in ppm after Rinsing with EtOH

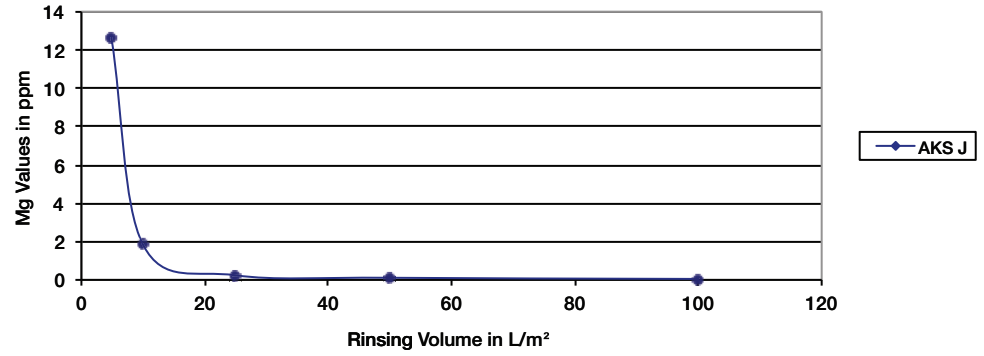


**Table 6**  
Mg in ppm

	Mg (ppm) in WFI			Mg (ppm) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	1.83	0.11	0.05	2.53	0.08	0.05

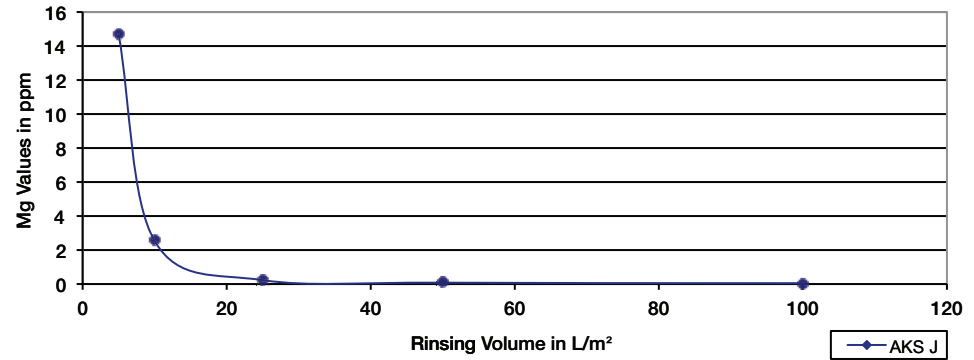
**Figure 5**

*Mg Values in ppm after Rinsing with WFI*



**Figure 6**

*Mg Values in ppm after Rinsing with EtOH*



**Table 7**

*Fe in ppm*

	Fe (ppm) in WFI			Fe (ppm) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	<0.05	<0.05	<0.05	0.09	0.06	<0.05

**Table 8**

*Cu in ppm*

	Cu (ppm) in WFI			Cu (ppm) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

**Table 9**

*Ni in ppb*

	Ni (ppb) in WFI			Ni (ppb) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	<5	<5	<5	6.67	<5	<5

**Table 10***Cr in ppb*

	Cr (ppb) in WFI			Cr (ppb) in EtOH		
	Rinsing Volume in L/m <sup>2</sup>			Rinsing Volume in L/m <sup>2</sup>		
Seitz AKS Filter Media Grade	5 - 10	50	100	5 - 10	50	100
AKSJ	<5	<5	<5	<5	<5	<5

**4.4.3 Conclusion****Table 11***Extractable Results*

Extractables in WFI	Typical Values after Rinsing with 50 L/m <sup>2</sup> WFI
Ca	< 1.0 ppm
Mg	< 0.1 ppm
Fe	< 0.1 ppm
Al	< 0.1 ppm
Ni	< 0.01 ppm
Cu	< 0.1 ppm
Cr	< 0.01 ppm
pH	4 - 6
Conductivity	< 30 µS/cm
TOC	< 2 ppm

**4.5 Total Extractables****4.5.1 Method**

Title 21 of the FDA's Code of Federal Regulations (Chapter I: 'Food and Drugs', Subchapter B, Part 177) refers to indirect food additives/polymers, and Subchapter C refers to substances for use only as components of articles intended for repeated use.

21 CFR 177.2260 refers to resin-bonded filters and states the limits for extractables in different extraction media and under different extraction conditions. The following limitations are stated here.

**Table 12***Extraction Limitations*

Extraction Solvent	Extraction Conditions	Limits
Deionized Water	100 °C	< 4% by the weight of the filter
50% ethanol	Ambient Temperature	< 4% by the weight of the filter
50% acetic acid	Ambient Temperature	< 4% by the weight of the filter
n-hexane	Reflux	< 4% by the weight of the filter

Although these regulations are not primarily intended for pharmaceutical products, they provide additional supportive data for the suitability of filters for pharmaceutical applications.

The total extractables of all Pall Activated Carbon (AKS) depth filter media was significantly below the prescribed limits and therefore meet the requirements of 21 CFR 177.2260. Detailed reports are available upon request.



## 5. Endotoxins

In filter manufacturing there is a potential risk of contamination by endotoxins. Therefore the verification of low endotoxin levels of the filter extracts is an important issue during validation.

### 5.1 Methods

Human Albumin LAL Gel Clot Test

For the extraction and desorption of endotoxins from filters, human albumin can be demonstrated to be most effective. Thus, filtering a human albumin solution and demonstrating that endotoxins are below the detectable limit in the filtrate is often used as a routine test in quality control. Filtration of a human albumin solution without pre-rinsing was performed and an endotoxin-specific LAL-gel clot test was used to determine the level of endotoxins in EU/mL (endotoxin units/mL).

### 5.2 Results

**Table 13**

*Test Results in Human Albumin\* without WFI Pre-Rinse*

Seitz AKS Filter Media Grade	Endotoxin Content (EU/mL)
AKSJ	< 0.12

\* Control sample human albumin: < 0.06 EU/mL

### 5.3 Conclusion

The endotoxin content of the tested Seitz AKS filter media grade AKSJ sheets in human albumin without pre-rinsing was below 0.12 EU/mL. Detailed reports are available upon request.

## 6. Biological Reactivity Tests of Seitz AKS Filter Media Grade AKSJ

### 6.1 Method

According to the United States Pharmacopeia (USP), the biocompatibility of a material can be checked in biological reactivity tests either *in vitro* or *in vivo*. The Biological Reactivity Tests listed in the current revision of the USP for Class VI - 121 °C Plastics are a combination of *in vivo* tests that are designed to determine the biological response of animals to specific extracts prepared from the material under test. The USP defines six plastic classes based on the response to these tests for which extracts, materials and routes of administration are specified. In testing of filter sheets, the following tests were performed:

- Acute systemic injection test
- Intracutaneous test
- Implantation test

As extraction media for systemic and intracutaneous injection, the following media are used:

- Saline
- Saline in alcohol
- Polyethylene glycol 400
- Sesame oil

The extraction is performed at 121 °C for 1 hour.

### 6.2 Results

All tested materials met the specifications for Biological Reactivity Tests, *in vivo*, listed in the current revision of the USP for Class VI - 121 °C Plastics. Certificates and test reports are available upon request.



## Life Sciences

### Corporate Headquarters

Port Washington, NY, USA  
+1.800.717.7255 toll free (USA)  
+1.516.484.5400 phone  
biopharm@pall.com e-mail

### European Headquarters

Fribourg, Switzerland  
+41 (0)26 350 53 00 phone  
LifeSciences.EU@pall.com e-mail

### Asia-Pacific Headquarters

Singapore  
+65 6389 6500 phone  
sgcustomerservice@pall.com e-mail

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**E-mail us at [biopharm@pall.com](mailto:biopharm@pall.com)**

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