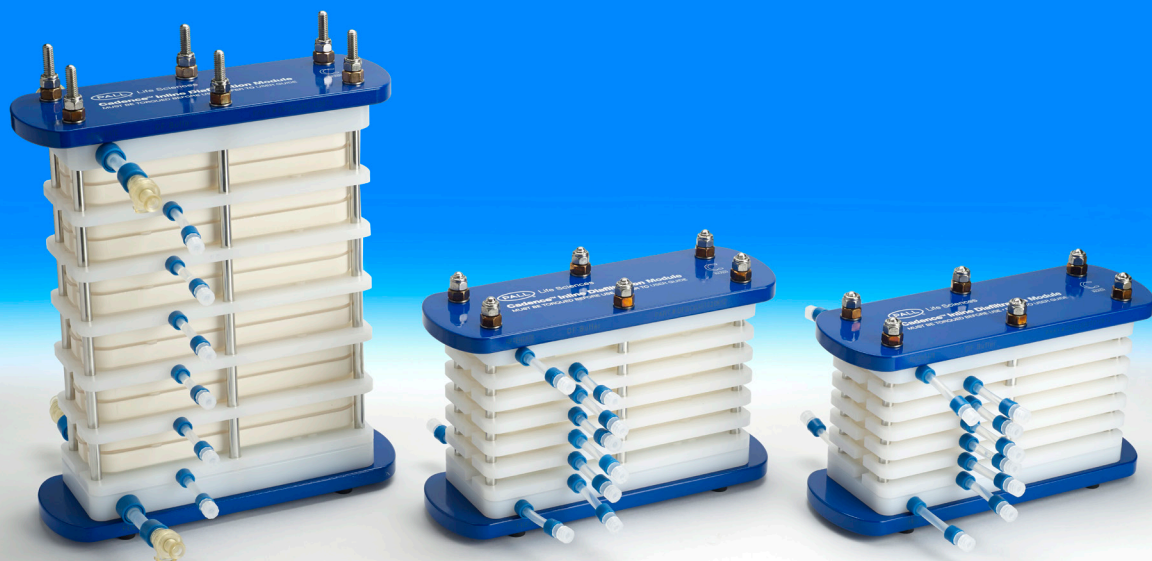




## Cadence™ Inline Diafiltration Module



### *Single-pass continuous diafiltration made simpler with Delta 30 kDa regenerated cellulose and Omega™ 30 kDa PES membrane*

Single-pass tangential flow filtration (SPTFF) has revolutionized the implementation of TFF in biotech, vaccine, blood plasma and other applications. The Cadence inline diafiltration (ILDF) device addresses a gap in the biopharmaceutical industry, by completing the product/technology offering for the realization of continuous processing of the final ultrafiltration/diafiltration (UF/DF) of drug substance. The Cadence ILDF module moves the biopharm industry one step closer to an end-to-end integrated continuous bioprocessing platform.

This latest addition to the Pall portfolio has many benefits, including:

- ▶ Fully continuous diafiltration in the downstream processing (DSP) steps
- ▶ Significantly reduced system hold-up volume
- ▶ Easy to use, holderless design
- ▶ Potential reduction of product damage or aggregation due to reduced residence time and shear exposure



## Overview

Cadence inline diafiltration modules are preassembled and do not require a holder. Each device includes a pre-configured tubing set that is connected to a feed pump and a diafiltration buffer pump. Torque the module to the recommended setting and it is ready to operate.

The Cadence ILDF technology allows for removal factors of  $\geq 3$ -log. Utilizing conventional TFF cassette building blocks in either Delta regenerated cellulose or Omega polyethersulfone membrane ensures accurate scalability and proven selectivity, and low protein binding attributes.

These products utilize proprietary technology, as well as technology licensed from SPF Innovations, and may be covered by one or more patents. See [pall.com/patents](http://pall.com/patents).

## Applications and Operational Benefits

The Cadence inline diafiltration module is designed for continuous processing, in-process buffer exchange or contaminant removal in various processes throughout a wide range of applications in the biopharmaceutical industry. These applications include buffer exchange for final drug substance, desalting or buffer exchange before or after column chromatography, and small molecule contaminant removal.

**Enable continuous processing** - Until now, there has been a gap in the technology offering for enabling diafiltration in a truly continuous, single-pass method. The Cadence ILDF device fills that gap and is facilitated through the use of staging, providing repetitive dilution / concentration cycles without a re-circulation loop and with significantly smaller system hold-up volume.

**High removal factors** - The Cadence ILDF technology allows for removal factors of  $\geq 3$ -log. Dialing in the number of diavolumes is easily achieved by adjusting the flow rate on the buffer addition pump and performance is stable over extended operation times.

**Optimize processing of highly shear-sensitive products** - Processing results in only one pass through the pump and module, therefore reducing shear exposure. Further benefits are achieved by eliminating any mixing or foaming issues associated with the feed tank.

**No holder required** - Cadence ILDF modules come assembled, and the cassettes and manifolds are configured between two end plates with no extra holder needed. A pre-configured tubing manifold is also provided. Simply torque the device to the recommended setting and attach the tubing manifold to a feed pump and diafiltration buffer pump.

### Product Platform

Similar to other Cadence SPTFF devices, the Cadence inline diafiltration device utilizes standard Pall T-Series cassettes as the building blocks for the module. These modules are offered with either Delta regenerated cellulose or Omega polyethersulfone membranes providing the high flux, high selectivity and low protein binding characteristics that are associated with these membranes. They are available in a range of size formats to accommodate various processing volumes.

A standard PharmaPure<sup>♦</sup> tubing manifold is provided with each device, and Sta-Pure<sup>♦</sup> tubing manifolds can be ordered separately for extended operation applications (see ordering information).

The Cadence ILDF device requires two standard peristaltic pumps for operation. A 2-headed pump to control the feed and retentate, and a 6-headed pump to control the buffer injection. The feed and retentate lines on the supplied tubing set include PendoTECH pressure transducers and conductivity sensors. A PendoTECH PMAT pressure monitoring device is required to monitor the feed and retentate pressure, and a PendoTECH CMONT device is required to measure conductivity. A torque wrench is also required to torque the module to the recommended level.

## Specifications

The operating characteristics for any SPTFF process must be established by performing trials and analyzing the results. Pall's team of technical specialists is available to assist in conducting trials to develop operating conditions necessary to achieve the desired process objectives.

### Materials of Construction

Cassettes	Delta regenerated cellulose or Omega polyethersulfone 30 kDa membranes with polypropylene screen, white polyurethane encapsulant with white pigment (TiO <sub>2</sub> ), and medical grade silicone for the permeate seals
Gaskets	Medical grade, platinum-cured silicone
Manifold Plates	Ultra high molecular weight polyethylene
Connections	T01/T02 – female luer connection and cap: Polypropylene T12 – female MPC quick disconnect connector and plug: Polysulfone
Flowpaths	Polypropylene, polysulfone, and platinum-cured silicone
Pump Head Tubing	PharmaPure (platinum-cured silicone) or Sta-Pure (expanded polytetrafluoroethylene (ePTFE) and platinum-cured silicone) Flowpath connections on tubing sets are open to the feed container/vessel
Operating Limits	Maximum Pressure: 4.1 barg (60 psig) Processing Temperature Range: 15 – 25 °C for extended use (freezing may damage the module) Up to 40 °C for 4 hour cleaning
pH Range	2 – 13

### Typical Feed Flow Rates

Module	Area (m <sup>2</sup> )	10 g/L Feed Flow Range (mL/min)	55 g/L Feed Flow Range (mL/min)
T01	0.11	0.5 – 10	0.5 – 4
T02	0.22	1.0 – 18	1.0 – 10
T12	1.20	5.0 – 90*	5.0 – 55

\* Scaled calculation due to pump selection

### Module Integrity Test

Delta	4.1 barg (60 psig)
Omega	2.1 barg (30 psig)
Acceptable Forward Flow Rate	Delta: < 538 sccm/m <sup>2</sup> (< 50 sccm/ft <sup>2</sup> ) Omega: < 1600 sccm/m <sup>2</sup> (< 150 sccm/ft <sup>2</sup> )

Each Cadence module has a unique serial number for full traceability.

## Shelf Life

The shelf life of the Cadence ILDF modules, packaged in preservative, is expected to be 5 years from the date of manufacture when the modules are stored unopened in the original packaging at a temperature up to 25 °C and protected from direct light. The shelf life studies to confirm this are ongoing.

## Biological Safety

Materials of construction for the Cadence ILDF modules have been tested and meet the requirements for the Biological Reactivity Tests listed in the United States Pharmacopeia (USP) <88> for Class VI – 70 °C Plastics.

## Documentation

Each module is supplied with the following comprehensive documentation to ensure the Cadence ILDF module is operated successfully.

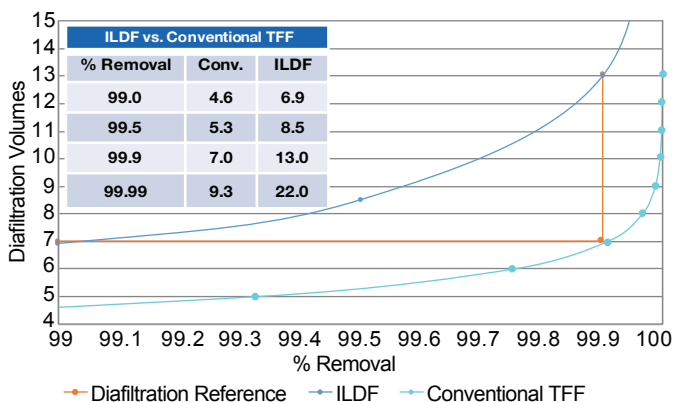
- ▶ Certificate of quality
- ▶ Installation guide
- ▶ Material and safety data sheet (MSDS) for the module preservative solution
- ▶ Care and use manual\*
- ▶ Validation guide\*
- ▶ Validation service for your specific tests such as compatibility testing with your product fluid\*
- ▶ Training and technical support to optimize your process using Cadence inline diafiltration modules\*

\*Visit [www.pall.com/biopharm](http://www.pall.com/biopharm) or contact your local Pall representative to obtain these documents.

## Performance

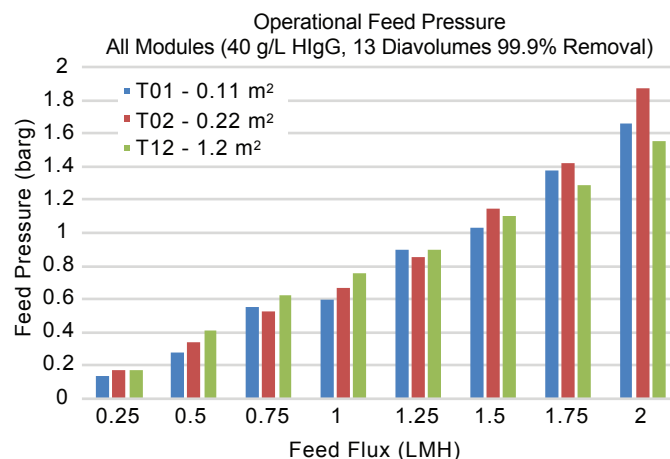
**Figure 1**

Number of diafiltration volumes needed for Cadence inline diafiltration system compared with conventional TFF



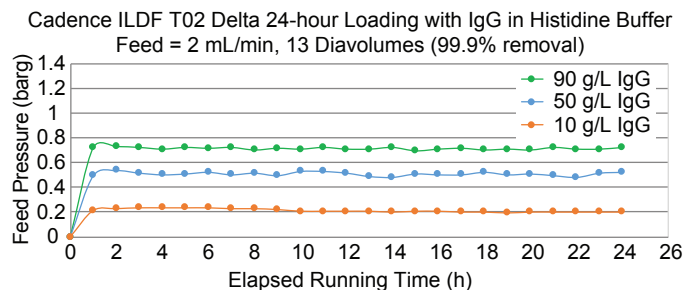
**Figure 2**

Scaled operational performance across different sizes of the Cadence inline diafiltration modules. All modules tested with 40 g/L HlgG and 13 diafiltration volumes.



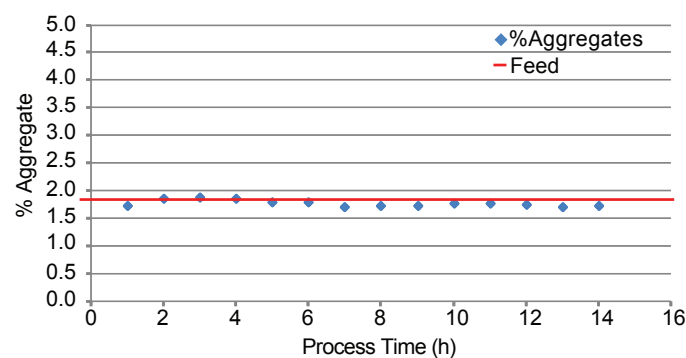
**Figure 3**

Stable performance when operating over extended time. T02 modules tested with varying concentrations of IgG.



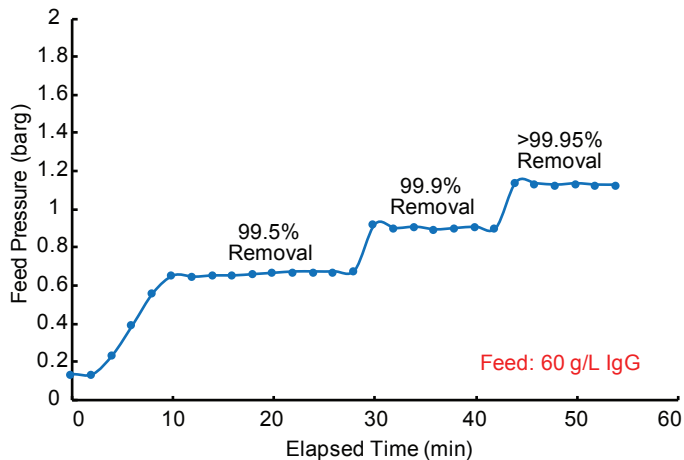
**Figure 4**

Stable aggregate profile over extended continuous processing performance when operating over extended time. T12 module tested with Pall in-house mAb.



**Figure 5**

Ability to adjust % removal with instantaneous adjustment of applied diafiltration volumes through pumping adjustment. Removal % adjustment at a constant feed flow rate using 60 g/L IgG.



## Ordering Information

Identify and order Cadence inline diafiltration modules using the table below.

### Guide to Cadence Inline Diafiltration Module Part Numbers

<b>DF</b>	Inline diafiltration device
<b>DC/OS</b>	Delta regenerated cellulose or Omega polyethersulfone membrane
<b>030</b>	Nominal molecular weight cut-off (MWCO)
<b>T02</b>	Cassette format
<b>06</b>	Number of stages in series
<b>12</b>	Number of cassettes per module

For example, a T02 module with 30 kDa Delta regenerated cellulose membrane area of 0.22 m<sup>2</sup> is part number DFDC030T020612.

### Cadence Inline Diafiltration Part Number and Membrane Area (m<sup>2</sup>)

Part Number	Membrane	Cassette Format	Membrane Area (m <sup>2</sup> )	MWCO (kDa)
DFDC030T010612	Delta	T01	0.11	30
DFDC030T020612	Delta	T02	0.22	30
DFDC030T120612	Delta	T12	1.2	30
DFOS030T010612	Omega	T01	0.11	30
DFOS030T020612	Omega	T02	0.22	30
DFOS030T120612	Omega	T12	1.2	30

### Tubing Set Part Numbers

Note: Every Cadence ILDF module includes a PharmaPure tubing set.

Description	Part Number
Cadence ILDF T01/T02 PharmaPure	5390-0565M
Cadence ILDF T01/T02 Sta-Pure	5390-0565N
Cadence ILDF T12 PharmaPure	5390-0565P
Cadence ILDF T12 Sta-Pure	5390-0565Q

### Additional Recommended Equipment for Operation (not provided by Pall)\*

Description	Vendor	Part Number	Qty
Masterflex <sup>♦</sup> L/S pump	Cole-Parmer	EW-07522-20	2
Masterflex Easy Load II pump head	Cole-Parmer	EW-77201-60	2
Masterflex L/S cartridge pump head (6 channel, 6 roller)	Cole-Parmer	EW-07519-15	1
Masterflex L/S pump head cartridges, large	Cole-Parmer	EW-07519-75	6
PendoTECH PMAT 4 pressure monitor	PendoTECH	PMAT4A	1
PendoTECH CMONT conductivity monitor	PendoTECH	CMONT	1
PendoTECH software licenses, 1 per PC	PendoTECH	PMATP-GUI	1
Masterflex mounting hardware (for 2 pumps heads)	Cole-Parmer	SC-77200-02	1
Torque driver	McMaster-Carr	5716A21	1
9/16 in. deep socket	McMaster-Carr	5544A45	1

\*This is the equipment that is recommended by Pall and has been demonstrated to perform as required. It is possible that other similarly functioning equipment could be used.



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