![SHIMADZU logo] **SHIMADZU**
Excellence in Science

Fully Automated Sample Preparation Module for LCMS

CLAM-2000

CLAM-2000 provides users seamless integration of automated sample preparation and LC-MS/MS to improve data quality, sample throughput, laboratory efficiency and safety

Simple workflows allow users to go from blood collection tubes to results without any additional sample handling

Fully Automated Sample
Preparation Module for LCMS

CLAM-2000

■ Seamless Integration of Sample Preparation and LC-MS/MS Analysis

- Simply place the blood collection tubes to be analyzed, necessary reagents, and specialized pretreatment vials into the CLAM-2000 which then performs all processes automatically.

- Each sample is processed successively in parallel, to optimize instrument usage and sample throughput.

- The CLAM-2000 frees up time spent by laboratory staff performing tedious sample preparation steps, thus increasing laboratory efficiency.

■ Thorough Precision Control of Analytical Results.

- Easy to access software controlled management of reagents, calibration curves, control samples, and system maintenance ensures system performance and reliability.

- Easy to interpret charts and figures alert users to decreasing reagent volumes or variable QC sample results.

■ Reduces Operator Errors and Enhances Laboratory Safety During Procedures.

- Eliminates manual operations involving biological samples, such as dispensing. Not only does this improve reproducibility of data, but it minimizes user contact with biohazardous material.

- Potentially infectious waste products are kept isolated inside the system. This allows such waste to be disposed of after the analysis is finished, according to the procedures specified for that laboratory.

With the diversification of pharmaceuticals and increasingly individualized medicine, there is a need to control the concentrations of multiply administered low-dose drugs, evaluate metabolic variations between and within individuals, and to determine the narrow concentration range of drug treatments. Consequently, there has been growing interest in using ultra high performance HPLC or high-sensitivity high-throughput LCMS for identification or quantitative research of immuno-suppressants, pain treatment drugs, antiretroviral drugs, anti-seizure drugs, and antipsychotic drugs. The CLAM-2000 fully automated sample preparation module for LCMS is based on the extensive blood coagulation analyzer technology that Shimadzu has cultivated over many years. Simply place blood collection or other tubes in position and the system fully automates everything from pretreating blood or other samples for analysis to LCMS analysis. Consequently, the system is able to minimize human error and variability in sample pretreatment procedures. Therefore, it helps achieve a high-precision workflow for clinical research that is safer, faster, and simpler.

Perform All Processes from Collection of Samples in the Blood Collection Tubes to Sample Pretreatment and Analysis Automatically

User-Friendly Experimental Design and Execution

Depending on the samples being analyzed, operations involve two simple steps - placing the blood collection tubes and reagents in the system and then requesting the desired sample analyses in the software. Using a liquid crystal touch panel display, the CLAM-2000 interface was designed to make LCMS sample preparation and analysis accessible to all users, regardless of the level of experience. The CLAM-2000 offers a next-generation workflow for routine LC-MS/MS analysis that helps ensure reliable and rapid operations.
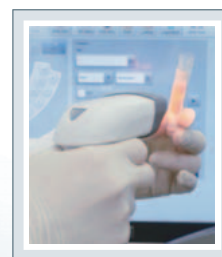
Prepare blood collection tubes in advance.

- Whole blood
- Blood plasma
- Blood serum
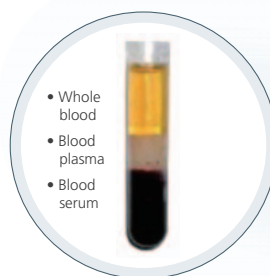
Place blood collection tubes and reagents.
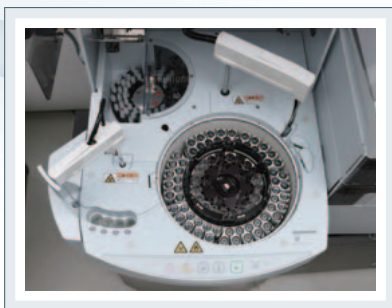
Handheld barcode reader input (option)
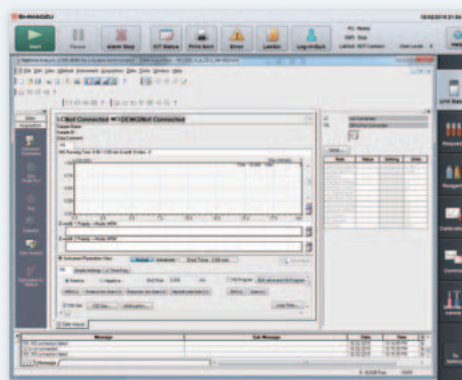
Enter samples and reagents.

Examples of Analysis Windows

Main CLAM-2000 GUI Window ← Click to switch between → LabSolutions Data Window
these windows

Advanced options for displaying, reporting, and managing data results can be easily accessed through the CLAM-2000 software by linking to LabSolutions.

Note: An optional LCD screen can be installed for monitoring LCMS analysis.

For Research Use Only. Not for use in diagnostic procedures.

Precise Control of Analytical Results

## Improves Accuracy and Reproducibility of Analytical Data

Sample batches are easily created through a barcode reader or by direct entry to facilitate sample analysis. CLAM-2000 software ensures reliable results and continuous operation by tracking solvent levels, calibration curves, QC samples and instrument parameters. These measures help to ensure a routine analysis workflow that continues to provide high-quality results.
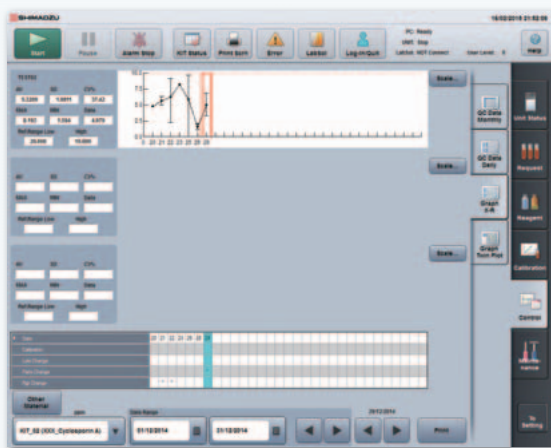
Reagent Management
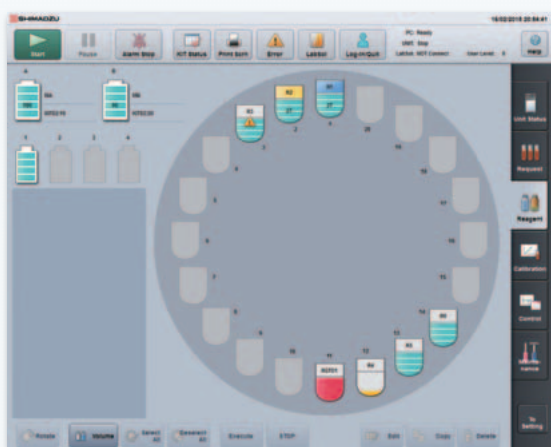
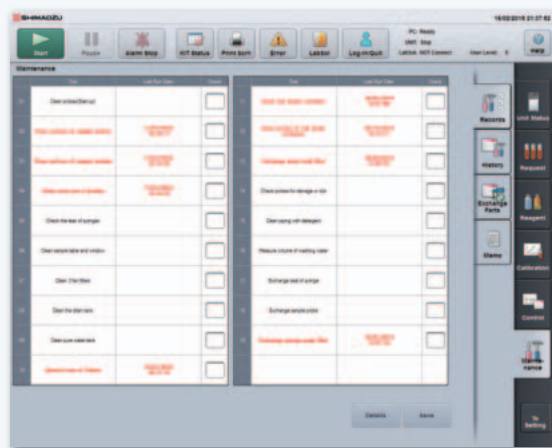Reagent information registration

Calibration Curve Management
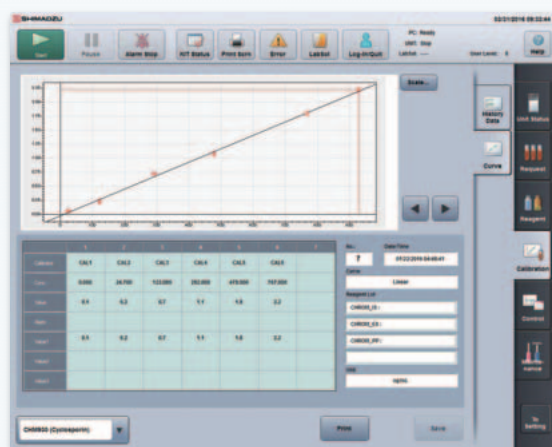
Calibration curve

Control Management

Daily variance control data

System Maintenance Management

Maintenance record

The Benefits of CLAM-2000 Automation on LC-MS/MS Workflows

Reduces Operator Errors

Once the samples and the filtration/collection vials are loaded into the sample carousel, users use a touch panel screen to queue the samples and order the methods. Once loaded, all steps are automatically performed including the LC-MS/MS analysis. Removing the operator from the process in effect removes operator error, thus increasing reproducibility.

❶ Table for samples and reagents
❷ Table for dedicated vials
❸ Probe for dispensing samples
❹ Probe for dispensing reagents

Seamless Automation

The CLAM-2000 not only automates common steps in LC-MS/MS sample preparation protocols, but it delivers the sample to the LC autosampler for injection. Most often, sample preparation involves protein precipitation and derivatization and the CLAM-2000 provides all of the functions required to execute these critical steps.

Dispensing Samples	Dispensing Reagents	Shaking

For Research Use Only. Not for use in diagnostic procedures.
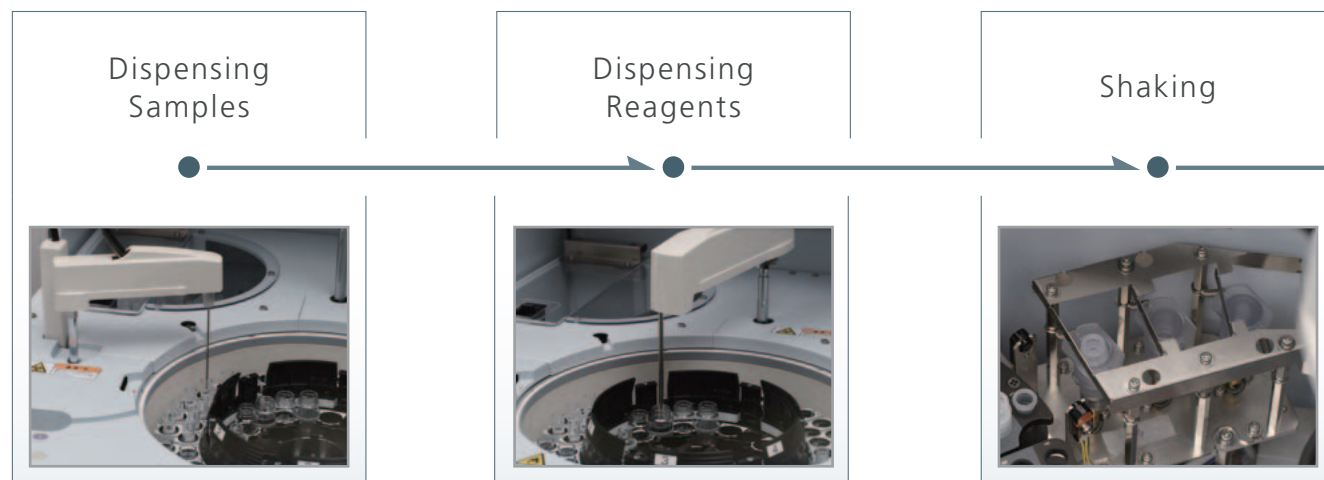
Increased Laboratory Efficiency and Safety

Laboratory staff will no longer be tied to a bench, processing samples. Operators will simply need to load samples and reagents, create the batch and press start. Exposure to samples are minimized and all potentially hazardous waste is isolated inside the CLAM until it can be disposed of according to proper laboratory safety procedures.

LCD touch panel (option)

Waste tank

Disposal box
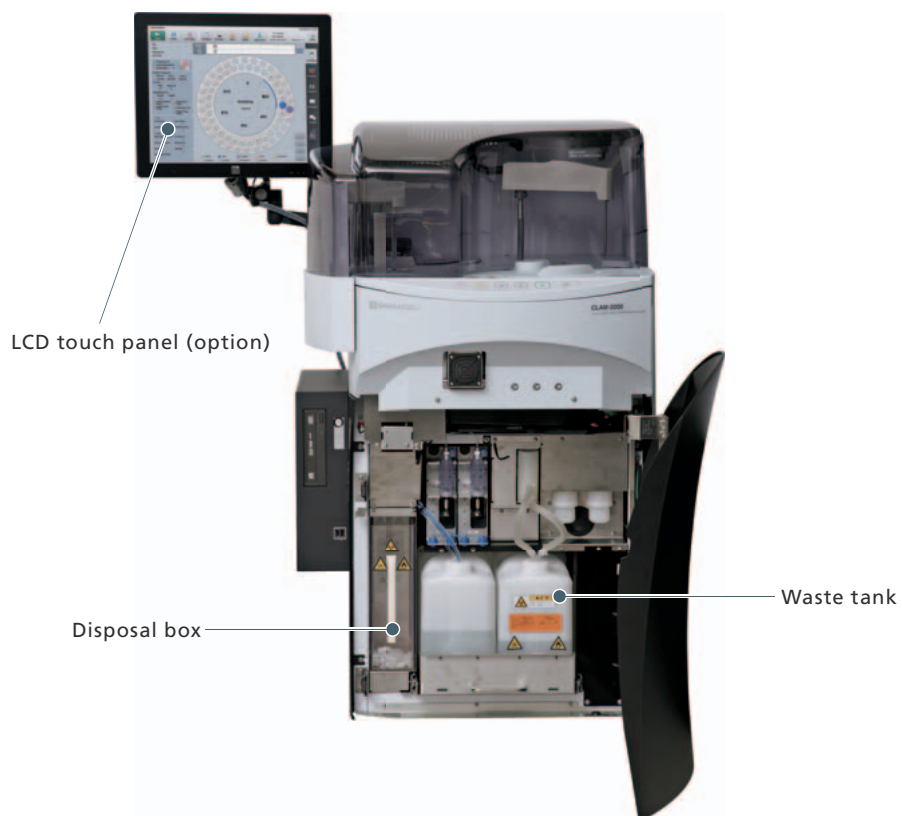
Filtering

Incubation

Autosampler Delivery

Applications examples using CLAM-2000 combined with LC-MS/MS

Steroids

This analysis flow is an example of a simultaneous multicomponent analysis of steroids in serum using a fully automated preparative LCMS analysis system consisting of a Nexera X2 ultra high performance liquid chromatograph, LCMS-8060 triple quadrupole mass spectrometer, and CLAM-2000 fully automated sample preparation module for LCMS.

Pretreatment Conditions and Analysis Flow

Comparison with the time required for sample preparation
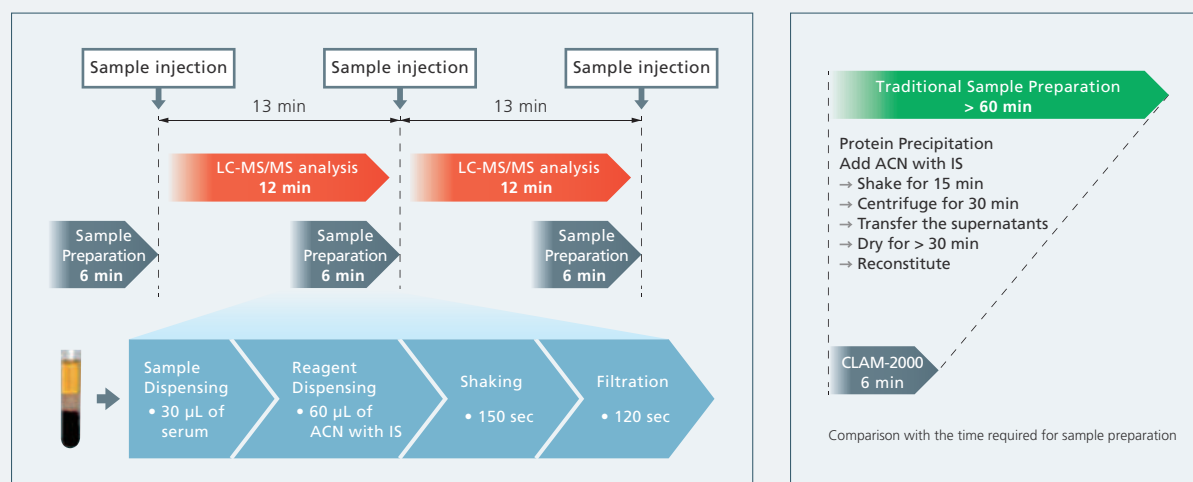
Quantitative Results of Drug Spiked into Serum

Compounds	Polarity	Range (ng/mL)	r²	QC sample concentrations (ng/mL)			Accuracy (%)			%RSD (n=3)		
				LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ
Aldosterone	+	0.03 – 1.14	0.997	0.03	0.46	1.14	96.5	102.0	102.8	6.3	7.9	3.6
Cortisol	+	1.51 – 320	0.999	1.51	20.8	320	104.4	100.4	98.6	1.6	0.5	0.7
DHEAS	+	12.9 – 2750	0.999	12.9	179	2750	104.3	101.3	99.6	3.9	3.6	1.9
Corticosterone	+	0.29 – 62	0.998	0.29	4.03	62	101.8	101.0	98.4	4.6	0.8	1.0
11-Deoxycortisol	+	0.08 – 18	0.997	0.08	1.17	18	103.0	102.7	96.1	5.5	0.9	0.2
Androstenedione	+	0.08 – 18	0.999	0.08	1.17	18	116.5	99.1	100.1	4.6	1.3	1.1
Testosterone	+	0.03 – 7.2	0.999	0.03	0.47	7.2	93.8	101.4	100.1	3.7	1.0	1.0
17-OHP	+	0.12 – 26	0.998	0.12	1.69	26	103.6	103.3	99.6	6.2	1.6	1.8
DHEA	+	0.31 – 65	0.999	0.31	4.22	65	93.1	98.1	99.0	6.5	3.9	6.5
Progesterone	+	0.12 – 26.5	0.999	0.12	1.72	26.5	103.3	101.0	99.2	3.9	1.1	1.5
Aldosterone (neg)	–	0.03 – 1.14	0.996	0.03	0.46	1.14	115.0	97.3	97.4	6.6	7.5	8.0
DHEAS (neg)	–	12.9 – 444	0.997	12.9	20.8	444	101.7	103.0	99.7	2.1	1.2	7.1

Anticoagulants

Compounds	Polarity	Range (ng/mL)	r²	QC sample concentrations (ng/mL)			Accuracy (%)			% RSD (n=6)		
				LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ
Apixaban	+	5 – 500	0.992	5	50	500	95.7	99.1	107.1	9.16	4.95	1.53
Rivaroxaban	+	5 – 500	0.993	5	50	500	104.8	107.8	106.0	4.65	5.84	2.21
Edoxaban	+	5 – 500	0.996	5	50	500	100.0	109.1	99.2	2.52	2.92	1.26
Dabigatran	+	5 – 500	0.994	5	50	500	101.7	111.4	96.9	0.85	2.19	1.05

Antiarrhythmic Drugs

Compounds	Polarity	Range (ng/mL)	r²	QC sample concentrations (ng/mL)			Accuracy (%)			% RSD (n=6)		
				LLOQ	Middle	H	LLOQ	Middle	ULOQ	LLOQ	Middle	H
Sotalol	+	100 – 5000	0.999	100	1000	2000	107.0	101.2	101.1	3.20	1.83	1.80
Amiodarone	+	100 – 5000	0.999	100	1000	2000	99.2	102.6	100.6	3.78	1.66	1.99
N-Desethylamiodarone	+	100 – 5000	0.999	100	1000	2000	101.2	103.3	100.1	4.22	1.48	3.01

Antiepileptic Drugs

Compounds	Polarity	Range (ng/mL)	r²	QC sample concentrations (ng/mL)			Accuracy (%)			% RSD (n=6)		
				LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ	LLOQ	Middle	ULOQ
Levetiracetam	+	10 – 750	0.999	10	100	750	94.6	106.1	99.2	3.42	1.23	1.98
Felbamate	+	25 – 1000	0.999	25	250	1000	98.6	101.8	99.6	6.28	1.88	1.50
Carbamazepine-10,11-epoxide	+	5 – 1000	0.999	5	100	1000	92.9	107.8	99.3	7.48	3.32	1.41
Carbamazepine	+	10 – 1000	0.999	10	100	1000	90.6	110.3	99.1	3.79	3.42	1.19
Tiagabine	+	50 – 1000	0.999	50	250	1000	98.5	101.9	99.6	1.95	2.00	1.26
Diazepam	+	5 – 1000	0.999	5	250	1000	98.1	102.4	99.5	4.61	1.50	1.53
Topiramate	–	500 – 10000	0.999	500	2500	10000	102.3	97.1	100.6	6.71	3.58	2.96

Note:
Polarity: LC-MS/MS ion mode, +: positive, –: negative
r²: Linear regression value of the calibration curve
QC sample concentrations: Spiked concentrations in serum
LLOQ: Lower limit of quantification
ULOQ: Upper limit of quantification
H: High concentration of quantification

CLAM-2000 Specifications

Pretreatment Method	Volume for Sample Treatment	Max. 350 μL
	Processing Capacity	Max. 20 samples per hour Note: when using simple pretreatment protocol with 1 min LCMS cycle time in R&D verification
	Pretreatment Processes	Sample dispensing, reagent dispensing, shaking, suction filtration, and incubation Note: Up to 20 processes can be specified.
	Pretreatment Methods	Each sample processed successively in parallel
	Number of Vials Placed	Max. 60 filteration vials and 60 collection vials
	Number of Samples	Max. 60 samples*
	Number of Reagents	Max. 20 bottles
	Sample and Reagent Cooling Temperature Ranges	4 to 15°C (room temperature 18 to 23°C) 4 to 8°C below room temperature (room temperature 23 to 28°C)
Pretreatment Functions	Dispensing Sample Volumes	Setting range from 30 to 100 μL in 0.5 μL steps, liquid level sensor function, and collision-stop function
	Dispensing Reagent Volumes	Setting range from 10 to 300 μL in 0.5 μL steps, liquid level sensor function, and collision-stop function
	Shaking	Eccentric vial rotation method, with rpm settings from 1,000 to 2,600 rpm
	Incubation	Setting range from 35 to 60°C, with ± 5°C precision
External Dimensions		W670 × D700 × H1,190 mm (LCD touch panel and computer are not included.)
Weight		185 kg
Power Source		120 V/230 V AC, 50/60 Hz, 700 VA
Operating Environment		Temperature: 18 to 28°C, Humidity: 40 to 70% RH

Note(*): The numbers of samples successively treatable may be different depending on applications.

CLAM-2000 Software Specifications

Connectable Instruments	LCMS-8060/8050/8040 systems that include an SIL-30AC autosampler Note: Specialized LC and LCMS tables (options) Note: For other connectable instruments, contact your Shimadzu representative.
Managing, Displaying, and Outputting Data	Determined by LabSolutions LCMS version 5.85 functionality
Key Functionality	Precision management functions: reagent management, calibration management, control management, and instrument maintenance management Pretreatment parameter settings (max. 20 pretreatment processes per condition × max. 60 conditions) Indirect LC or LCMS control by linking to LabSolutions Supports interrupting analysis for priority samples (if within the max. number of placeable vials)
Control Unit	LCD touch panel (also requires specialized LCD mounting arm) (option) Handy barcode reader (option)

Computer System Specifications   Note: The system does not include a control computer. Please obtain the computer system separately.

Item	Remarks
PC for LCMS-8060/8050/8040	For connecting to an LCMS-8060/8050/8040 systems Note: LabSolutions LC is required for connecting to a Nexera system.

Item	Main Specifications
PC Unit	CPU: Intel Core i5-3470 (3.20 GHz) RAM: 4 GB, HDD: 500 GB Super Multi Drive, with one serial port (RS-232C compatible) OADG keyboard 100BASE-T/100BASE-TX/10BASE-T LAN interface
Display Monitor	22-inch LCD monitor with 1920 × 1080 pixel resolution
Required Software	Microsoft Windows 7 Professional (English Edition) LabSolutions LCMS version 5.85 Adobe Acrobat Reader (read-only version that cannot create PDF files) Printer driver

Specifications for Dedicated Pretreatment Vials

CLAM-2000 is compatible with dedicated disposable pretreatment vials from Shimadzu. Filteration and Collection vials are used as a pair.

Dedicated
Filteration Vial

Dedicated
Collection Vial

P/N	Description		
241-16531-41	Vial set	Set of 100	* Sold as a set
241-16531-42	Vial set	Set of 500	* Sold as a set

Vial Material	Polypropylene (PP)
Filter Material	PTFE, with 0.45 μm pore size
Reusability	No (disposable)

Specifications of Applicable Sample and Reagent Vials

Sample Containers	13 mm body diameter × 75 mm tall Examples: BD brand Vacutainer blood collection tubes Terumo brand Venoject II blood collection tubes Nipro brand Neotube blood collection tubes, etc.	
	2 mL cup P/N 038-00180 Sample Cup, 1270016HIT	
	Micro-volume cup P/N 241-94045-01 Sample Cup, Micro	
Reagent Vials	2 mL vial P/N 038-00083-01 Vial, 2.0mL Glass Shell Vial	
	6 mL vial P/N 038-00199-04 Vial, SCREW NO.2-C	
	12 mL vial P/N 038-00199-06 Vial, SCREW NO.4-C	

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