## YMC

## From Analysis to Plant-Scale Purification

# **Chiral Separation**



YMC CO., LTD. http://www.ymc.co.jp

PB-0081E

## **Chiral Technology offered by YMC**

Chromatography using chiral stationary phase (packing material) is an effective and popular method for optical isomer separation. However, cost for purification can be an issue because of expensive packing materials when a large scale purification is required. YMC has developed various products for chromatography for a wide range of scale from microanalysis to plant-scale preparation. Based on our experience and achievement, we reduce the cost of chiral separation by using optimized products or/and high efficiency separation methods and by providing contract purification service.

**P.8** 

P.9, 10

### HPLC and SFC columns/packing materials P.2-7

CHIRAL ART, HPLC columns/packing materials with polysaccharide derivatives chiral selector for chiral separation offer outstanding stability and high resolution by utilizing high-strength super wide pore silica and optimal packing technology. Alcyon SFC CSP, columns for supercritical fluid chromatography, are useful for improving efficiency of analysis and purification by reducing separation time and solvent consumption.

## Preparative LC systems and columns

YMC has a great selection of preparative LC systems and columns which are effective for separation of chiral compounds. Our preparative systems with a recycle function improve efficiency of preparative separation and reduce solvent consumption. We provide the best solution from dynamic axial compression columns (DAC), preparative systems, and packing materials depending on the scale from a laboratory-scale to a pilot-scale and to a plant-scale.

## Contract purification

YMC offers contract purification service for isolating optical isomers using various chromatography techniques such as HPLC, SFC, and SMB. We provide services using in-house manufactured packing materials and preparative systems for chiral separation to accommodate a wide scale of purification from milligram to kilogram that are compliant with GMP. We propose high efficiency and cost effective methods by selecting the optimal products based on our expertise.







# HPLC Columns/Packing Materials CHIRAL ART

# SFC Columns Alcyon SFC CSP

- Features
- Columns for chiral separation with polysaccharide derivatives
  - Applicable to various chiral compounds
  - Applicable from LC/MS microanalysis
    - to large-scale preparative purification
  - Enhanced resolution and durability

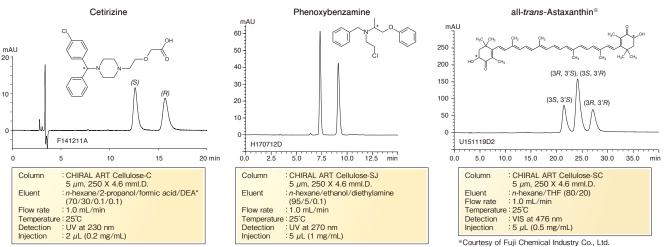
Immobilized type	Columns/p	acking materials useful for both normal-ph	ase and reversed-phase	chromatography
Column/ Packing material	Particle size (µm)	Chiral selector	USP Classification	
Amylose-SA		$\begin{bmatrix} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & $	CH <sub>3</sub>	L99
Cellulose-SB	35	$\begin{bmatrix} O^{R} & O^{R} \\ O^{R} & O^$	R: 3,5-Dimethylphenylcarbamate	_
Cellulose-SC	10 20	$\begin{bmatrix} O^{R} & O^{R} \\ O^{R} & O^{R} \\ O^{R} & O^{R} \\ O^{R} & O^{R} \end{bmatrix}_{n}$ Cellulose tris(3,5-dichlorophenylcarbamate)	Ci NH R: 3,5-Dichlorophenylcarbamate	_
Cellulose-SJ		$\begin{bmatrix} & & & & \\ & & & & \\ & & & & \\ & & & & $	R: 4-Methylbenzoate	_

#### Coated type Columns/packing materials with high resolution for various compounds Column/ Particle size USP Chiral selector Packing material $(\mu m)$ Classification Amylose-C L51 Amylose-C Neo 3 5 10 Amylose tris(3.5-dimethylphenylcarbamate) 20 3,5-Dimethylphenylcarbamate Cellulose-C L40 Cellulose tris(3,5-dimethylphenylcarbamate)

\*Please see `Care and Use Instruction` of CHIRAL ART columns on our web site for usable solvents \*Amylose-C Neo columns/packing materials are upgraded products of Amylose-C

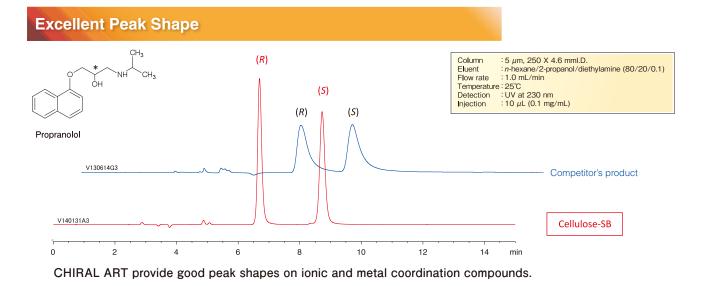
# HPLC Columns/Packing Materials

## Useful for Separation of a Wide Range of Chiral Compounds

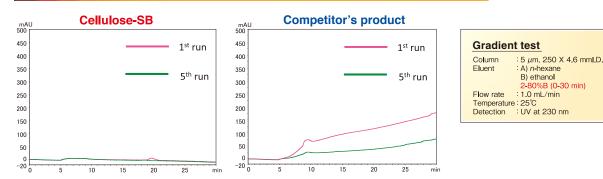


diethylamine

CHIRAL ART are suitable for separation of a wide range of compounds.

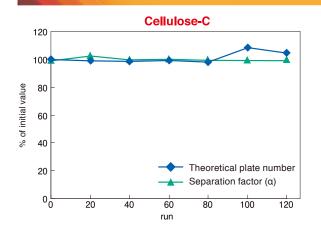


### Low Column Bleeding (Immobilized Type)



CHIRAL ART immobilized type show remarkably reduced background signal under the typical gradient conditions. CHIRAL ART immobilized type offer excellent robustness on gradient analysis and highly sensitive analysis on LC/MS due to the very low ion suppression as well as a stable baseline.

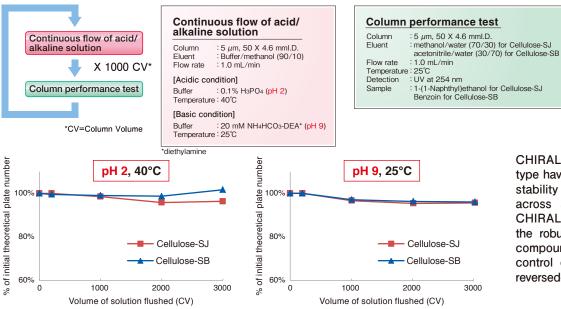
#### Extended Packing Durability



Column	5 μm, 250 X 4.6 mmI.D
Eluent	: A) n-hexane, B) ethanol
	0-100%B (0-15 min)
Flow rate	3.0 mL/min
Pressure	10-30 MPa/run

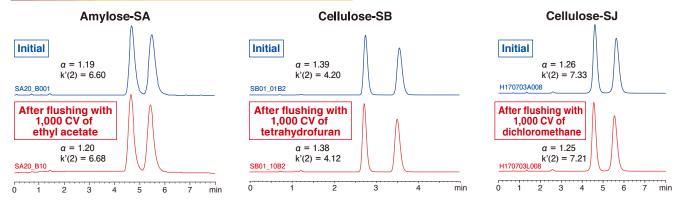
CHIRAL ART have outstanding packed bed stability provided by using high-strength super wide pore silica and innovative packing technology. The column efficiency and selectivity are maintained even after the sequential gradient tests at a high flow rate (three times higher than normal flow rate) and under high pressure (rapid pressure change). CHIRAL ART are useful for shortening analysis time, (re-)equilibration time, or/and column cleaning time by increasing the flow rate. CHIRAL ART are also effective when using highly viscose solvents as a mobile phase on immobilized type columns.

#### Wide Usable pH Range (Immobilized Type)



CHIRAL ART Immobilized type have excellent chemical stability and can be used across a wide pH range. CHIRAL ART also enable the robust analysis of ionic compounds requiring pH control of mobile phase in reversed-phase conditions.

#### High Solvent Versatility (Immobilized Type)



Retention rate of initial column performance (After flushing with 1,000 CV of each solvent at 40°C) \*CV=Column Volume

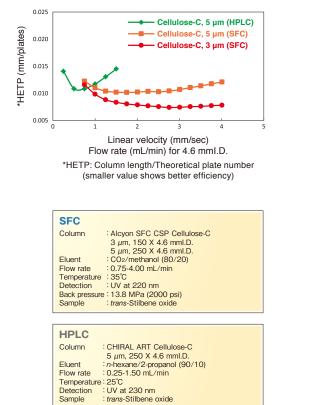
	Amylose-SA		Cellulo	ose-SB	Cellulose-SJ	
	α	k'(2)	а	k'(2)	α	k'(2)
Ethyl acetate	100.3%	101.2%	100.0%	99.1%	99.3%	99.0%
Tetrahydrofuran	100.0%	100.0%	99.3%	98.0%	99.2%	99.7%
Dichloromethane	100.3%	100.6%	101.3%	99.6%	99.6%	98.4%

CHIRAL ART immobilized type have high solvent versatility. After flushing with various solvents, the losses of initial column performances were less than 2%.

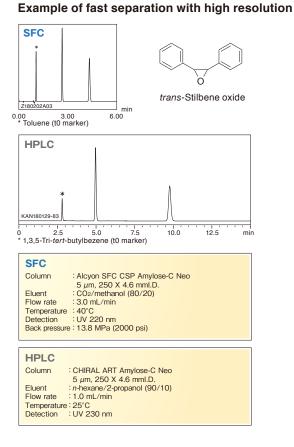
4

# **SFC Columns Alcyon SFC CSP**

#### Faster Separation Than Conventional HPLC



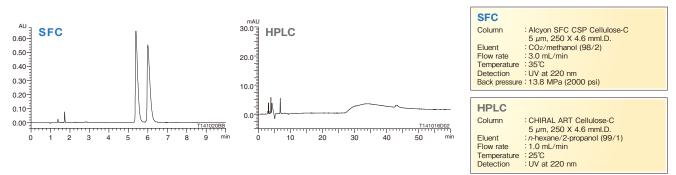
#### Correlation between linear velocity and column efficiency



Faster chiral separation is achieved on supercritical fluid chromatography (SFC) compared to HPLC separation due to lower viscosity and larger diffusion coefficient of supercritical fluid.

#### Excellent Peak Shapes

Sample



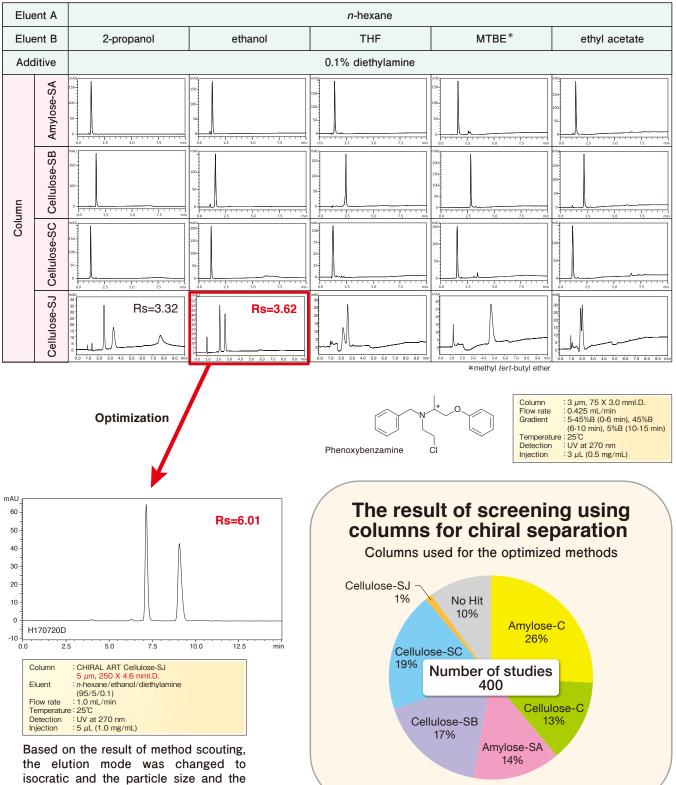


2-Phenylpropionic acid

Excellent peak shape of 2-phenylpropionic acid is obtained on SFC chiral separation. In HPLC, a mobile phase without acidic additives gave very broad peak shapes of acidic compounds. On the other hand, both peak shape and resolution are very good under SFC conditions even without adding any acid. It is considered that supercritical carbon dioxide acts as weak acid.

# **Example of Method Scouting**

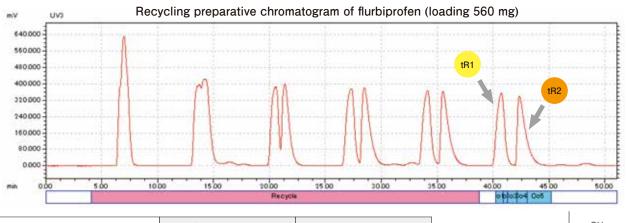
Method scouting is effective for method development of chiral compound separation. Rapid method development can be achieved by studying combination of mobile phases and columns comprehensively, and then optimizing a candidate condition.



column size were optimized.

# **Purification of Chiral Compounds**

### High Purity Preparative Purification of Optical Isomer Using Recycling HPLC



	Single column		Recy	rcling	C * OH	
	tR1	tR2	tR1	tR2		
Enantiomeric purity (%ee)	>99	>97	>99	99	F Flurbiprofen	
Yield (%)	87	74	89	90		
Productivity (mg product/hr)	122	103	335	336 <	Productivity : about 3 times higher	
Solvent consumption (L/g-product)	22	26	2.0	2.0 <	Solvent consumption : about 1/10	

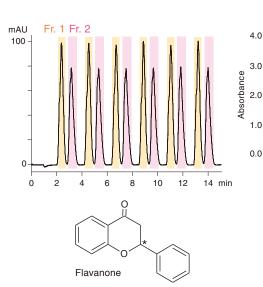
Productivity of single column preparation is estimated based on the stacking injection of the sample every 2.5 minutes

Column	CHIRAL ART Cellulose-C
	5 μm, 250 X 30 mml.D.
Eluent	: n-hexane/2-propanol/TFA
	(95/5/0.1)
Flow rate	: 45 mL/min
Detection	: UV at 280 nm
Injection	: 560 mg
injeotion	. 000 mg

Above is the result of preparative separation of optical isomer, flurbiprofen. Recycling preparation can achieve high purity and high yield on purification of the compound which is difficult to optimize preparative separation conditions using a single column method. Recycling preparation greatly contributes to reduction of solvent consumption and costs on purification as mobile phase is circulated during recycling mode.

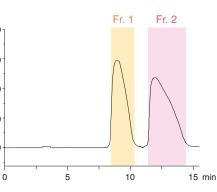
#### High Efficiency Preparation of Optical Isomer Using SFC





Alcyon SFC columns show excellent peak shape even on preparative separation at high loading condition. As a result, purification with high purity and high recovery will be achieved. Alcyon SFC columns offer purification with higher efficiency and lower solvent consumption.

#### **HPLC**



5 10			ie (20 mg/me)		
	SFC		HP	LC	
Column : $250 \times 20$ mml.D.	Fr. 1	Fr. 2	Fr. 1	Fr. 2	
Enantiomeric purity (%ee)	>99.9	99.8	>99.9	99.7	
Yield (%)	94.5	95.6	95.7	93.7	
	340	344	172	169	
Productivity (mg product/hr)	Productivity is doubled				
Volume of purified fraction	0.39	0.57	1.15	2.88	
(L/g-product)	Volume of purifi	ed fraction is 1/4	, easy removal of	residual solvent	
Solvent consumption	ca. 2 ca. 7				
(L/g-product)	Solvent consumption is about 1/3				
Cost (Yen/g product)	5,0	000	12,0	000	
(Mobile phase, waste liquid treatment)		Cost is ha	If or lower		
Productivity is estimated based on the stocking injection of the sample every 0 minutes for					

SFC

Column

Eluent Flow rate

Temperature Detection

HPLC

Column

Eluent

Flow rate Temperature

Detection

Injection

Alcyon SEC CSP Amylose-C

5 μm, 250 X 20 mml.D. CO<sub>2</sub>/ethanol (80/20)

CHIRAL ART Amylose-C

5 μm, 250 X 20 mml.D. n-hexane/ethanol (90/10)

60 mL/min

20 mL/min ambient UV at 220 nm

: 3 ml (20 mg/ml)

Back pressure: 15 MPa (2180 psi) Injection : 1.5 mL (20 mg/mL)

30°C UV at 280 nm

Productivity is estimated based on the stacking injection of the sample every 9 minutes for HPLC and every 2.5 minutes for SFC.

# **Preparative HPLC Systems/Columns**

YMC offer a wide range of product lineup such as a system featured a recycling preparation function which is useful for preparative purification of chiral compounds, and large scale preparative systems which can meet GMP requirements. We can propose the optimal systems and columns depending on the purification scale and its purposes.

**Features** 

**Versatile Preparative HPLC Systems** 

## LC-Forte/R



- Recycling mode as a standard feature
  Laboratory-scale enantiomeric separation of a few grams of the target in one day
   Low cost preparative separation enabled
- Eow cost preparative separation enable by reducing solvent consumption
   Featured both HPLC and flash
- chromatography

## **Preparative HPLC Systems**



- Usable for a wide range of scale from a laboratory-scale to a plant-scale
   Fully extension by PO
- Fully-automatic operation by PC
  Maximum flow rate: up to 25 L/min
- GMP compliant and explosion proof type is also available

### **Dynamic Axial Compression Columns**



- Cost-effective self-packing dynamic axial compression columns
- Superior column performance, durability, and reproducibility provided by constant pressurization
- Inner diameter: 50 to 1000 mm
- GMP compliant and explosion proof type is also available

# From Laboratory to Plant-Scale Separation/Purification Contract Purification

## Purification method development is also available Fast service achieved by accumulated experience and knowledge

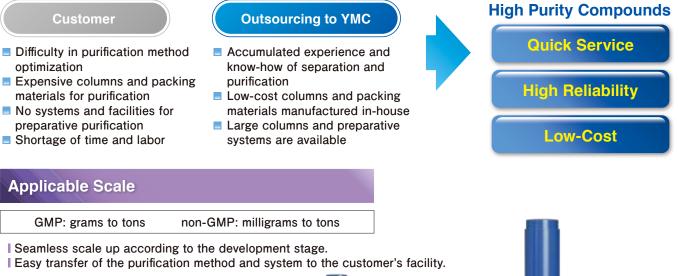
- Smooth transfer of the purification method and system to clients
- GMP compliant simulated moving bed (SMB) continuous chromatography equipment
- Prompt racemic resolution at a kilogram scale

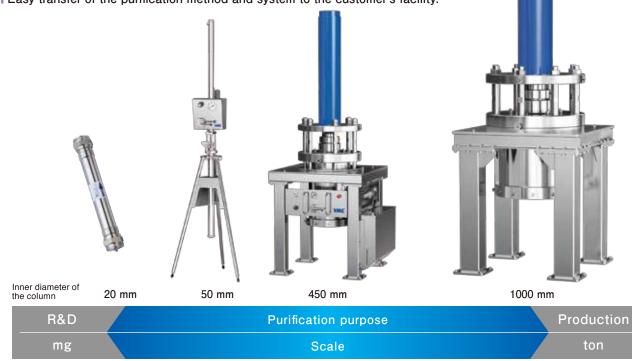


### **Advantages of Contract Purification**

Features

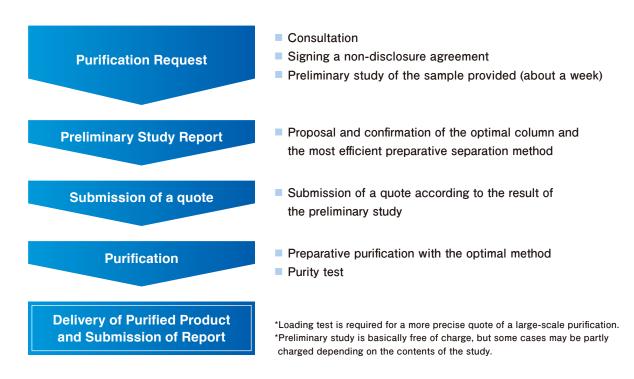
Separation and purification using chromatography can require advanced technology, time, and cost. YMC provides purification services with our accumulated experience, know-how, and excellent equipment. In addition to ensuring qualification of a target substance according to your request, we will also propose an efficient separation method that may result in a cost reduction.





#### **Flow of Purification Service**

We respond flexibly to your need including confidentiality, GMP requirements, and budget. Please feel free to ask for consultation about purification of any scale from small production to mass production.



## Facilities and Quality Assurance System



**API Purification Plant** 

Our GMP compliant API Purification Plant is equipped with large scale preparative HPLC systems and dynamic axial compression columns as well as a lyophilizer and various analytical instruments. Low-cost purification can be achieved by utilizing in-house products such as preparative chromatography systems, packing materials, and columns along with our experience and know-how in chromatography purification. We also established GMP quality management system for appropriate manufacturing control and quality control. Our quality assurance and quality control units are independent from our manufacturing control units, ensuring product quality and maintaining the quality system.



SMB preparative system

Dynamic axial compression HPLC column

Preparative HPLC system

## HPLC columns CHIRAL ART

#### Columns

Particle	Column size	Product number								
size	inner diameter x length		Immobili	zed type			Coated type	Coated type		
(µm)	(mm)	Amylose-SA	Cellulose-SB	Cellulose-SC	Cellulose-SJ	Amylose-C	Amylose-C Neo	Cellulose-C		
3	2.0 X 75	KSA99S03-L502WT	KSB99S03-L502WT	KSC99S03-L502WT	KSJ99S03-L502WT	KAN99S03-L502WT	KBN99S03-L502WT	KCN99S03-L502WT		
	2.0 X 100	KSA99S03-1002WT	KSB99S03-1002WT	KSC99S03-1002WT	KSJ99S03-1002WT	KAN99S03-1002WT	KBN99S03-1002WT	KCN99S03-1002WT		
	2.0 X 150	KSA99S03-1502WT	KSB99S03-1502WT	KSC99S03-1502WT	KSJ99S03-1502WT	KAN99S03-1502WT	KBN99S03-1502WT	KCN99S03-1502WT		
	2.0 X 250	KSA99S03-2502WT	KSB99S03-2502WT	KSC99S03-2502WT	KSJ99S03-2502WT	KAN99S03-2502WT	KBN99S03-2502WT	KCN99S03-2502WT		
	3.0 X 50	KSA99S03-0503WT	KSB99S03-0503WT	KSC99S03-0503WT	KSJ99S03-0503WT	KAN99S03-0503WT	KBN99S03-0503WT	KCN99S03-0503WT		
	3.0 X 75	KSA99S03-L503WT	KSB99S03-L503WT	KSC99S03-L503WT	KSJ99S03-L503WT	KAN99S03-L503WT	KBN99S03-L503WT	KCN99S03-L503WT		
	3.0 X 100	KSA99S03-1003WT	KSB99S03-1003WT	KSC99S03-1003WT	KSJ99S03-1003WT	KAN99S03-1003WT	KBN99S03-1003WT	KCN99S03-1003WT		
	3.0 X 150	KSA99S03-1503WT	KSB99S03-1503WT	KSC99S03-1503WT	KSJ99S03-1503WT	KAN99S03-1503WT	KBN99S03-1503WT	KCN99S03-1503WT		
	3.0 X 250	KSA99S03-2503WT	KSB99S03-2503WT	KSC99S03-2503WT	KSJ99S03-2503WT	KAN99S03-2503WT	KBN99S03-2503WT	KCN99S03-2503WT		
	4.6 X 50	KSA99S03-0546WT	KSB99S03-0546WT	KSC99S03-0546WT	KSJ99S03-0546WT	KAN99S03-0546WT	KBN99S03-0546WT	KCN99S03-0546WT		
	4.6 X 75	KSA99S03-L546WT	KSB99S03-L546WT	KSC99S03-L546WT	KSJ99S03-L546WT	KAN99S03-L546WT	KBN99S03-L546WT	KCN99S03-L546WT		
	4.6 X 100	KSA99S03-1046WT	KSB99S03-1046WT	KSC99S03-1046WT	KSJ99S03-1046WT	KAN99S03-1046WT	KBN99S03-1046WT	KCN99S03-1046WT		
	4.6 X 150	KSA99S03-1546WT	KSB99S03-1546WT	KSC99S03-1546WT	KSJ99S03-1546WT	KAN99S03-1546WT	KBN99S03-1546WT	KCN99S03-1546WT		
	4.6 X 250	KSA99S03-2546WT	KSB99S03-2546WT	KSC99S03-2546WT	KSJ99S03-2546WT	KAN99S03-2546WT	KBN99S03-2546WT	KCN99S03-2546WT		
5	4.6 X 150	KSA99S05-1546WT	KSB99S05-1546WT	KSC99S05-1546WT	KSJ99S05-1546WT	KAN99S05-1546WT	KBN99S05-1546WT	KCN99S05-1546WT		
	4.6 X 250	KSA99S05-2546WT	KSB99S05-2546WT	KSC99S05-2546WT	KSJ99S05-2546WT	KAN99S05-2546WT	KBN99S05-2546WT	KCN99S05-2546WT		
	10 X 250	KSA99S05-2510WT	KSB99S05-2510WT	KSC99S05-2510WT	KSJ99S05-2510WT	KAN99S05-2510WT	KBN99S05-2510WT	KCN99S05-2510WT		
	20 X 250	KSA99S05-2520WX	KSB99S05-2520WX	KSC99S05-2520WX	KSJ99S05-2520WX	KAN99S05-2520WX	KBN99S05-2520WX	KCN99S05-2520WX		
	30 X 250	KSA99S05-2530WX	KSB99S05-2530WX	KSC99S05-2530WX	KSJ99S05-2530WX	KAN99S05-2530WX	KBN99S05-2530WX	KCN99S05-2530WX		

#### Guard cartridge columns (inner diameter 4.0 mm or smaller: 5/pack, 10/20/30 mm: 2/pack)

Particle	Column size				Product number					
size	inner diameter x length				type		Coated type			
(µm)	(mm)	Amylose-SA	Cellulose-SB	Cellulose-SC	Cellulose-SJ	Amylose-C	Amylose-C Neo	Cellulose-C		
3	2.1 X 10	KSA99S03-01Q1GC	KSB99S03-01Q1GC	KSC99S03-01Q1GC	KSJ99S03-01Q1GC	KAN99S03-01Q1GC	KBN99S03-01Q1GC	KCN99S03-01Q1GC		
	3.0 X 10	KSA99S03-0103GC	KSB99S03-0103GC	KSC99S03-0103GC	KSJ99S03-0103GC	KAN99S03-0103GC	KBN99S03-0103GC	KCN99S03-0103GC		
	4.0 X 10	KSA99S03-0104GC	KSB99S03-0104GC	KSC99S03-0104GC	KSJ99S03-0104GC	KAN99S03-0104GC	KBN99S03-0104GC	KCN99S03-0104GC		
5	4.0 X 10	KSA99S05-0104GC	KSB99S05-0104GC	KSC99S05-0104GC	KSJ99S05-0104GC	KAN99S05-0104GC	KBN99S05-0104GC	KCN99S05-0104GC		
	10 X 10	KSA99S05-0110CC	KSB99S05-0110CC	KSC99S05-0110CC	KSJ99S05-0110CC	KAN99S05-0110CC	KBN99S05-0110CC	KCN99S05-0110CC		
	20 X 10	KSA99S05-0120CC	KSB99S05-0120CC	KSC99S05-0120CC	KSJ99S05-0120CC	KAN99S05-0120CC	KBN99S05-0120CC	KCN99S05-0120CC		
	30 X 10	KSA99S05-0130CC	KSB99S05-0130CC	KSC99S05-0130CC	KSJ99S05-0130CC	KAN99S05-0130CC	KBN99S05-0130CC	KCN99S05-0130CC		

A cartridge holder will need to be purchased separately before using this product for the first time.

#### SFC columns Alcyon SFC CSP Columns

Particle	Column size				Product number				
size	inner diameter x length		Immobili	zed type		Coated type			
(µm)	(mm)	Amylose-SA	Cellulose-SB	Cellulose-SC	Cellulose-SJ	Amylose-C	Amylose-C Neo	Cellulose-C	
3	2.1 X 150	KSA99S03-15Q1WTS	KSB99S03-15Q1WTS	KSC99S03-15Q1WTS	KSJ99S03-15Q1WTS	KAN99S03-15Q1WTS	KBN99S03-15Q1WTS	KCN99S03-15Q1WTS	
	3.0 X 50	KSA99S03-0503WTS	KSB99S03-0503WTS	KSC99S03-0503WTS	KSJ99S03-0503WTS	KAN99S03-0503WTS	KBN99S03-0503WTS	KCN99S03-0503WTS	
	3.0 X 100	KSA99S03-1003WTS	KSB99S03-1003WTS	KSC99S03-1003WTS	KSJ99S03-1003WTS	KAN99S03-1003WTS	KBN99S03-1003WTS	KCN99S03-1003WTS	
	3.0 X 150	KSA99S03-1503WTS	KSB99S03-1503WTS	KSC99S03-1503WTS	KSJ99S03-1503WTS	KAN99S03-1503WTS	KBN99S03-1503WTS	KCN99S03-1503WTS	
	4.6 X 150	KSA99S03-1546WTS	KSB99S03-1546WTS	KSC99S03-1546WTS	KSJ99S03-1546WTS	KAN99S03-1546WTS	KBN99S03-1546WTS	KCN99S03-1546WTS	
	4.6 X 250	KSA99S03-2546WTS	KSB99S03-2546WTS	KSC99S03-2546WTS	KSJ99S03-2546WTS	KAN99S03-2546WTS	KBN99S03-2546WTS	KCN99S03-2546WTS	
5	2.1 X 150	KSA99S05-15Q1WTS	KSB99S05-15Q1WTS	KSC99S05-15Q1WTS	KSJ99S05-15Q1WTS	KAN99S05-15Q1WTS	KBN99S05-15Q1WTS	KCN99S05-15Q1WTS	
	4.6 X 150	KSA99S05-1546WTS	KSB99S05-1546WTS	KSC99S05-1546WTS	KSJ99S05-1546WTS	KAN99S05-1546WTS	KBN99S05-1546WTS	KCN99S05-1546WTS	
	4.6 X 250	KSA99S05-2546WTS	KSB99S05-2546WTS	KSC99S05-2546WTS	KSJ99S05-2546WTS	KAN99S05-2546WTS	KBN99S05-2546WTS	KCN99S05-2546WTS	
	10 X 250	KSA99S05-2510WTS	KSB99S05-2510WTS	KSC99S05-2510WTS	KSJ99S05-2510WTS	KAN99S05-2510WTS	KBN99S05-2510WTS	KCN99S05-2510WTS	
	20 X 250	KSA99S05-2520WTS	KSB99S05-2520WTS	KSC99S05-2520WTS	KSJ99S05-2520WTS	KAN99S05-2520WTS	KBN99S05-2520WTS	KCN99S05-2520WTS	

Before use (installation, operation, maintenance, or check-up) of our products, please read this instruction carefully and follow the safety rules and precautions in the manual.

#### – Worldwide Availability –

The above information is as of August, 2018 and is subject to change without notice. ©2018 YMC CO., LTD. All Rights Reserved.

#### YMC America, Inc. www.ymcamerica.com

YMC India Pvt. Ltd. www.ymcindia.com



YMC Korea Co., Ltd. www.ymckorea.com

YMC Europe GmbH

www.ymc.de

YMC CO., LTD.

#### YMC Switzerland LLC www.ymc-schweiz.ch

YMC Taiwan Co., Ltd. www.ymctaiwan.com

Distributor

YMC Shanghai Rep. Office www.ymcchina.com

YMC Singapore Tradelinks Pte. Ltd. www.ymc.sg

YMC Karasuma-Gojo Bldg., 284 Daigo-cho Karasuma Nishiiru Gojo-dori, Shimogyo-ku Kyoto, 600-8106, Japan TEL:+81-75-342-4515 FAX:+81-75-342-4550

www.ymc.co.jp sales@ymc.co.jp