C190-E214C

SHIMADZU
Excellence in Science

Ultra High Performance Liquid Chromatograph for Online Analysis

Nexera FV

Automates Online LC Analysis, from Sample Collection to Data Collection

Nexera™ FV

Nexera FV and LabSolutions™ FV together form a new UHPLC system capable of monitoring flow synthesis and batch synthesis reactions, and automating formulation dissolution testing.

From bulk drug to final product manufacturing, the Food and Drug Administration (FDA) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) look for consistency in the manufacturing of pharmaceuticals. There is an increasing need for a Quality by Design (QbD) approach using process analytical technology (PAT), and process monitoring, in which the quality of each product is controlled during each unit operation. In measuring the critical quality attributes (CQA), Nexera FV and LabSolutions FV automate all the steps for PAT, including collection and dispensing of the reaction solution, HPLC analysis, data analysis, and the creation of reports. This achieves substantial labor savings and provides highly reliable data by eliminating human error.

In dissolution testing as well, everything from periodic sample collection from the dissolution vessels to LC analysis is performed automatically, substantially reducing the burden on the analyst.

With its proprietary design, the Nexera FV flow through vial autosampler periodically collects samples that are sent into the flow through vial from the reaction tank or dissolution vessel. Two analytical modes can be selected depending on the sampling time and LC analysis time, to provide optimally timed analytical data collection. Further, the Nexera FV can also be used as a general-purpose UHPLC system, which contributes to increasing the asset's operating rate. Additionally, with just a few simple operations, LabSolutions FV implements settings for online analysis and data analysis for a wide range of applications, including process monitoring and dissolution testing.

Nexera FV and LabSolutions FV expand the possibilities for online LC, providing new solutions for pharmaceutical quality control.

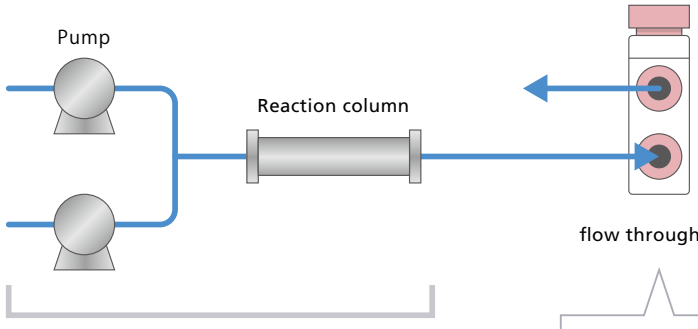
- **Compatible with Online Analysis of Flow Synthesis**
- **Reduces the Cost and Risk of Batch Reaction Monitoring**
- **Simultaneously Provides Labor Savings and Heightened Efficiency in Dissolution Testing**

Compatible with Online Analysis of Flow Synthesis

Online analysis can be performed by injecting reaction mixture into the flow through vial in the autosampler during flow synthesis. With simple settings using LabSolutions FV, the sampling program can be configured to collect samples at set intervals, enabling continuous monitoring. If high-speed separation analysis via the UHPLC conditions is used, the system can accommodate sampling at intervals as short as 5 minutes.

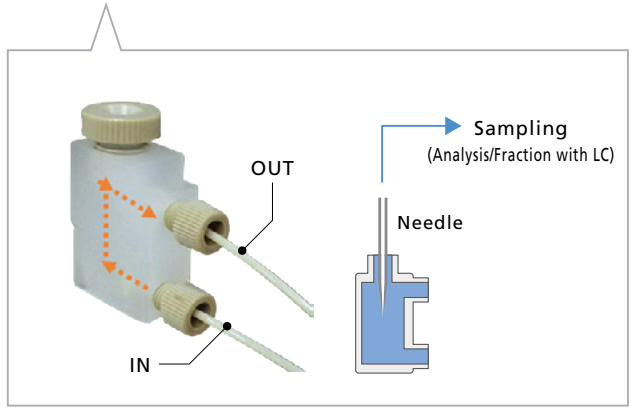
Nexera™ FV System

Flow synthesis system

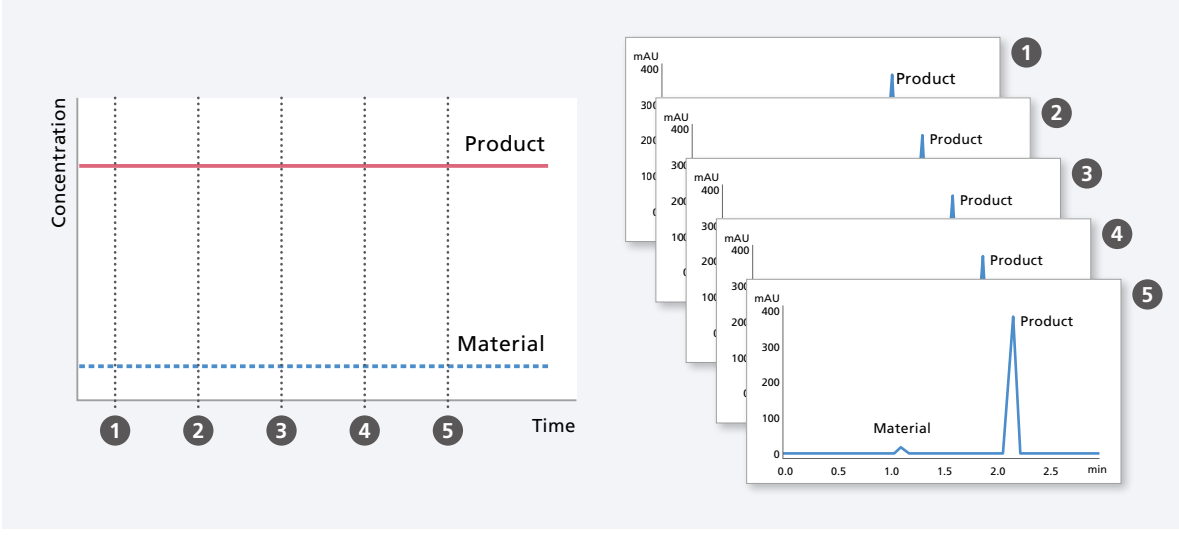


Flow synthesis system

Note: Separate preparations are required for the flow synthesis system.



Synthetic evaluation



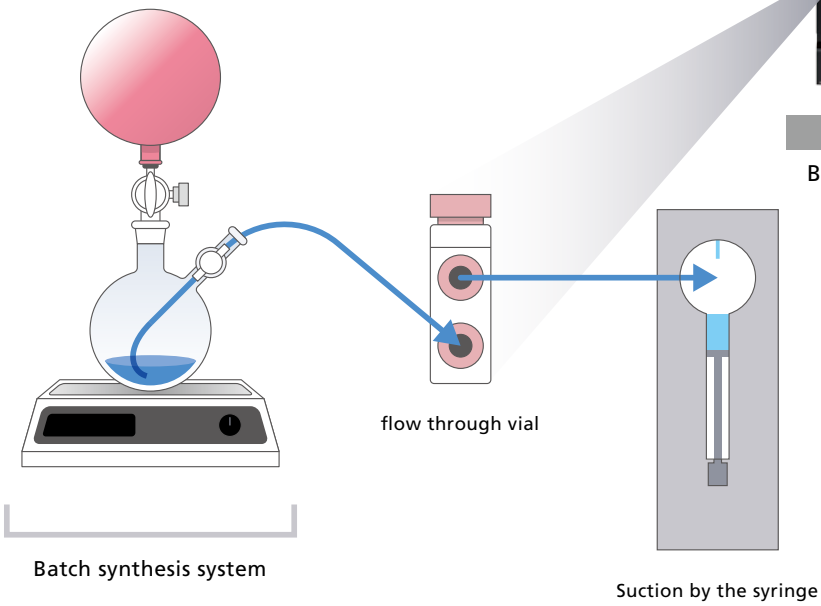
Confirmation of the status of continuously manufactured products

Reduces the Cost and Risk of Batch Reaction Monitoring

The reaction mixture can be injected from the batch synthesis flask into the flow through vial by combining an autosampler with an external syringe and valve. High-concentration samples can be automatically diluted with the autosampler pretreatment function, and then injected into the column. Automatic sampling of reaction mixture reduces the manual sampling time and eliminates the risk of human error during sample collection, making reaction monitoring even more efficient and increasing data reliability.

Nexera™ FV System

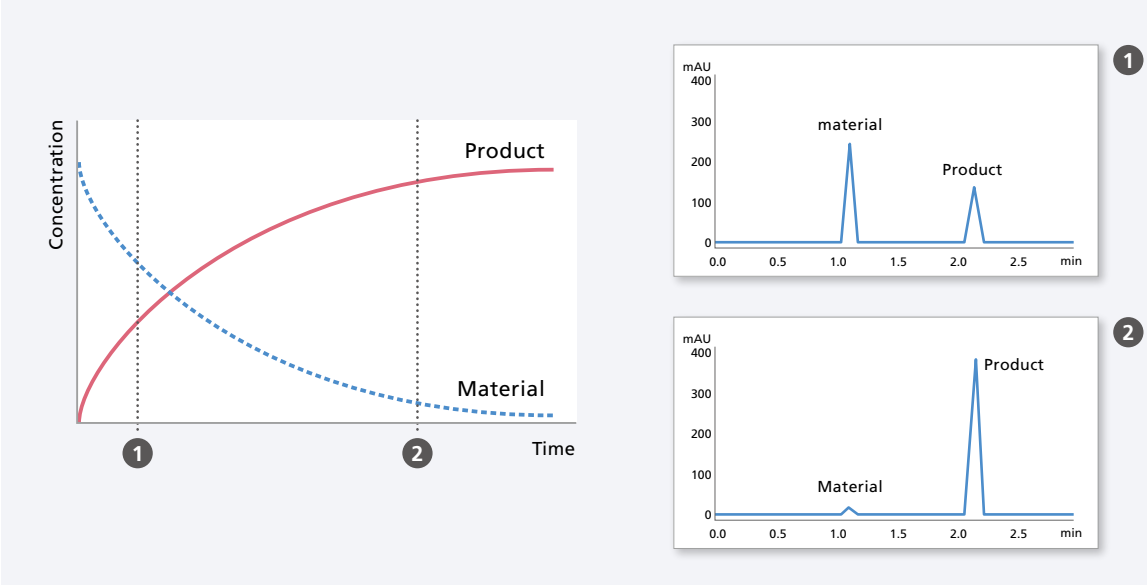
Batch synthesis system



Note: The autosampler needle is used for pretreatment, so a reaction mixture prone to precipitation cannot be used.

Note: Separate preparations are required for the batch synthesis system.

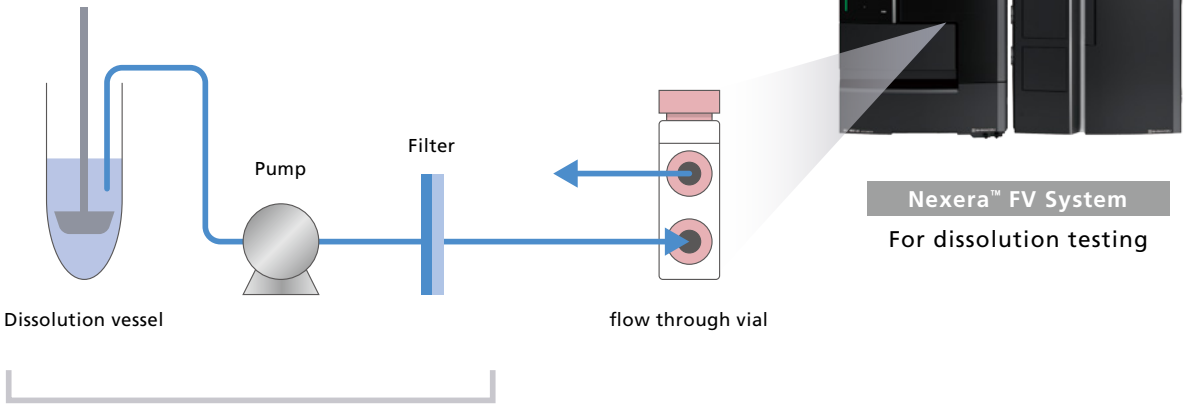
Synthetic evaluation



Confirmation of changes over time in products

Simultaneously Provides Labor Savings and Faster Speeds in Dissolution Testing

Everything is automated in dissolution testing systems containing the Nexera FV, from sampling, dilution, and other pretreatments to data acquisition, data analysis, and the creation of reports. As a result, there is less hands-on work for the operator, thereby supporting an increase in processing throughput. Further, there is no manual dispensing of samples, so sampling mistakes are eliminated, enabling safer testing.

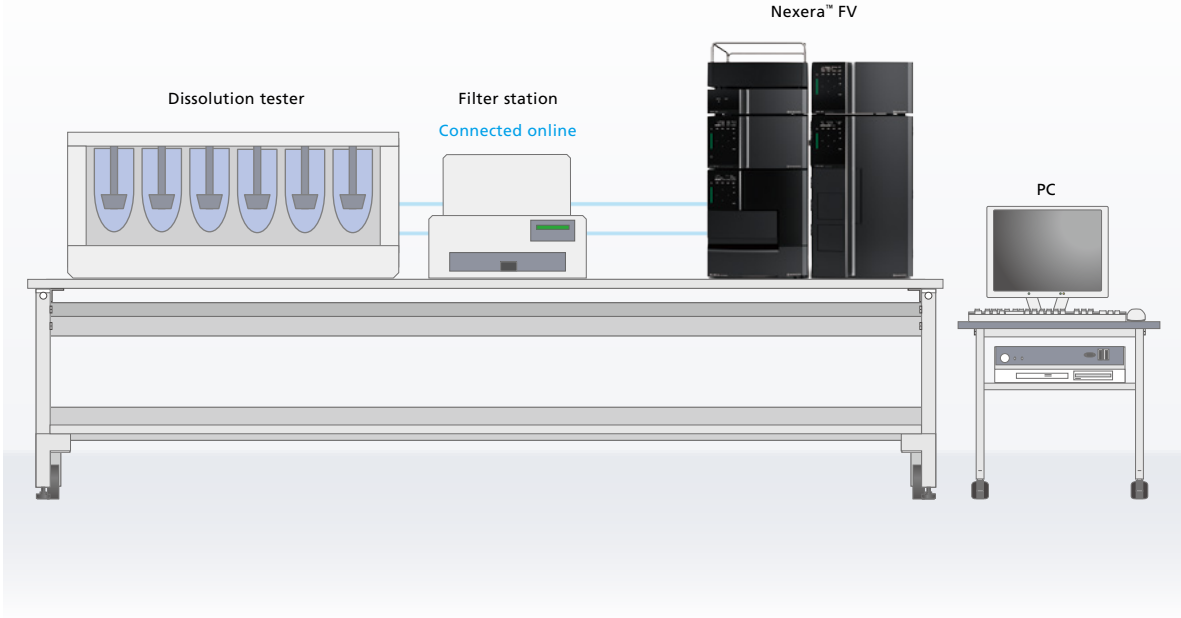


Nexera™ FV System

For dissolution testing

Note: Separate preparations are required for the dissolution tester and the filter station.

Typical System Configuration for Online Dissolution Testing

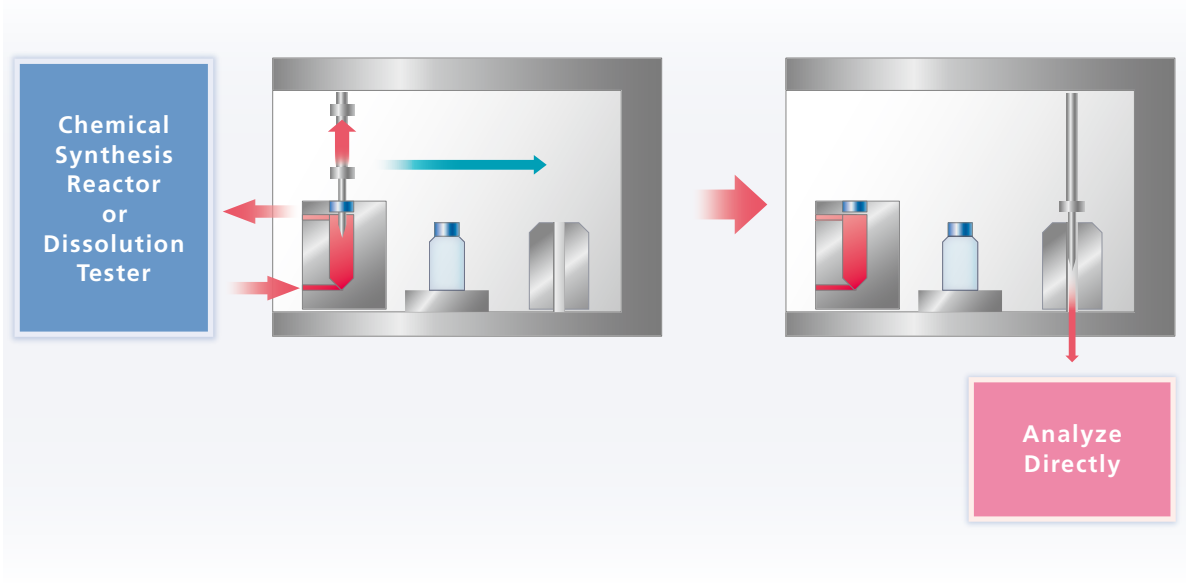


The test solution sent from the dissolution tester flows directly into the flow through vial installed in the autosampler.

Two Analysis Modes Promote Faster Online Analysis

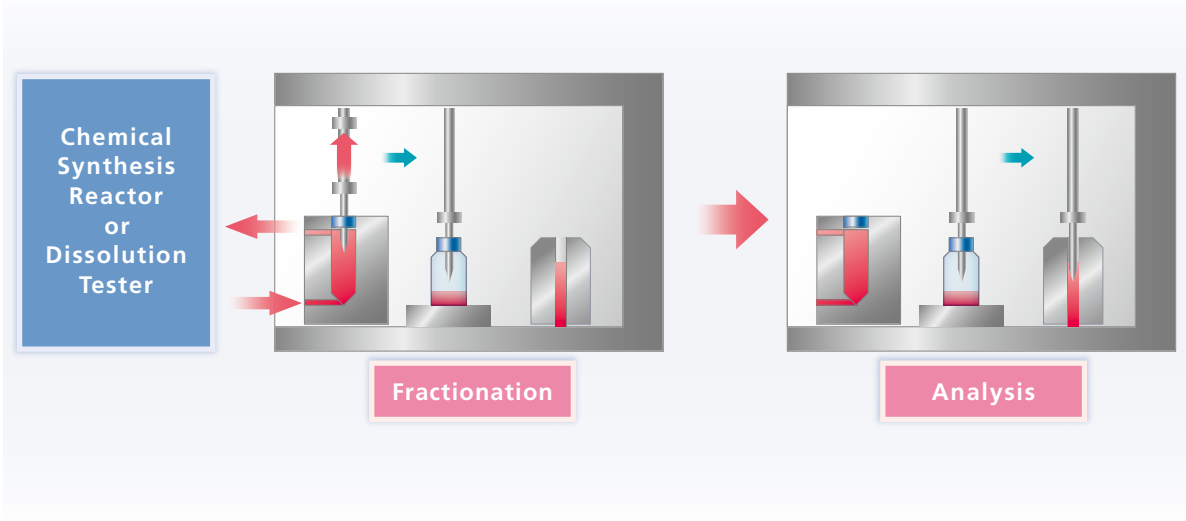
Direct Injection Mode: Exclusively with the Nexera System

This mode directly injects and analyzes the test solution sent from the reaction flask or dissolution tester vessels. It is effective if the analysis of the injected reaction mixture or test solution is completed by the next sampling interval.
This analysis mode can be selected because the Nexera FV is compatible with UHPLC analysis.



Fraction Mode: For Confirmation at Short Sampling Intervals

This analysis mode is used for tests in which the sampling interval is short. Thanks to the high-speed operation delivered by the Nexera autosampler, the system is compatible with sampling intervals as short as 5 minutes. Up to 384 samples can be fractionated. This is effective when dilution will be required.



Reliable Performance Expands the Range of Choices

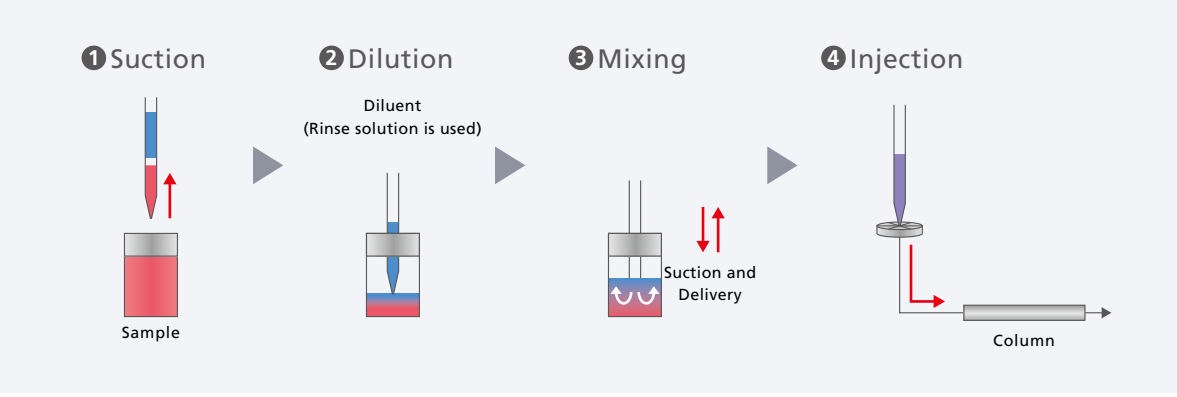
Automatic Dilution of High-Concentration Samples

High-concentration samples often require dilution. Samples can be diluted online using the fraction analysis mode. High injection accuracy is provided even at trace quantities, enabling reliable automatic dilution.
The table to the right shows the dilution accuracy of standard solutions using Nexera FV's automatic dilution method.
(Sample: Aqueous caffeine solution)

Dilution rate (times)	Dilution accuracy (%)
2	98
5	98
10	98
20	99
50	95
100	95

Note: Dilution accuracy varies depending on the solvent used. It is expected to be within ±10% when caffeinated water is used.

Automation of sample dilution and mixing



Automatic Addition of Internal Standard Substances

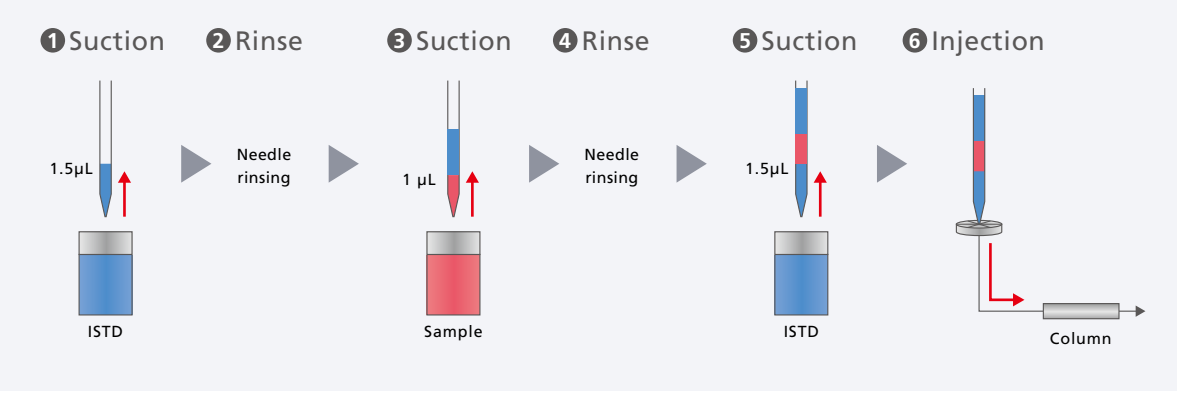
Internal standard substances are sometimes added to samples for the purpose of yield calculations. Using the Nexera FV automatic pretreatment function, a set amount of an internal standard substance can be automatically added to and mixed with the injection sample, after which the mixture can be injected onto a column.

Area ratio repeatability (n=6)

Sample concentration (mg/L)	Area ratio %RSD
40	0.165
80	0.266
160	0.116

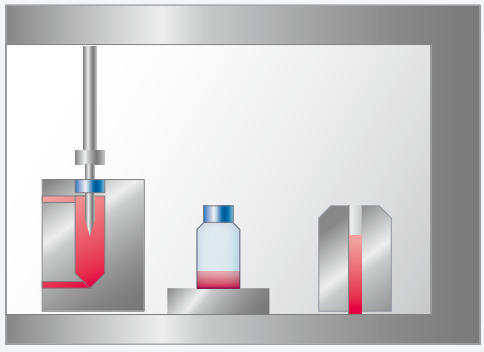
Sample : Loxoprofen Sodium Salt Dihydrate
ISTD : Methyl p-oxybenzoate

Simultaneous injection of internal standard substances

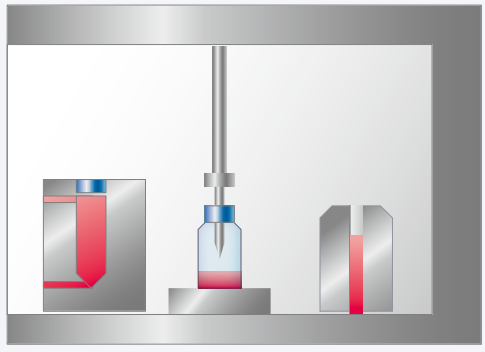


One System Plays Two Roles, Significantly Improving the Throughput of the Testing Lab

The Nexera FV is a multipurpose system since not only can it be used online as an LC by connecting it with a reaction vessel and dilution tester, but also as a standalone UHPLC system. This maximizes the equipment operation rate, increasing the utilization of laboratory assets.



As an on-line LC

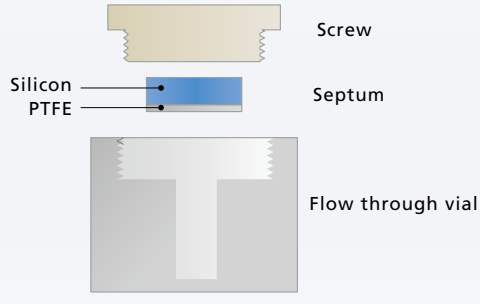


As a UHPLC system

Long-Lasting Consumables Provide for High Cost-Effectiveness

A special septum is used for the flow through vial that receives the dissolution medium. It boasts a better degree of adherence after needle penetration in comparison to a regular septum, and can be used for 200 continuous injections without leaking.* This greatly reduces maintenance, enabling continuous testing.

*The replacement period varies depending on the usage conditions.



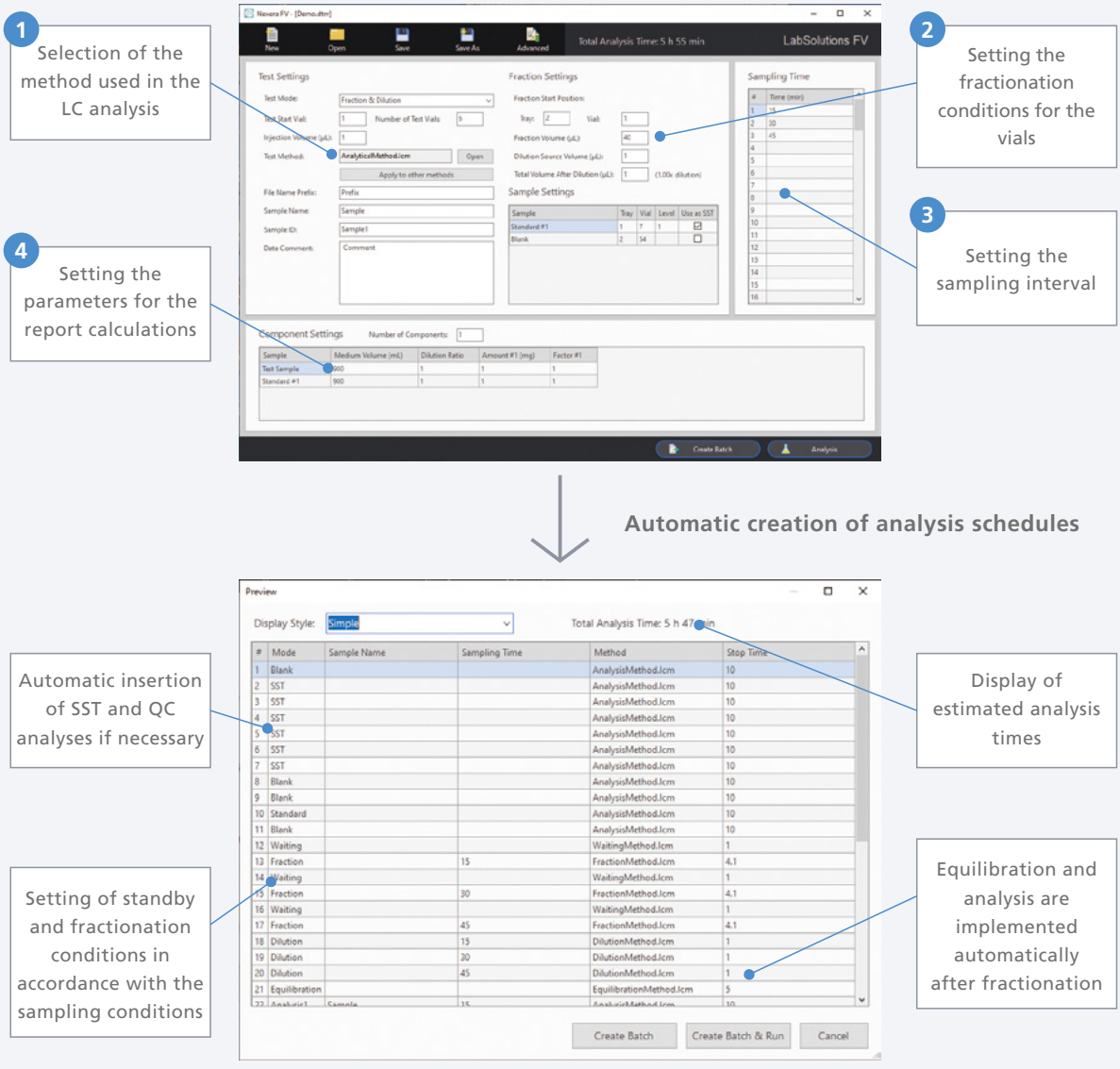
Heightening the efficiency of online analysis work:

LabSolutions FV

Easily Implement Batch Synthesis, Flow Synthesis, Dilution Tests, and Other Online LC Analyses

When monitoring is performed with an online LC, one of the laborious tasks that must be performed is the creation of an analysis schedule corresponding to the sampling conditions. The special LabSolutions FV software provides strong support for a range of time-consuming tasks prior to starting analysis.
In a single software window, not only can the user configure the LC analysis conditions, sampling interval, and other necessary information, but the LabSolutions analysis schedule can be created automatically, so online LC analysis can be started just by clicking the Start button. This reduces the time and labor expended prior to starting analysis and, at the same time, reduces the risk of analysis failures due to setting mistakes, thereby contributing to a more efficient workflow and improved data reliability.

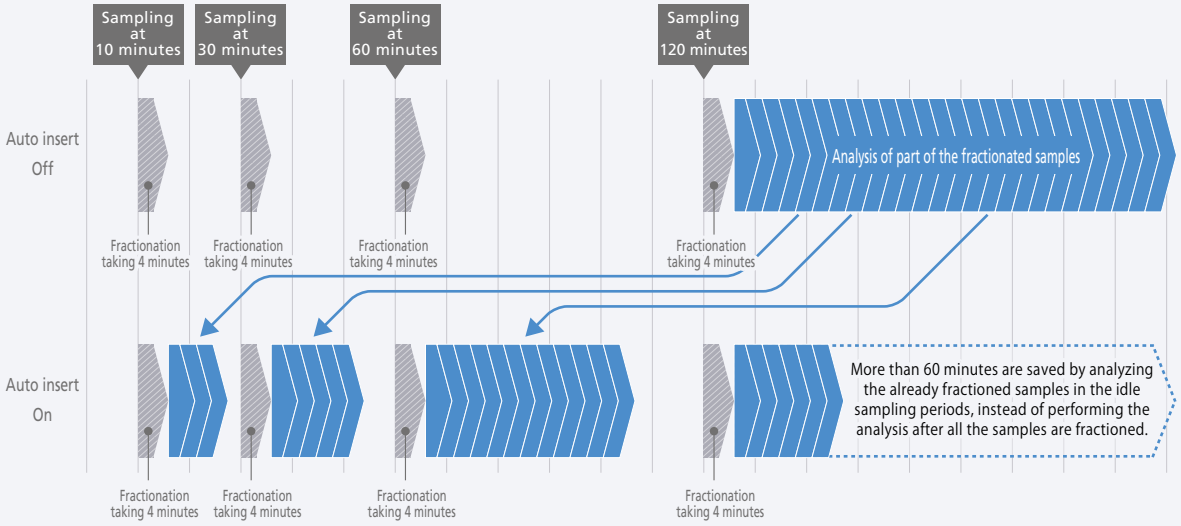
- **Automatically creates analysis schedules in accordance with the sampling conditions.**
- **Implements fraction and dilution automatically with the autosampler pretreatment program.**
- **Sampling can be started by an external signal input or at a specified time.**



Heightened Efficiency of the Entire Monitoring Analysis Workflow

Generally, in the later part of an online analysis schedule, the sampling interval becomes larger, and the LC instrument remains idle for longer periods. Using the automatic analysis insertion function provided by LabSolutions FV, when idle periods arise during sampling, LC data analysis of samples that have already been sampled is automatically conducted during the set analysis schedule, heightening the efficiency of the entire online analysis.

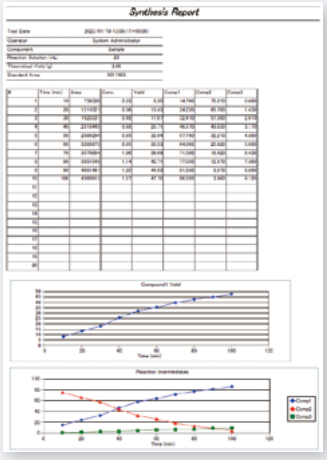
Analysis example ● 6 vessels, 1 analysis every 3 minutes ● Sampling time 10 minutes, 30 minutes, 60 minutes, 120 minutes

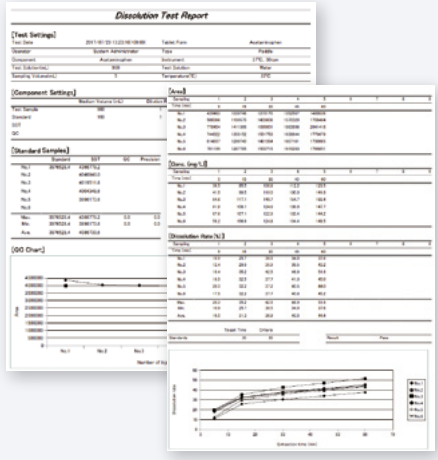


Online Confirmation of Analytical Results with Trend Plots

Using the multi-data report function, which can create and output reports in a spreadsheet-like format, the results for changes over time to the yield of the principal components of the synthesis, the creation of intermediate products, and the dilution rate in dilution testing can be output automatically.

Note: LabSolutions™ DB/CS is required to use the multi-data report function.





Shimadzu Corporation
www.shimadzu.com/an/