

Xtend™ – Automated Cleaning with ATS Xtend™ and ATF Xtend™



Purpose of this document

- How to run the automated cleaning routine of semi-automated ATS Xtend™ systems
- Explanation of the cleaning routine of fully automated ATF Xtend™ systems
- Difference between cleaning routines of semi- and fully automated systems

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1 Introduction

The ATS Xtend™ and ATF Xtend™ both have the ability to run an automated cleaning routine that flushes all fluidic paths that are part of the closed loop system. Once the cleaning routine of the ATS Xtend™ has completed, the user will only need to finish washing the shafts and vessels. Whereas the ATF Xtend™ will handle all washing activities that have been programmed in the method. This document will describe the cleaning routines available and explain how to run them at the end of a dissolution test.



Disclaimer

Automated procedures are meant to simplify the cleaning process and are not a guarantee of effective cleaning. The cleaning procedure can vary from product to product and a formal cleaning validation study should be executed in order to determine efficacy.

2 Automated Cleaning with the ATS Xtend™

2.1 Required hardware options

The ATS Xtend™ will need to be configured with the media selector valve attached to the right-hand side of the bath. There are two versions of this valve, one version uses a single sample inlet that is either plumbed to position 8 inside the bath or uses an external line that runs directly out the back of the media valve. The second version is a media selector valve that has 4 different media options that would be plumbed to an external media source. The cleaning process will work with either the AutoLift™ or HollowShaft™ sampling option.



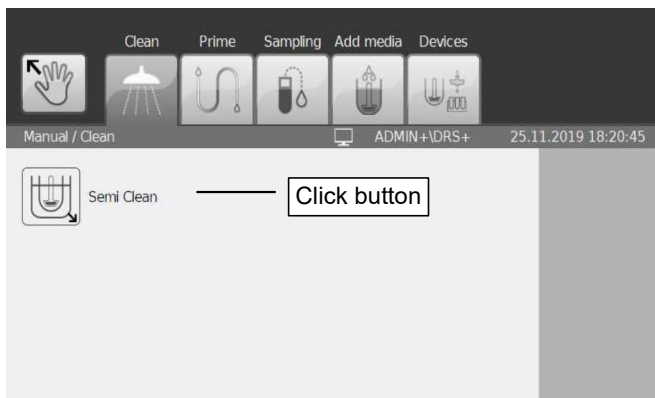
Medium valve (single sample inlet)



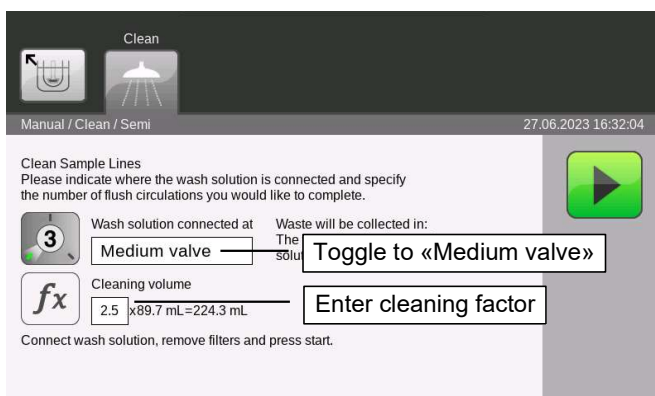
Media selector valve (4 media options)

2.2 How to access the cleaning routine on EasyTouch™

To access the semi-automated cleaning procedure of the ATS Xtend™ navigate to the “Manual” control menu and then select the “Cleaning” tab. Click the button “Semi Clean”.



- Toggle through “Wash solution is connected at” button until it says “Medium valve”
- Enter a cleaning factor for “Cleaning volume”



The cleaning volume is based on the following calculation:

$$\text{Cleaning volume} = \text{Cleaning volume factor} \times \text{Process-specific cleaning volume}$$

The factor defines how many times the tubing will be flushed with the attached wash solution. The “Clean Volume” displayed is the minimal volume the user must prepare for the wash solution.

Once the dissolution test has been completed, the user must remove any filters. The basket/paddle shafts or vessels should not be washed at this point in the process.

Once the wash solution is plumbed to the valve, the user can press the green play button to start the cleaning process. The routine will take about five minutes to complete. All fluidic paths are rinsed with the wash solution, this also includes the needles on the SAM fraction collector.

At the end of the routine, the lines are purged with air. All waste is collected inside the vessel. Once the routine has completed, the user will need to wash the paddle/basket shafts and vessels.



2.3 What to use for Cleaning Solution?

Water is the most common cleaning solution, however, an alternative cleaning solution may be required to clean out a particular analyte. After flushing with the alternative cleaning solution, the process should be repeated with DI water as a final rinse.

If surfactant-containing media types have been used with the system, it is recommended to run the cleaning procedure first with hot tap water, which is more effective at flushing out surfactant than DI water. Once sufficiently flushed with tap water, the cleaning procedure should be repeated using DI or purified water.

3 Automated Cleaning with the ATF Xtend™

The ATF Xtend™ is a fully automated system that is capable automating every aspect of a dissolution test including cleaning. There are three components that require attention during the cleaning process:

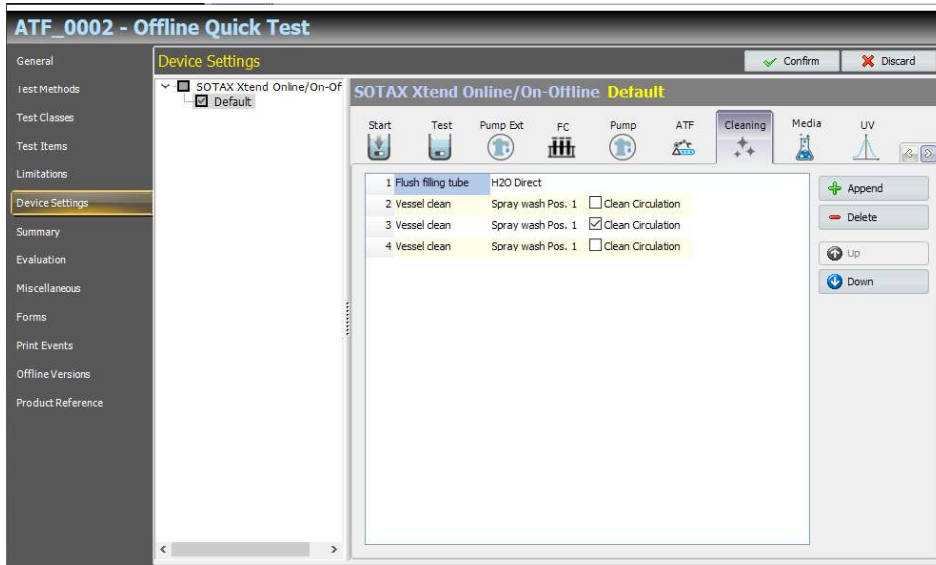
- Vessels
- Sample lines
- Media preparation tank

Although some cleaning actions can be accessed through the EasyTouch™ firmware, all cleaning routines can be programmed using q-doc® software. This allows users to customize a specific cleaning routine for a specific product to maximize efficiency.

By default the ATF Xtend™ will have DI water plumbed directly to the system, but an extended cleaning option is available that adds another pressurized media as a possible cleaning solution, for example hot DI water.

3.1 How to program Cleaning Routine in q-doc®

The cleaning functions for the ATF Xtend™ can be found in the product's device settings.



The default cleaning routine is broken down into four (4) steps.

3.1.1 Flush Filling Tube

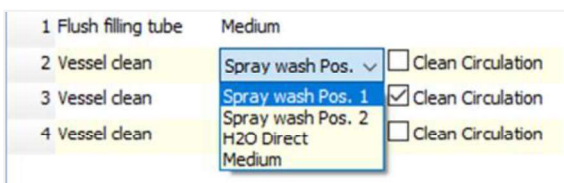
This process will flush a cleaning solution through the fluidic path that is used to fill a vessel. DI is used by default, but an alternative cleaning solution can be used by selecting "Medium" from the drop down menu.



3.1.2 First Vessel Clean

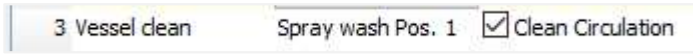
There are three rounds of vessel cleans that serve a specific function. The first vessel clean is used to wash the vessel so that there is no more undissolved drug remaining inside the vessel. There are four potential cleaning sources for this step.

#	Cleaning Source	Medium
1	Spray Wash Position 1	Pressurized DI
2	Spray Wash Position 2	Pressurized cleaning media
3	H ₂ O Direct	DI water that flows from the vessel fill position
4	Medium	Cleaning media that's prepared in the media tank



3.1.3 Second Vessel Clean

The second vessel clean is used to rinse all the sample lines with clean wash solution from the vessel. The box labeled “Clean Circulation” must be checked for this step to work properly. This process will circulate media through the sample lines. The waste is collected inside the vessel and the lines are purged with air at the end of this step.

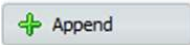


3.1.4 Third Vessel Clean

The third and final vessel clean step is used to clean the vessel after the sample line flush. Cleaning solutions can be selected from the same drop down menu as before.

3.1.5 Additional rounds of cleaning

Extra vessel cleans can be added to the list by selecting the green “Append” option.

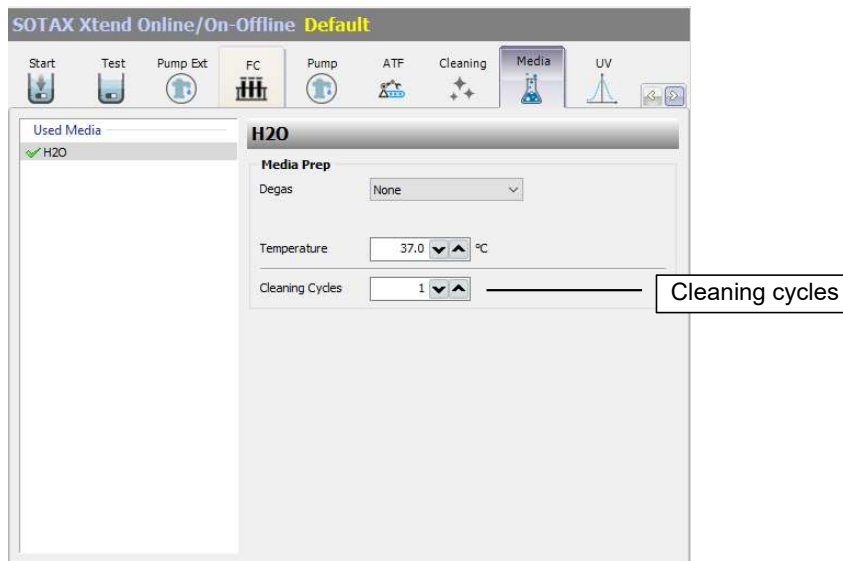


How ever it is always recommended to end the cleaning routine with the same sequence of steps found in the default program, i.e. the last three steps need to be as follows:

Vessel clean	Spray Wash Position 1	Clean circulation (no)	<input type="checkbox"/>
Vessel clean	Spray Wash Position 1	Clean circulation (yes)	<input checked="" type="checkbox"/>
Vessel clean	Spray Wash Position 1	Clean circulation (no)	<input type="checkbox"/>

3.1.6 Cleaning Cycles for Media Tank

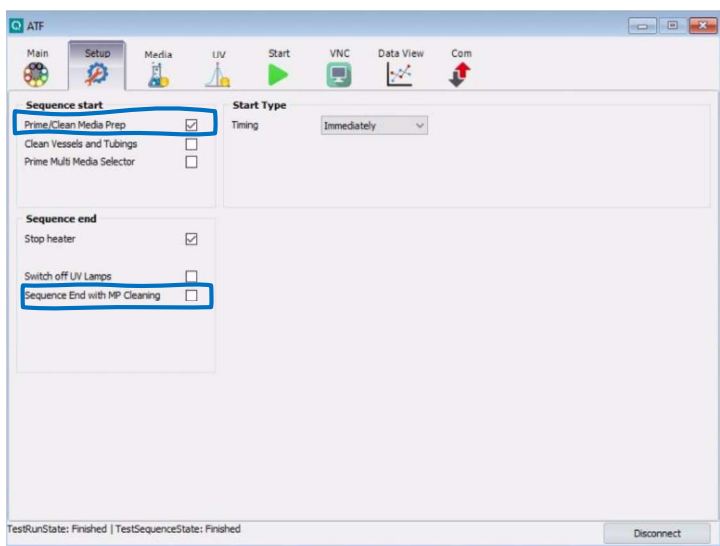
The last item to program for the ATF Xtend™ cleaning routine is found in the media tab of the device list. Here the user has control over how many cycles DI water flushed are performed after this media was used prior to filling the media prep tank with new media. This can be selected by increasing the number of cleaning cycles.



3.2 Options at Run Start

When starting a batch sequence on the ATF Xtend™ the user can select to have the vessel cleaned. If this option is selected then the ATF Xtend™ will follow the default cleaning parameters. This option is useful if the system has not been used for a while to help flush all the tubing with clean DI water. However, if the previous run completed successfully, then this step is not needed.

It is important to end the batch sequence with an MP cleaning so that any remaining dissolution media in the media prep tank is flushed out with DI water. This step becomes even more crucial if a caustic media source was last used.



4 Criteria for an Effective Cleaning Procedure

Special attention should be given when determining a cleaning routine for the ATF Xtend™. Since the intent of this system is to run sequential batches in a row, an effective cleaning process must address all sources of carry over between runs. It is common to use the same criteria for the blank injection of the HPLC's system suitability as the benchmark which is typically set to 1% or less.

Additional steps can be taken when running a fully automated batch sequence such as starting with the lower dosage strength products first before testing a higher strength.

In the end, the cleaning routines available for the ATS Xtend™ and ATF Xtend™ should always be evaluated, and their use should be modified to fit the needs of the product being tested. Wash solutions can vary from water to a mild cleaning solution or even possibly some amount of diluted solvent solution. If an organic solution is used, proper care should be given to thoroughly flush with DI water and material compatibility information is noted in the respective user manuals.

5 SOTAX Pharma Services

SOTAX offers a full range of product and contract Pharma Services including method automation, filter studies, and method development. If you are interested, please contact your local SOTAX representative.

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