

Preparative and Purification Liquid Chromatograph

# Nexera Prep



# Be simple. Be Flexible.

**The Shimadzu Preparative Purification System provides the optimal solutions for laboratory issues.**

For Example:

- Easy optimization of preparative parameter and scale up  
Fractionation simulation for supporting optimization of parameter  
Column line-up for scale-up from analysis to preparative
- Time- and energy-saving by automation of the work process for purification  
Collection of target components at high purity by automation of remove of salts
- Expandable to suit the sample/fraction number and volume  
Select of best suitable system for your work

Problems are resolved simply, to accommodate a variety of needs.



## Saves on Labor When Investigating the Conditions for Preparative Work

— P. 4

Using the Nexera™ Prep system saves on labor when scaling up from the investigation of analysis conditions to the conditions for preparative work.

Nexera Prep System



## Preparative Work for Non UV

### Adsorptive Components — P. 6

The FRC-40 Fraction Collector can perform preparative work utilizing up to four detector signal channels. Preparative work is performed with the LCMS signal corresponding to the target component, enabling high purity purification.

Nexera Prep LCMS™ Preparative System



## High Separation via Recycle Preparation

— P. 8

By repeatedly injecting the sample into the column, the target component can be fractionated with a degree of separation impossible from a single preparation.

Recycling Preparative System



## Excellent System Expandability

— P. 10

The solvent delivery unit and fraction collector can be selected to suit the recovery volume.

Additionally, the Shim-pack™ Scepter features excellent scalability from analysis to preparative work, and the preparation of a variety of components is supported by an ample lineup.



# ✦ Saves on Labor When Investigating the Conditions for Preparative Work

Fully Equipped with Functions to Reliably Prepare Target Components

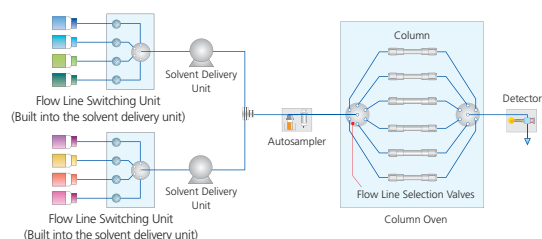
## Nexera Prep System

Smoothly Proceeding Investigation of Analysis Conditions and Optimization of Preparative Parameters

In order to prepare multiple components, the analysis and fractionation parameters must be optimized, which involves a great deal of work. Shimadzu provides the Method Scouting system, which investigates conditions at the analysis level. This system fully automates method scouting in which the combination of mobile phase and column is changed, enabling efficient method development. Further, the preparative system performs automatic simulations using the pre-preparative results, enabling the optimization of the fractionation parameters.

In this way, the work involved in investigating conditions is reduced, which saves on mobile phase solvent and samples.

### Investigation of Analysis Conditions



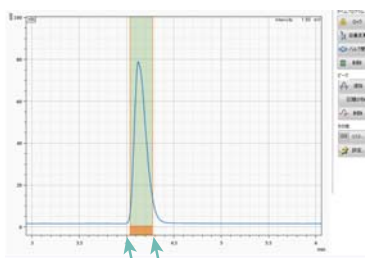
An investigation is performed in order to separate out the target compounds at the analysis level.

Using the Shimadzu Method Scouting system together with Method Scouting Solution, a special software program, provides a fast and accurate method scouting work flow, which supports heightened efficiency in method development.

### Significantly Reduces the Process of Setting Fractionation Parameters

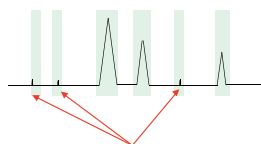
LabSolutions™ software provides simulation functions that reduce the labor involved in investigating conditions for analysis and preparative work.

With the LabSolutions fractionation simulator (patent pending), specify the peak segment in the chromatogram to fractionate, and the system automatically sets the parameters required for fractionation. This reduces the time spent on setting fractionation conditions to about 1/4 the conventional value.

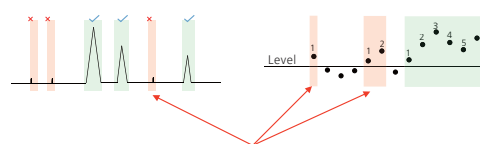


<input checked="" type="checkbox"/>	Use
Peak Detection Parameter	
<input checked="" type="checkbox"/>	Slope
<input checked="" type="checkbox"/>	Use Slope
Front Slope:	4321 uV/sec
Back Slope:	-1017 uV/sec
<input type="checkbox"/>	Level
<input type="checkbox"/>	Use Level
Level:	1000 uV
<input checked="" type="checkbox"/>	Slope Disable Level
	10 %
Peak Collection Sensitivity:	3
Delay Time (Detector Filter):	1.00 sec

When configuring fractionation via automatic peak recognition, noise in the chromatogram is sometimes mistaken for component peaks during fractionation, resulting in an insufficient number of test tubes or other fractionation containers being positioned in the fraction collector. With the LabSolutions software peak sensitivity determination function (patent pending), peaks are recognized from the number of data points consecutively exceeding the configured threshold value, in order to determine whether or not to fractionate.



Conventionally, Noise is Also Sometimes Fractionated



Thanks to the Peak Sensitivity Determination Function, Noise is Distinguished from the Component Peaks (Peak Sensitivity Setting: 5)

## Fraction Purity Checks (LH-40)

A fraction purity check can easily be performed with a single system. Purity checks can be performed without changing the fraction recovery container, so the workload is reduced and throughput is improved.

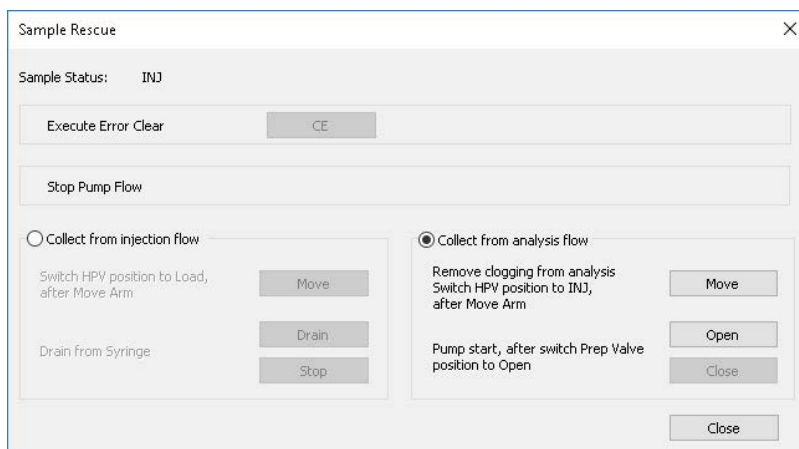


Results of a Purity Check of the Chromatogram During Fractionation and the Recovered Fraction

Note: The fraction reanalysis option is required.

## Sample rescue function prevents the loss of precious samples (LH-40、FRC-40)

With the LabSolutions software's sample rescue function, even if a problem occurs during preparative work, the sample remaining within the preparative system can be recovered. By following the procedures according to the rescue instructions appearing on screen, the precious sample is recovered into the specified container rather than being discarded. Additionally, by using the optional waste collector, samples that cannot be recovered due to fractionation mistakes can be retained.

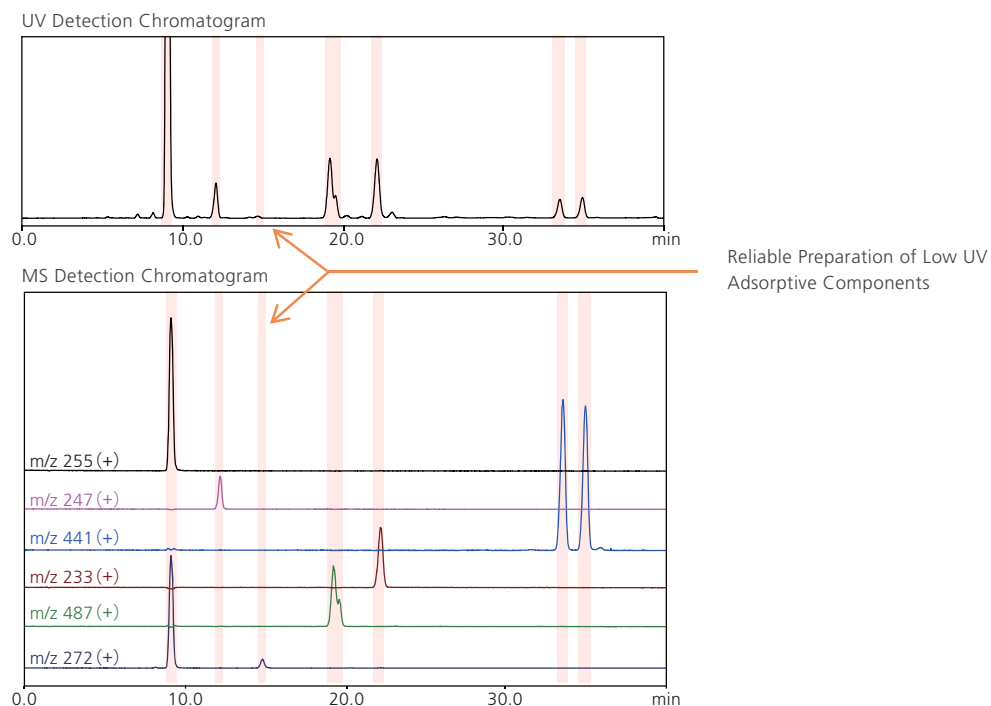


# Preparative Work for Non UV Adsorptive Components

## Capable of High Purity Preparation Triggered by Up to Four Detector Channel Signals Nexera Prep LCMS Preparative System

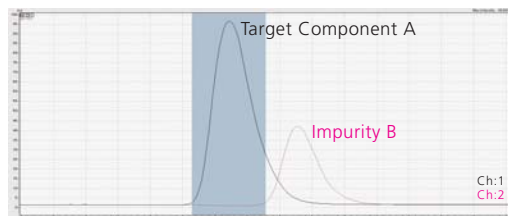
### Using MS Signal Triggers Enables Recovery with No Target Fraction Omissions

It can be difficult to prepare low UV adsorptive components using just a UV signal as the trigger, so there is a risk that the fraction will be missed. By using the MS signal as the trigger, the preparative work can be performed simply, with nothing missed, just by specifying the  $m/z$  of the target component, even for low UV adsorptive components. The LCMS-2020 mass spectrometer enables high sensitivity and high resolution detection and preparative work with no target components omitted.



### High Purity Recovery of Target Components Using Multiple Signal Triggers

By combining up to four detector signal channels, target components can be recovered at high purity levels.



The MS signal from the detection of target component A is used as the trigger to start the preparative work. The MS signal from the detection of impurity B, which is eluted in proximity, is used as the trigger to stop the preparative work. By combining multiple triggers in this way, it is possible to recover only the target component, at high purity levels. By combining a variety of detector signal as triggers, targets can be recovered at high purity levels, with no omissions.

High Purity Recovery of Target Component A  
(Using two MS signals as triggers)



UV-VIS Detector  
SPD-20A



Differential Refractive Index Detector  
RID-20A



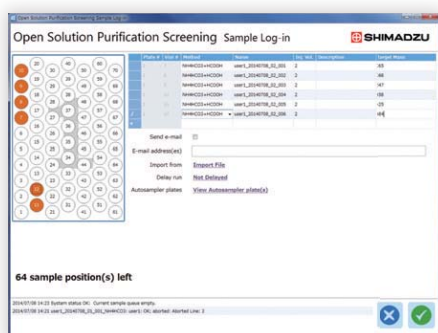
Evaporative Light Scattering Detector  
ELSD-LT II



Mass Spectrometer  
LCMS-2020

## Optional Analytical and Preparative Open Solution\* Software Simplifies Preparative Operations and Data Analysis

### Efficient System Sharing via Open Access



Sample Registration Window

Open Solution simplifies the sharing of preparative systems between several people.

There is a special sample registration window, so preparative work can be performed easily just by having users log in and then specify their method, injection volume and target *m/z*.

### Preparative Operations and Data Analysis Can Be Performed from a Single Window

With the Open Solution data browser, preparative results can be checked from a single window.

When the test tubes are selected, the peaks are highlighted, and the MS spectrum and UV spectrum for the applicable peak are displayed. The information for the fractionated compound can be checked easily.



MS spectrum (Positive/Negative) UV spectrum

Select the vial into which the sample is injected

Fractionated test tube information

Sample and Fraction Information Are Aggregated in a Single Window

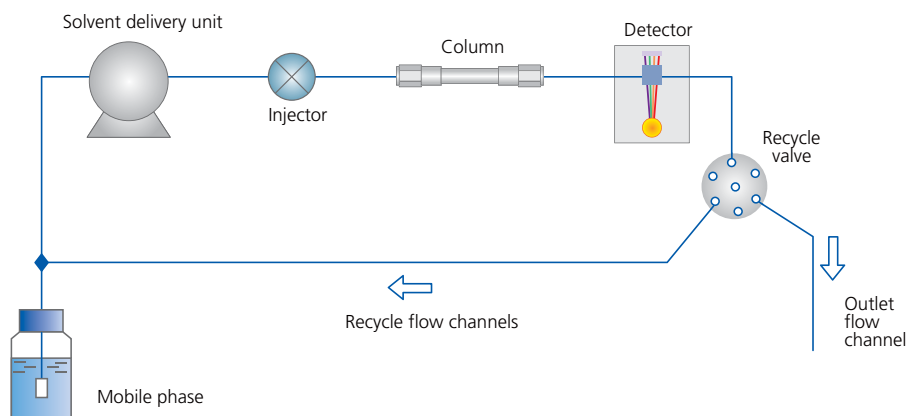
\* This is compatible with the FRC-10A.

# High Separation via Recycle Preparation

## Components Difficult to Separate Can Be Recovered at High Purity Levels and at Low Cost Recycling Preparative System

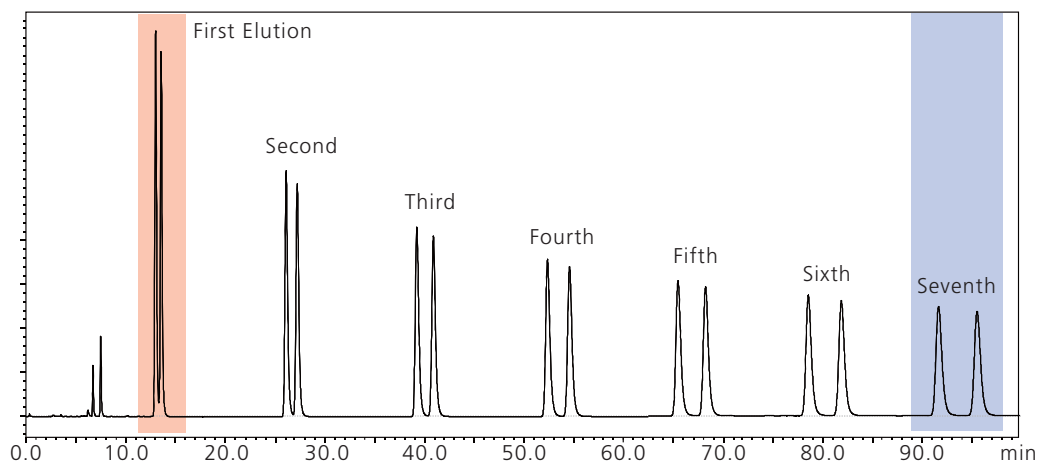
### What is the recycling separation method?

Long preparative columns are expensive, so there is a need to use comparatively cheap short columns effectively. In the recycling separation method (closed valve recycling), the elution liquid containing the target components eluted from the separation column is re-injected into the column, enabling an equivalent separation capacity to that of a longer column.



Flow Lines for the Recycling Preparative System

The figure below shows the results of a seven cycle recycling separation. In the first injection (typical separation), the separation of the two components is insufficient (red area). However, when the column liquid elution is returned to the column from the detector, it is re-injected, and separated a second time. If this recycling is repeated, the results obtained are equivalent to connecting a number of columns in series corresponding to the number of repetitions. In this example, a 4.0 or better degree of separation was ultimately obtained with seven recycling separation cycles (blue area).



Example of the improvement in separation by recycling : The unseparated peaks (red) are completely separated (blue).

Flowrate : 10 mL/min  
Detection wavelength: 254 nm  
Column : Shim-pack PREP-ODS(H) 20 mm I.D. × 250 mm L.  
Mobile phase : Water/methanol = 1/9 (v/v)  
Sample : Mixed 1% n-butylbenzene/iso-butylbenzene solution

## Recycle-Assist — Special Preparative Recycling Software

### Perform Automatic Preparative Recycling with a Simple GUI-Based Operating Environment

The graphical user interface (GUI) provides an environment where even novices to preparative recycling can perform operations simply and reliably. Furthermore, only a single main window is used for the workflow from recycling to fractionation, thus reducing the risk of wasting precious samples through setting mistakes.

Configure settings for automatic fractionation but following wizard instructions.

Manually time recycling and fractionation steps while viewing the chromatogram.

Drain (initial state)

Recycling

Fractionation

Visually identify current flow lines.

The chromatogram monitor enables confirmation of the current chromatogram and acquired data.

### Recycling Conditions Are Completely Set in Three Steps

Just click three points corresponding to the recycling start and stop points and the automatic preparative start point to complete the settings for the recycling preparation conditions.

Entering complicated numerical parameters is completely unnecessary, so recycling preparative work can start easily.

Consideration of Recycling Conditions

- Click the recycling start point.
- Click the recycling end point.
- Click the fractionation start point.

The automatic preparative recycling method is created.

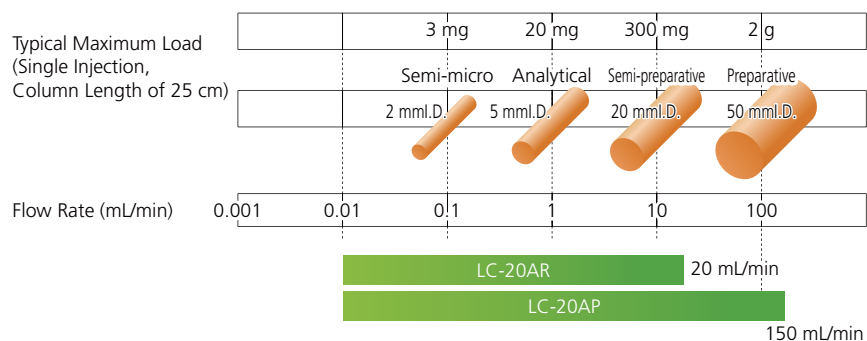
\* This is compatible with the FRC-10A

## System Configuration Responds Flexibly to Applications

### Solvent Delivery Unit Accommodates a Wide Range of Recovery Volumes

#### Guidelines for Preparative Scale and Maximum Load

The figure at right shows the guidelines for total component capacity per 250 mm long column when the target component is highly soluble in the mobile phase, and separates from impurities, and ions are suppressed. For isocratic elution, in principle, the total component capacity is proportional to the column volume.



Supports Semi-Preparative and Recycle Preparative

#### LC-20AR

- This solvent delivery unit can handle flow rates as high as those used in semi-preparative scale (up to 20 mL/min).
- Using a recycle kit enables semi-preparative recycling.



Supports Large-Scale Preparative Fractionation

#### LC-20AP

- High flow rates (up to 150 mL/min) enable highly efficient, large-scale preparative fractionation.
- Large-scale preparation and superior solvent delivery fully support the preparative fractionation workflow, including scaling up to large preparation or assessing purity after preparation.
- Combine with an FCV-200AL low-pressure gradient unit to perform gradient analysis using up to four mobile phases.

### Specifications

	LC-20AR	LC-20AP
Solvent delivery method	Parallel-type double plunger	Parallel-type double plunger
Plunger capacity	47 $\mu$ L	250 $\mu$ L
Maximum discharge pressure	49 MPa	42 MPa
Flow rate setting range	0.01 to 20.00 mL/min	0.01 to 150.00 mL/min
Flow rate accuracy	No more than $\pm 1\%$ or $\pm 10$ $\mu$ L/min, whichever is greater (0.1 to 5.0 mL/min)	No more than $\pm 1\%$ (1 mL/min), 10MPa
Flow rate precision	No more than 0.08% RSD or 0.02 min SD, whichever is greater	No more than 0.1% RSD or 0.02 min SD, whichever is greater
Constant pressure solvent delivery	Supported	Supported
Plunger rinsing mechanism	Syringe or rinsing pump	Syringe or rinsing pump
Operating temperature range	10 to 40°C	4 to 35°C
Size and Weight	W260 x D500 x H140 mm, 16 kg	W260 x D500 x H210 mm, 19 kg

## Shim-pack Scepter LC Columns

### Excellent stability & performance could be achieved under a wide range of LC conditions

Excellent stability and performance could be achieved under a wide range of LC conditions with Shim-pack Scepter LC columns, which are the next generation organic silica hybrid based columns. With different chemistry characteristics, Shim-pack Scepter columns are effective for method development/scouting with suitability for use in a wide variety of applications.

With different particle sizes (1.9  $\mu\text{m}$ , 3  $\mu\text{m}$ , 5  $\mu\text{m}$ ) and different column dimensions, Shim-pack Scepter LC columns are fully scalable between UHPLC, HPLC and preparative LC making method transfer seamless between different laboratory instrumentation.

### Shim-pack Scepter Chemistries

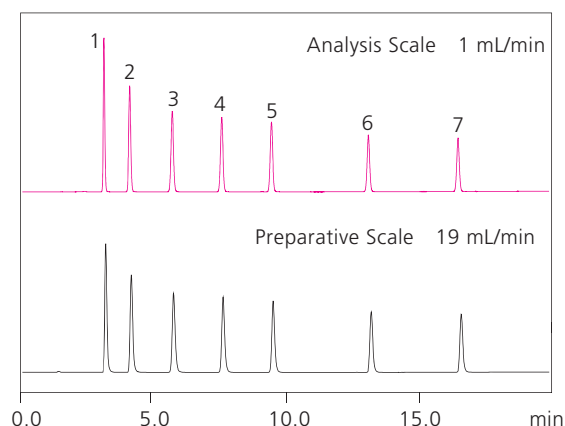
Shim-pack Scepter	Reversed Phase					HILIC
	C18	HD-C18	C8	Phenyl	PFPP	Diol-HILIC
Ligand Type	Trifunctional C18 Generic Purpose Type	Trifunctional C18 High Density Type	Trifunctional C8	Trifunctional Phenylbutyl	Trifunctional Pentafluorophenylpropyl	Trifunctional Dihydroxypropyl
Particle	Organic Silica Hybrid					
Particle Size	1.9 $\mu\text{m}$ , 3 $\mu\text{m}$ , 5 $\mu\text{m}$					
Pore Size	12 nm	8 nm	12 nm			
End Capping	Proprietary				None	
pH Range	1 - 12			1 - 10	1 - 8	2 - 10
100% aqueous condition	Yes	No	No	Yes	Yes	N/A
USP Classification	L1	L1	L7	L11	L43	L20

### Example of Scaling Up from Analysis to Semi Preparative Work

This is an example of scaling up in which seven types of parabens are targeted using a 150 mm long column with particle size of 5  $\mu\text{m}$ .

The gradient elution conditions investigated at the analysis scale are transitioned to the semi preparative scale. A comparable chromatogram is obtained at both scales.

Column : Shim-pack Scepter C18-120 (4.6 mm $\times$ 150 mm, 5  $\mu\text{m}$ )  
 Column : Shim-pack Scepter C18-120 (20 mm $\times$ 150 mm, 5  $\mu\text{m}$ )



- 1 : Methylparabene
- 2 : Ethylparabene
- 3 : Propylparabene
- 4 : Butylparabene
- 5 : Pentylparabene
- 6 : Heptylparabene
- 7 : Nonylparabene

Example of Scaling Up for Parabens

## System Configuration Responds Flexibly to Applications

### The New LH-40 Liquid Handler, Equipped with an Auto Injection Function and a Fraction Collection Function



#### Provides Both a Sample Injection Function and a Fraction Collection Function

A single unit can perform everything from sample injection to fraction recovery.

#### Suppresses Contamination

Thanks to a proprietary injection method, carryover is minimized, significantly limiting contamination to subsequent samples.

(When a 4000 mg/L caffeine sample is injected, the carryover is 0.004 % or less.)

#### Capable of Injection from a Variety of Containers

Thanks to a long needle stroke, the system is compatible with containers of varying depths, including microtiter plates (MTP), vials, test tubes, and sample bottles.

## Options

### Large Capacity Injection Kit

This kit enables large capacity injections of 2 mL or more at one time. The maximum injection volume is 20 mL.

### Washing Pump

This reduces the washing time for the injection needle, increasing throughput while reducing carryover.

### Reinjection Options

The recovered fraction can be reanalyzed, to check the purity.

### Liquid Surface Detection Needle

This detects the liquid surface level, and automatically determines whether there is any sample present. As a result, only the remaining volume is injected, which prevents the injection of air into columns. Additionally, if no sample is present, the system proceeds to the next sample, reducing needless labor.

#### Autosampler

### SIL-10AP

#### Sample Racks

- Sample rack S for 1.5 mL vials
- Reagent bottle rack for 15 mL reagent bottles
- Sample rack L for 4.0 mL vials
- Sample rack LL for 13 mL vials\*<sup>1</sup>
- Sample rack MTP2\*<sup>2</sup>

\*<sup>1</sup> Sample rack LL is a standard accessory of the SIL-10AP

\*<sup>2</sup> For 96-well microtiter/deep-well plates.

#### Sample Coolers

(Block Cooling/Heating: 4 to 70°C)

- S • L



#### Manual Injector

### Rheodyne 7725

#### Optional Sample Loops (Material: SUS)

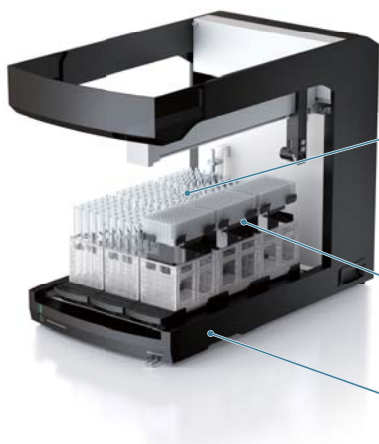
Volume
100 µL
200 µL
500 µL
1 mL
5 mL



## Specifications

	LH-40	SIL-10AP
Maximum Number of Containers	Up to 540 pcs* (10 mm I.D. test tubes)	Up to 100 pcs* (1.5 mL vials)
Maximum Injection Volume	Up to 20 mL (with the Large Capacity Injection Kit)	Up to 5 mL
Cooling Function	None	Yes (Optional available)
Compatible Containers and Quantities	10 mm I.D. Test Tubes 540 pcs 18 mm I.D. Test Tubes 216 pcs 25 mm I.D. Test Tubes 108 pcs 35 mm I.D. Test Tubes 54 pcs MTP/DWP 96-Well 9 pcs	1.5 mL Vials 100 pcs 4.0 mL Vials 80 pcs 13 mL Vials 25 pcs
Size and Weight	W 390xH 560xD 730 mm 40 kg	W 260xH 280xD 320 mm 18.5 kg

## The New FRC-40, Highly Flexible Fraction Collector



### Accommodating Up to 3,240 Test Tubes

Large-scale fractions of the order of liter can also be accommodated, including flasks in addition to 96 well MTPs and a variety of test tubes. Up to six units can be connected, enabling the number of fractions to be even further increased.

### A Variety of Containers Can Be Selected

The system is compatible with various capacities of racks for use to suit the volume of fractionated liquid and the processes after fractionation, which reduces the work involved in switching containers.



### Space-Saving Design

With its small installation footprint, up to nine MTP standard vial racks or test tube racks can be stored, contributing to the effective use of laboratory space.

## Sample Racks

A variety of containers can be placed including MTPs, vials, various types of test tubes, and 50 mL sample bottles. Six colors are available, so a separate color can be apportioned to each user in order to avoid confusing samples.



## Multi Fraction Collector Kit

Up to six FRC-40 fraction collectors (up to five LH-40 liquid handlers) can be connected, making it easy to increase the number of fractions.



Compact Design for Small Volume Samples

## FRC-10A

In consecutive preparative work, peak separation and shape sometimes change due to fluctuations in room temperature, mobile phase composition, and sample load. In addition to the time-based fractionation method, the BAND method and other fractionation functions enable target components to be prepared at high purity levels and with high recovery ratios.



## Specifications

	FRC-40	FRC-10A
Maximum number of fractions	Up to 540 pcs*	Up to 144 pcs*
Maximum flow rate	150 mL/min	
Fractionation mode	Configured through a combination of basic mode (initial parameter mode) and time program mode (14 parameters)	
Cooling function	None	Configured through sample cooler L
Compatible Containers and Quantities	10 mm I.D. Test Tubes 540 pcs 18 mm I.D. Test Tubes 216 pcs 25 mm I.D. Test Tubes 108 pcs 35 mm I.D. Test Tubes 54 pcs 4 mL Vials 252 pcs 50 mL Sample Bottles 54 pcs 250 mL Sample Bottles 20 pcs 500/1000 mL Sample Bottles 12 pcs MTP/DWP 96-Well 9 pcs	10 mm I.D. Test Tubes 144 pcs 18 mm I.D. Test Tubes 164 pcs 35 mm I.D. Test Tubes 16 pcs
Size and Weight	W 390xH 560xD 730 mm 30 kg	W 260xH 280xD 420 mm 15 kg

\*Depends on the type of racks used.

## Suited to the Target Preparative Method

Column Hub  
Column Holder  
Column Holder SLIM

Preparative columns with an I.D. of 20 mm to 50 mm, as well as manual switching valves can be attached. The valves can be used for column switching.

### Specifications

	Installable Valves	Installable Columns	Size
Column Hub	Automatic Switching Valves Up to 4 pc.	Preparative Columns 2 pcs Analysis Columns 2 pcs*	W 250×H 465×D 400 mm
Column Holder	Manual Switching Valves Up to 4 pcs	Preparative Columns 2 pcs Analysis Columns 1 pcs	W 250×H 465×D 400 mm
Column Holder SLIM	Manual Switching Valves Up to 5 pcs	Preparative Columns 2 pcs** Analysis Columns 1 pc	W 110×H 625×D 500 mm

\* If one preparative column and two or more analytical column are attached using the Column Hub, the optional column bracket ASSY is separately required.

\*\*If two preparative columns are attached using the column holder SLIM, the optional column clamp ASSY is separately required.



Column Holder SLIM



Column Holder



Column Hub

For Multiple Detection Triggers

### A/D Conversion Board Kit

This is required for preparative work using multiple detection triggers. Extend the hardware to suit the number of detection trigger channels required.

Degassing Units

### PrepPlus Degasser

- The PrepPlus Degasser has 4 channels of degassing capacity intended for flow from 50-100 mL/min per channel.
- A fifth analytical scale degassing chamber is incorporated for autosampler rinse solution degassing
- Based on proven semi-permeable fluororesin degassing technology, scaled for prep flow rates.



### High-Pressure Flow-Line Selection Valves

## FCV-20AH<sub>2</sub> / FCV-12AH

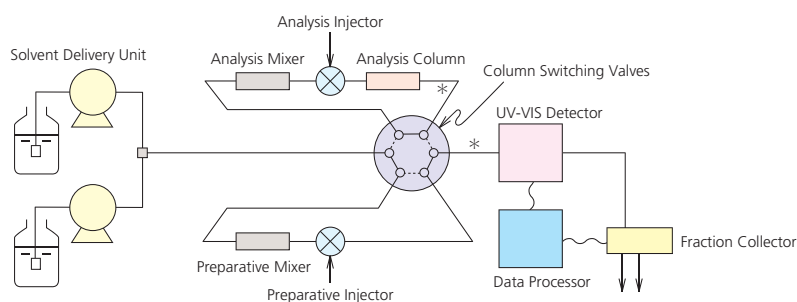
- The valve position is controlled by event signal input.
- Valve type: 2-position/6-port rotary valve (recycle valve : 2-position/3-port valve)
- Maximum operating pressure: 34.3 MPa
- Operating pH range: pH1 to 10
- Operating temperature range: 4 to 35°C
- Storing the FCV-12AH in the optional box, VP is useful for reducing the volume of preparative piping, including the recycling flow lines.



FCV-20AH<sub>2</sub>



FCV-12AH



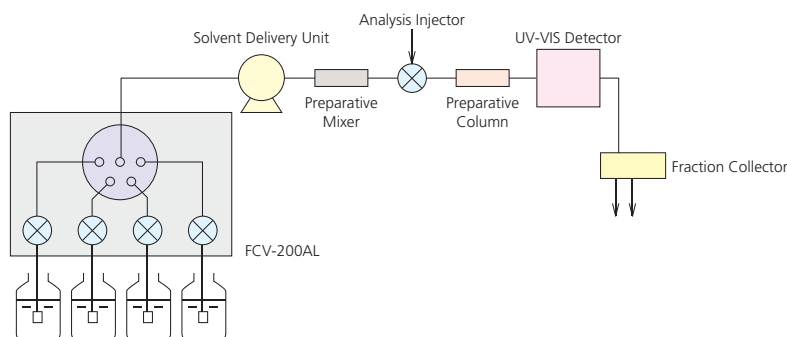
### Low-Pressure Gradient Unit

## FCV-200AL

- This low-pressure gradient unit is for the LC-20AP large volume solvent delivery pump.
- A gradient can be produced with a single pump, enabling gradient preparative work at low cost.
- A single unit is capable of providing up to a four-liquid gradient as well as solvent switching, reducing the work involved in mobile phase investigations during method development.



FCV-200AL



### Reservoir Selection Valves

## FCV-11AL / FCV-11ALS / FCV-230AL

- Capable of switching solvents using a solenoid valve.
- The FCV-11AL/FCV-11ALS can switch between two solvents. The FCV-11AL can handle for up to three solvent delivery units whereas the FCV-11ALS is used for one unit. It can be controlled from the LC-20AP/20AR or a system controller CBM-20A/20Alite or workstation.
- The FCV-230AL can switch between two solvents (option four solvents). It can be controlled from the LC-20AP/20AR or a system controller CBM-20A/20Alite or workstation.



FCV-11AL



FCV-230AL

# System Selection Guide

What is the total amount of sample load?

What is the sample injection volume?  
How many samples are there?

What are the characteristics of the samples?

~2000 mg

LC-20AP

Shim-pack Scepter (I.D. 20~50 mm)



~300 mg

LC-20AR

Shim-pack Scepter (I.D. 10~20 mm)



Injection Volume

Up to 20 mL\*<sup>1</sup>

LH-40

\*1 Optional equipment is required.  
The standard amount is 2 mL.

Up to 5 mL\*<sup>2</sup>

SIL-10AP

\*2 Optional equipment is required.  
The standard amount is 500 µL.

Number of samples\*<sup>3</sup>  
Up to 252 samples

LH-40

Up to 80 samples

SIL-10AP

\*3 When 4 mL vials are used.



UV adsorption

SPD-M20A SPD-20A/20AV



No UV adsorption

LCMS-2020



RID-20A



ELSD-LT II



Are there any other requirements?

Multi sample capability  
Multiple fractions



**Multi Fraction Collector System**

This is the optimal system when there are many fractions.  
The number of fraction collectors can be expanded up to six units.

High separation at low cost



**Recycling Preparative System**

This is the optimal system for obtaining high separation at low cost.

What is the number of fractions?

Up to 540 samples\*4

LH-40



FRC-40



Up to 144 samples\*4

FRC-10A



\*4: When test tubes with an I.D. of 10 mm are used

## Sample System Configuration

### Preparative LC System



Example of Selecting Units

LC-20AP  
Shim-pack Scepter (I.D. 50 mm)  
LH-40  
SPD-M20A

This system supports a wide range of loads, injection volumes, and number of fractions. It can be used as an all-purpose system to support a diverse range of samples.

### Preparative LCMS System



Example of Selecting Units

LC-20AP  
Shim-pack Scepter (I.D. 20 mm)  
LH-40  
SPD-M20A  
LCMS-2020

This is optimal when only preparing trace components. Trace components can also be selectively prepared with no omissions using LCMS.

## Purity checks



### Re-Chromatographic Preparative System

Everything up to fraction purity checks after preparation can be performed with a single system.

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