CombiFlash NextGen

Solutions for Organic Purification

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Teledyne Isco –
Innovators in Flash Chromatography

- First with automated flash chromatography
  - 1997 launched the CombiFlash Sg100
- First with multi-sample parallel and sequential systems
- Market leader in flash chromatography
  - 6th Generation of CombiFlash
  - 10,000 automated flash systems sold
- Complete line of chromatography
  - CombiFlash – flash chromatography
  - EZPrep – hybrid flash/prep chromatography
  - ACCQPrep – prep chromatography
- Same easy PeakTrak software

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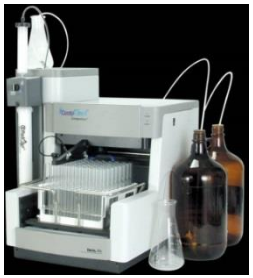
The Next in CombiFlash

Sg100

Sg100c



Companion

Rf

CombiFlash NextGen

- CombiFlash Rf launched 2007
- Over 5,000 sold globally

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Real differences

- PeakTrak Software

- Radically easy-to-use products
  - simplify operation
  - collapse learning curves
  - increase work efficiency
  - built in double checks
- Technology that ensures the separation is <u>successful the first time</u>

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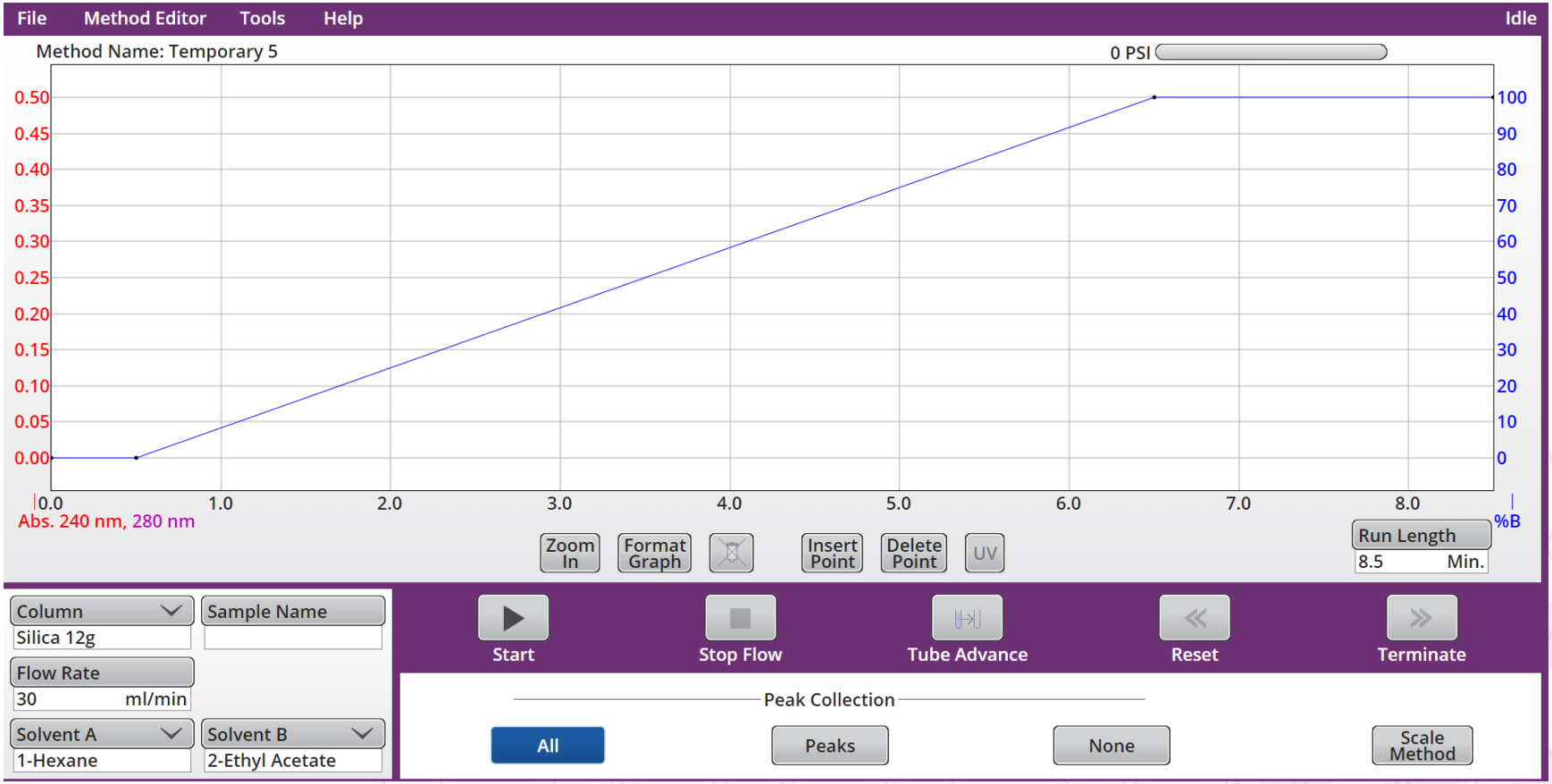
PeakTrak Main Screen

Everything on one screen



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What's New

- Enhanced feature options
- Up to 300 ml/min (NextGen 300+ and NextGen 300)
- Up to 300 psi (20 bar) (NextGen 300+)
- Capacitive touchscreen in choice of 12 or 15"
- Wider dynamic range UV detector
- New baseline correction
- Faster processer
- Able to fit 4 x 4 L bottles on top
- Improve "on instrument" rack access

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CombiFlash NextGen

CombiFlash NEXTGEN 300+

- CombiFlash Rf+ replacement
- System with standard options

CombiFlash NEXTGEN

- CombiFlash Rf150 replacement
- Basic system with limited options

CombiFlash NEXTGEN 300

- Custom configuration

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CombiFlash NextGen Family

	NextGen	NextGen300/+
Flow Rate	1-100 ml/min	1-300 ml/min
Pressure psi (bar)	150 (10.3)	300 (20)
Pumping	Single HPLC	Dual syringe
Detection	200-400 nm 200-800 nm ELSD MS	200-400 nm 200-800 nm ELSD MS
Injection Valve	No	Yes or No
Gradients	2 solvent binary	4 solvent binary with 3rd solvent modifier
Level Sensing	No	Yes or No
Air Purge	No	Yes or No
RFID/Level Sensing	No	Yes or No
User Interface	12”	12” or 15”

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Specs cont.

	NextGen	NextGen300/+
Sample Injection	Solid or liquid manual injection	Optional automated, self cleaning valve with injection through cartridge, syringe or directly on column
Solvent management	None	Optional active level sensing on inlet and waste
Dimensions (WxDxH)	14.1x17x26 in (36x43x66 cm)	
Weight	61 lb (27.7 kg) 74 lb (33.6 kg) w/ ELSD	
RFID on Column and Rack	No	Yes or No
Certification	CE, NRTL	CE, NRTL

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Options available for NextGen

- Vapor Sensor
- Hood enclosure
- Large column adaptor
- Detectors
  - Visible 200-800 nm
  - Evaporative light scattering
  - Mass spectroscopy

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Rack access

- Cut away right side
- Added lighting that is on when UV lamp is lit

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NextGen ELSD

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ELSD Specs

	Internal ELSD
Gas Inlet Pressure	60-70 psi
Gas Consumption	<2.5 SLPM
Spray Chamber Temperature	Setting range 10-60 °C
Drift Tube Temperate	Setting range 30-90 °C
Split Flow Rate	0.75 ml/min 5-30 ml/min Increases from 0.75 to 1.5 ml/min 30-60 ml/min 1.5 ml/min 60-300 ml/min
Sensitivity	High & Normal settings

ELSD detection is not recommended for flow rates below 5 ml/min

ELSD can be turned off for any runs below this recommendation.

-Note flash columns ≥ 4 grams are optimal over 15 ml/min.

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Two Modes of Operation

- Normal Sensitivity
  - Set to ½ of Lumen sensitivity
  - Gain default set to 2X
    - Results in same peak magnitude as current response
    - Ability to lower the sensitivity for strong signals
- High Sensitivity
  - Set to 6X Lumen sensitivity
  - Ability to cut peaks of <5mg samples

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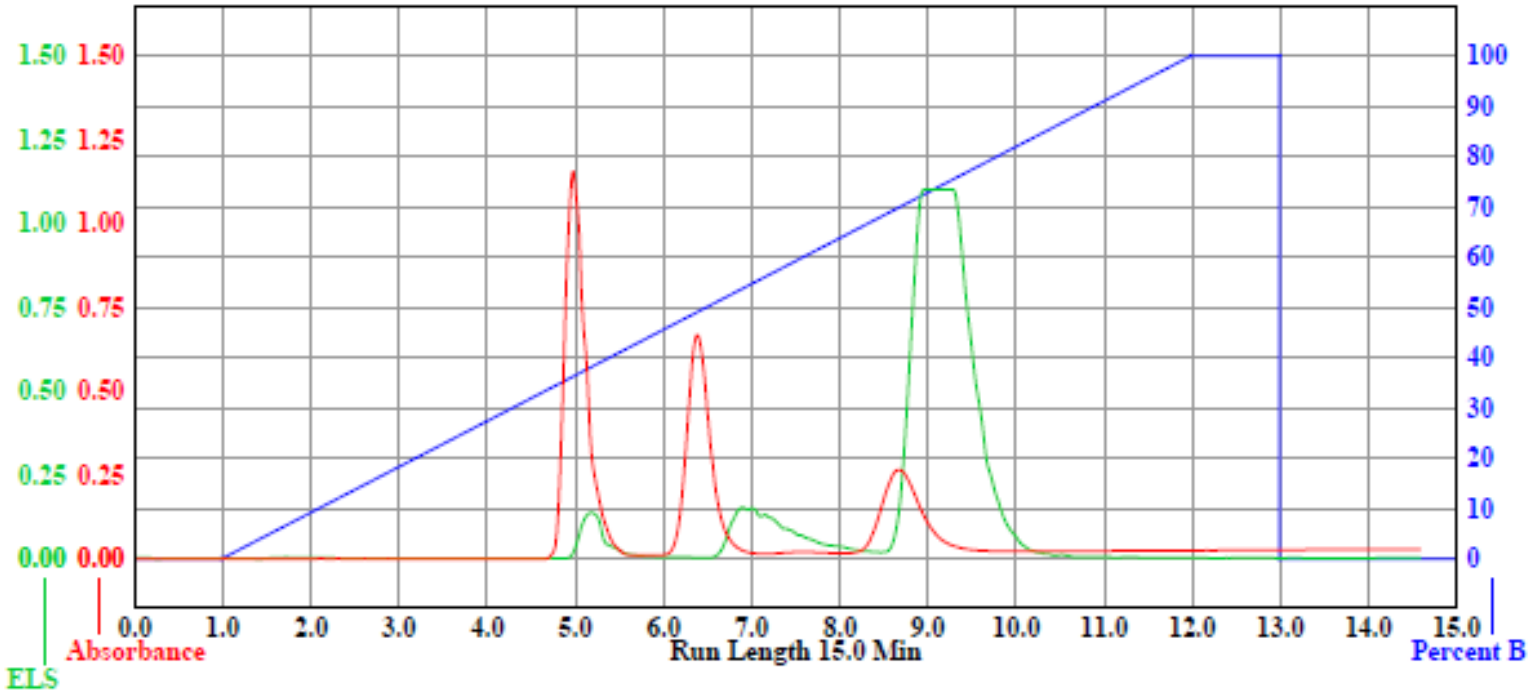
High Sensitivity X1



- 0.5gm of TMA.

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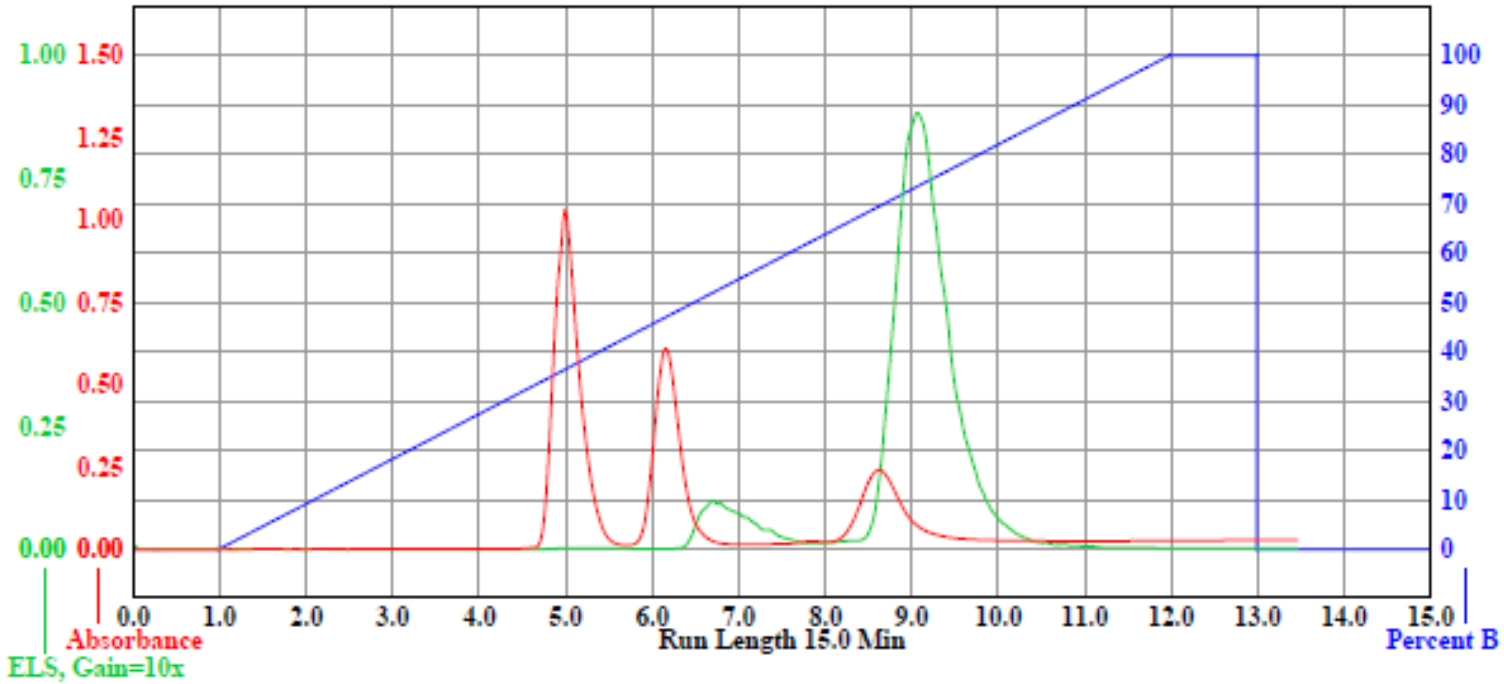
Normal Sensitivity X10



- 0.5gm of TMA.

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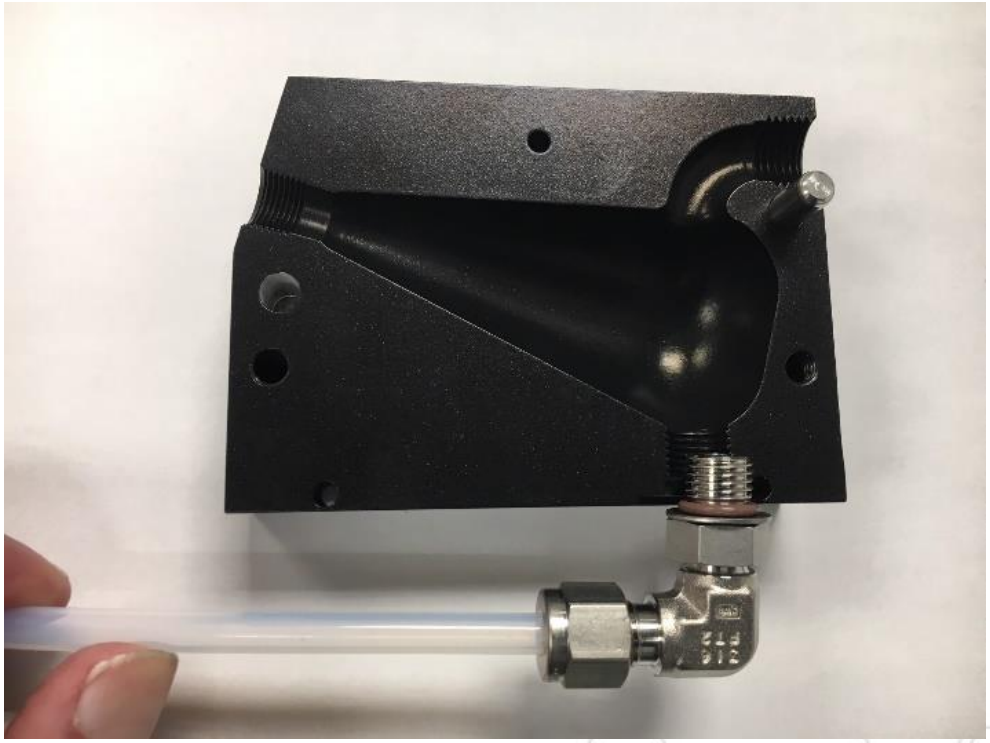
New ELSD Spray Chamber



- New spray chamber compatible with aqueous buffers
- Design is simple to clean
- Offers High and Normal sensitivity software selection

Integrated ELSD available on all CombiFlash models

- No additional lab space required

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NextGen UV

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Photo Diode Array Detector

- Variable Wavelength 200-400 nm
- Change Wavelength during the run
  - 2 wave length triggered collection
  - All wavelength triggered collection
- Purity Indicators
  - Dual Wavelength Monitoring
  - Purity Ratio

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Greater Dynamic Range

- New UV and UV-Vis detectors
  - Now up to 4 AU dynamic range
- 0.1mm fixed path length flow cell
  - Fixed allows you to count on the results
  - 0.1 mm keeps compounds on scale
  - 0.3, 0.5, 1 mm optional for increased sensitivity

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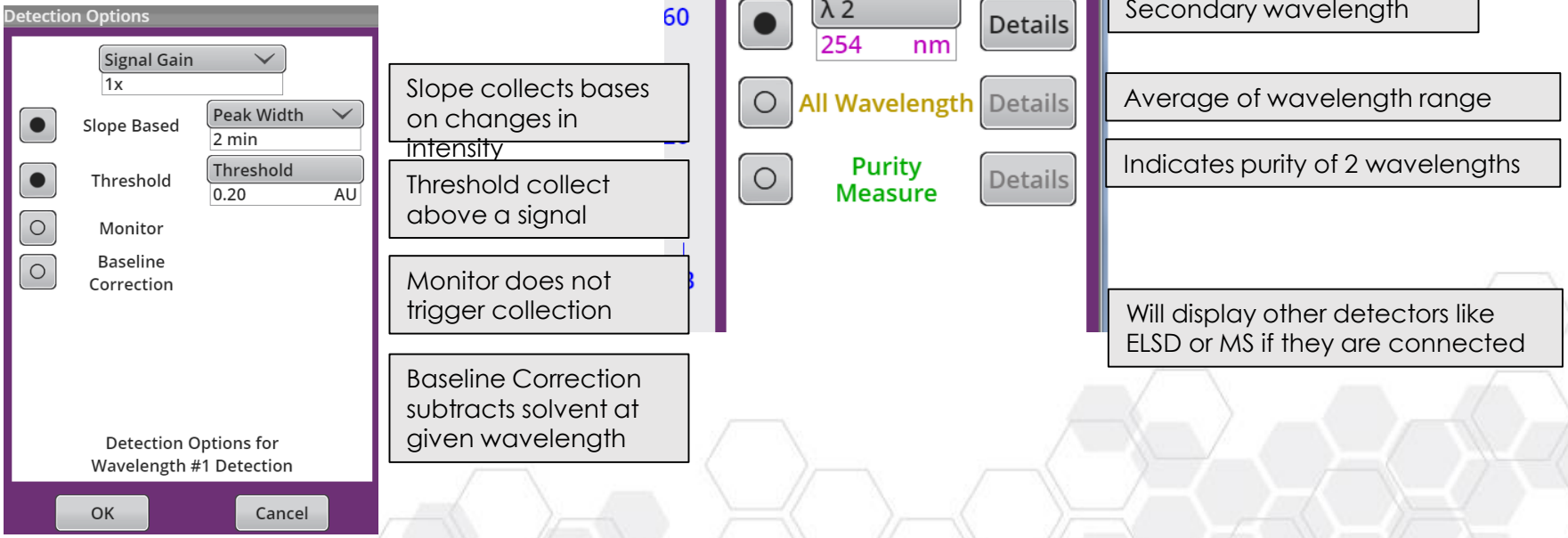
Detection Options

- Options allow for greatest sample recovery



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Baseline correction

- Solvent is subtracted from the base line
- See more of the compound
- Faster response time and increased recovery of compounds

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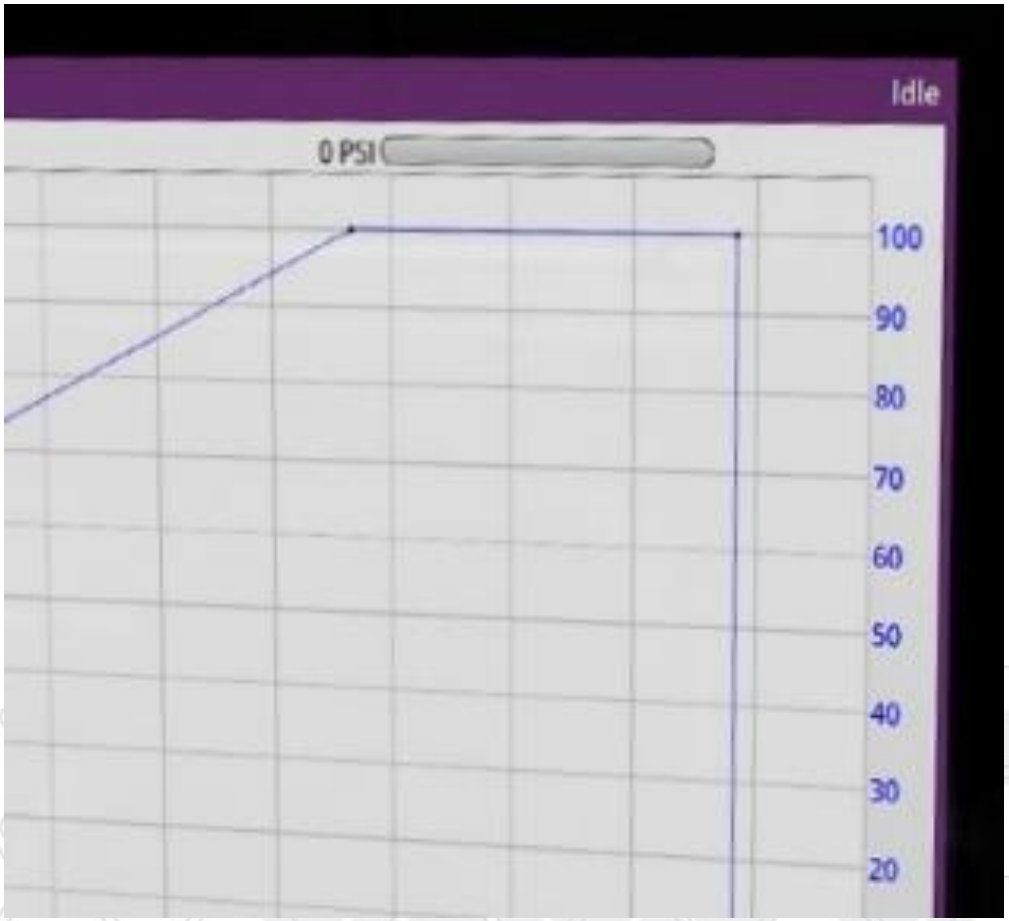
Speed

- New processor
- Updated OS
- Optimized operations by making several run in parallel
- Improved status reporting
- Audible alarms for errors



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NextGen MS

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CombiFlash PurIon MS

- Available on all NextGen models
- A fully integrated operation in PeakTrak software
  - Simple to operate
- Mass directed purification
- Compound verification
- UV/Vis and ELSD detection along with MS

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Purlon Module Specs

	"S" Model	"L" Model
Upgrade available	Rf+, Lumen, EZPrep, ACCQPrep, NextGen	
Dimensions (WxHxD)	11x26x22 in (28x66x56 cm) MS and FI 9x10x18 in (23x26x46 cm) Roughing Pump	
MS Detection	10-1200 Dalton 1 Dalton resolution	10-2000 Dalton 1 Dalton resolution
Ionization Mode	Positive and Negative Automatic Switching	
Capillary Cone Removal	Does not require vacuum shutdown	
Probes	ESI or APCI	
Sample injection	Direct Injection for MS Method Development	

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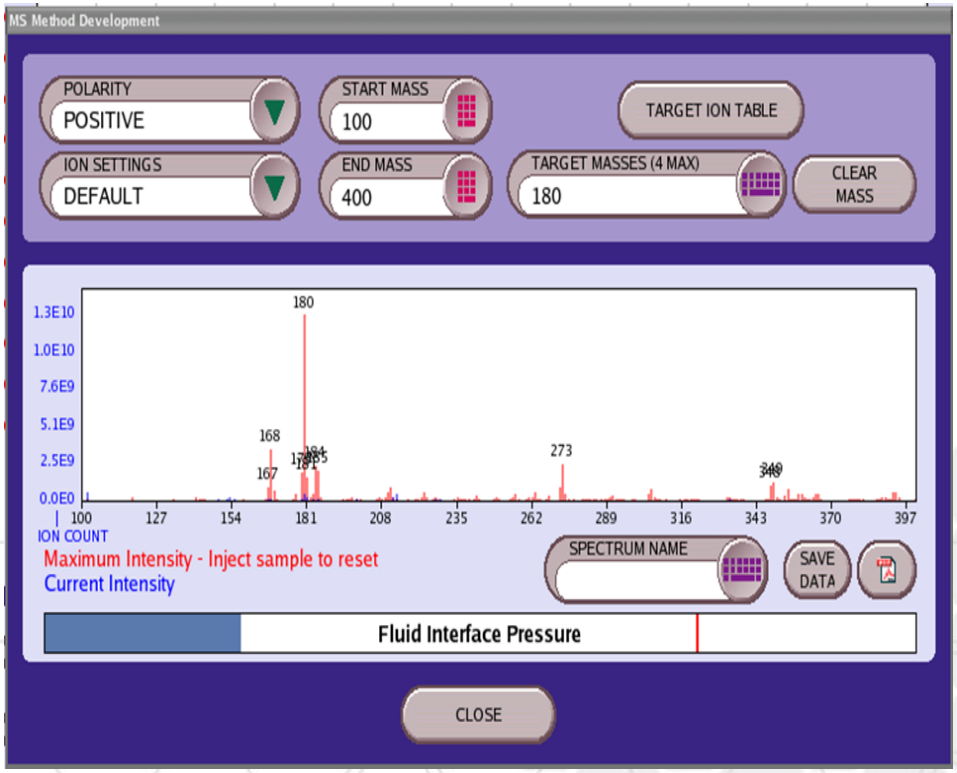
Benefits to the End User

- Determine presence of co-eluting impurity
  - Quickly determine that additional purification needed
- Collect only on target mass
  - Increase throughput
    - Shorten run times by terminating purification after target has eluted
    - Lower solvent consumption and costs
  - Eliminate the need for post-purification analysis
    - No more TLC
    - No post-run LC/MS
- Collect over a mass range
  - Eliminate unwanted masses
  - Useful in Natural Product Research

Terminate On Target

- Use MS Method Development screen
- Select desired masses



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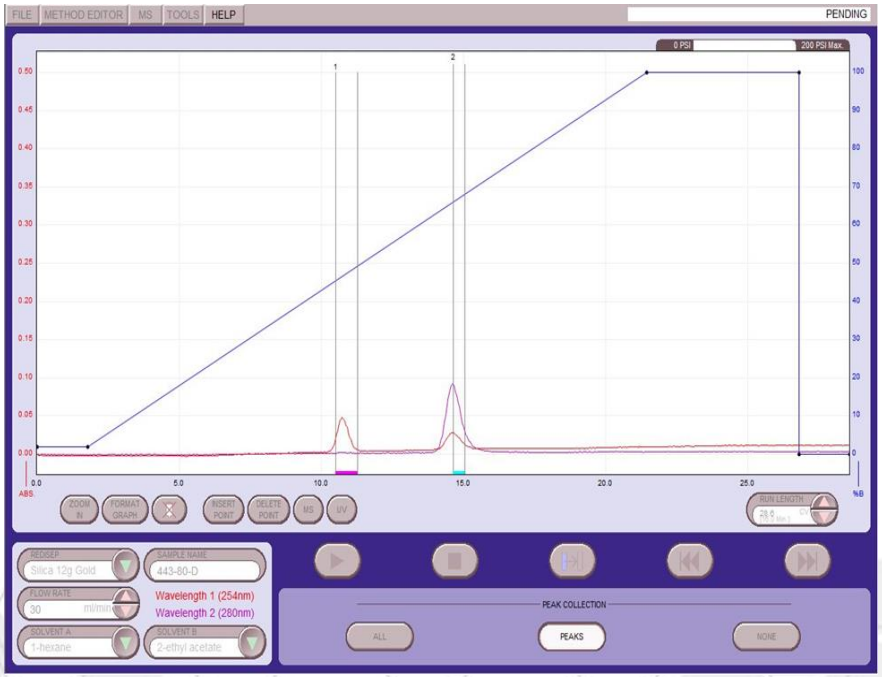
Sample run

- Weak UV absorbance
- Run entire program



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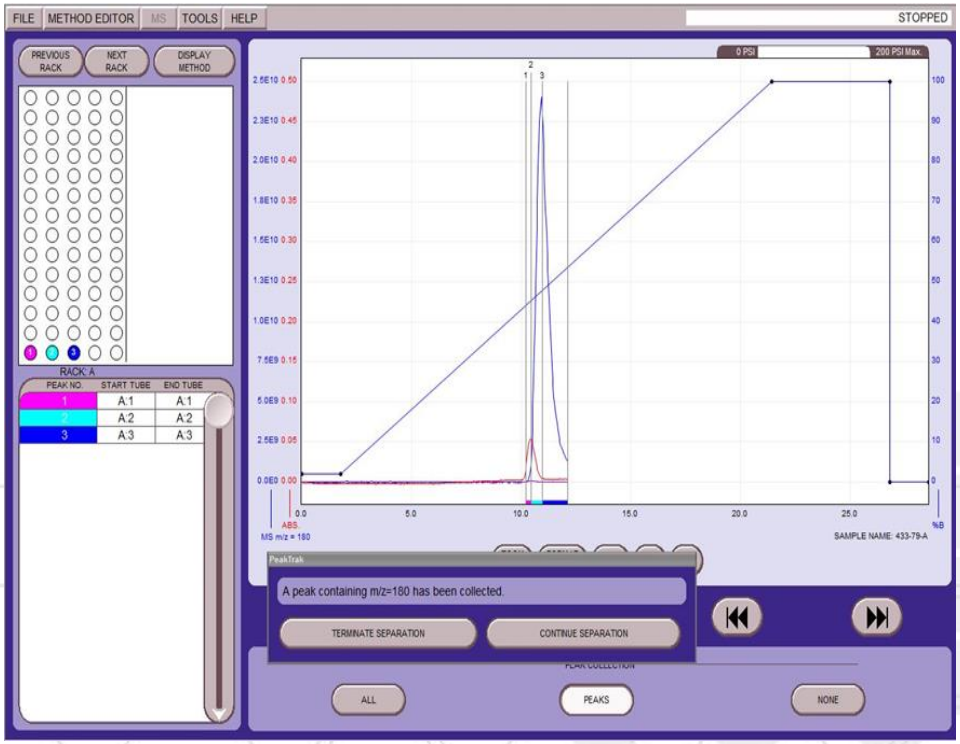
Terminate on Target

- Terminate run after peak with m/z=180 Da collected
- Collection with UV and MS
- Time and solvent saved



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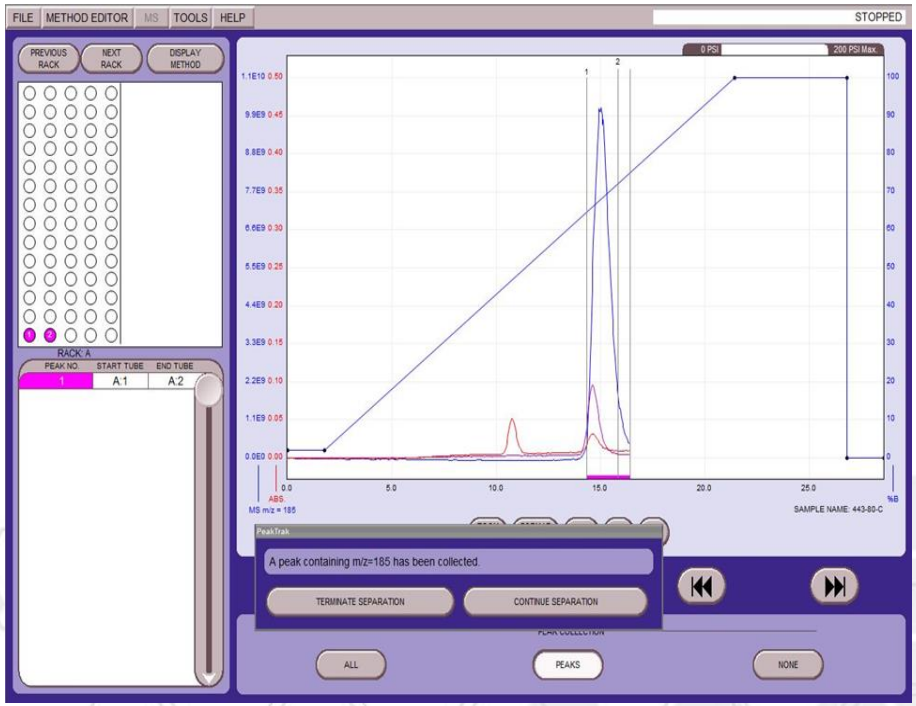
Terminate on Target

- Second peak collected, terminate on m/z = 185 Da
- Collection on SIM (single ion monitoring) 185 Da



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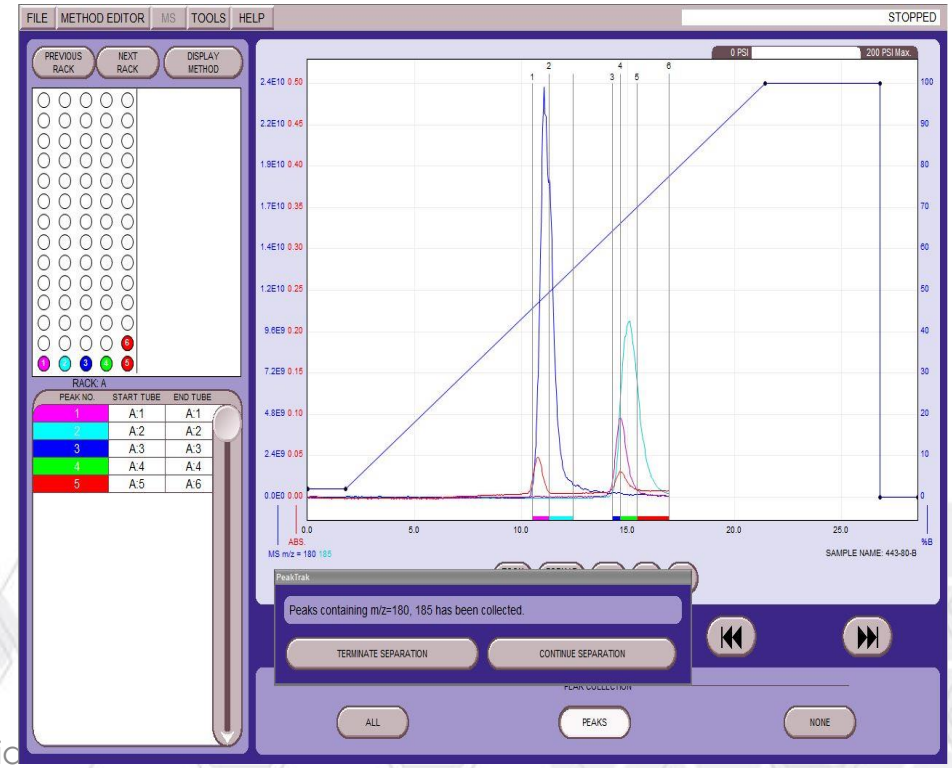
Terminate on target

- Terminate run after m/z 180 AND 185 Da collected.
- Up to 4 SIM or 3 SIM and 1 XIC (extracted ion current)



NextGen 300 and 300+ Pumps

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Sophisticated MPLC Pumping System

- Dual Piston Syringe Pumps
- High Pressure Gradient Formation
  - Better than 1% gradient accuracy
- Pumps Precisely and Accurately from 0 to 100%
  - Pumps Methylene Chloride/Methanol
  - Pumps from any solvent location
  - Pumps from 10 to 300 ml/min
  - Pumps up to 300 psi consistently
- Quiet

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4 Solvent Selection

- 4 solvent selection built into the system
  - Binary gradient
  - 3rd solvent modifier
- Can change solvents any time during the run
  - Chose any of 4 solvents
  - Program in solvent changes
- Solvent Monitor knows the solvent level
  - Never run a column dry or incorrect mixture
  - Never overfill a waste container

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NextGen Sample Injection

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Injection Options

- Equilibrate the column first
  - Best resolution results
- Direct Injection
- Liquid Injection
- Solid Sample Injection
  - Adjustable cap minimized gradient diffusion
  - Ability to evaporate off high polarity solvent to get accurate method development

Automatic Injection Valve

- Automatically loads sample after equilibration
- Ideal for solid samples
- Provides walk away automation
- Easy to maintain

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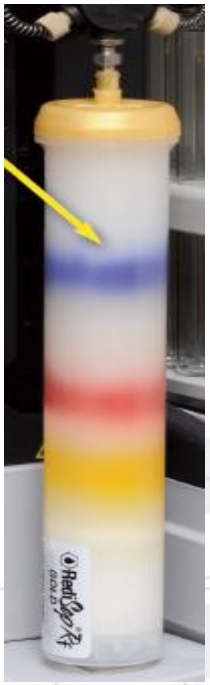
Benefits of Spherical Silica Gel

- **Higher bulk density** in Redisep GOLD columns (right) results in **reduced band broadening** and **sharper peaks**.

Standard Flash Column
(Irregular Silica)

RediSep Rf Gold
(Spherical Silica)



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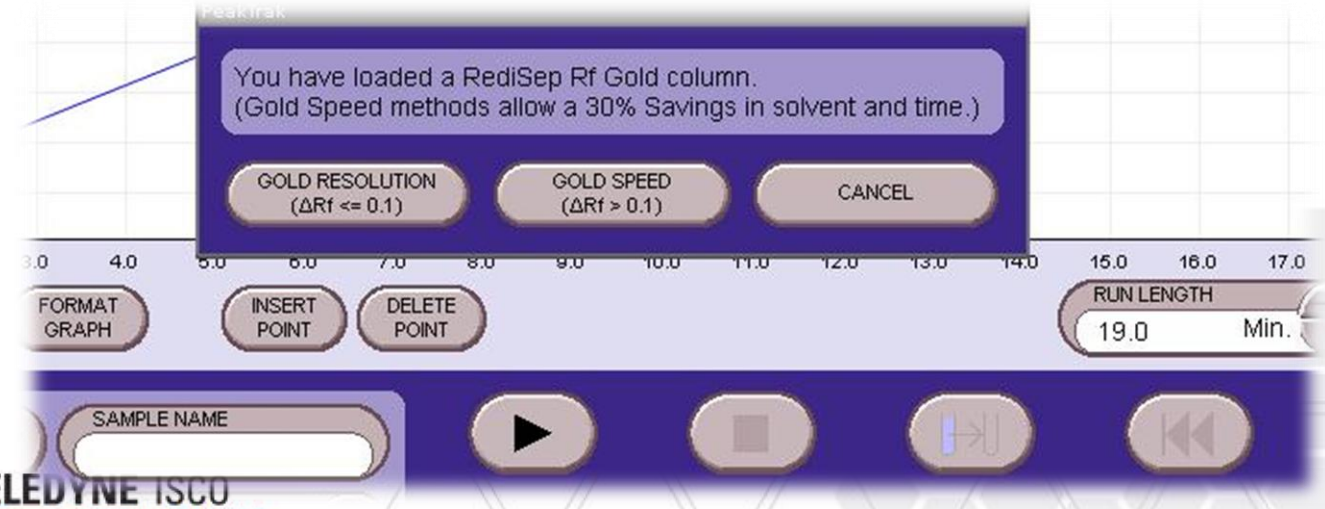
Seamless Automation with CombiFlash Rf

- With the CombiFlash Rf you get the option of running the RediSep Rf Gold columns under the best resolution conditions……
  - Ideal for compounds with ΔRf of ≤0.1



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Seamless Automation with CombiFlash Rf

- .....Or you can quickly purify your compounds using Gold Speed methods
  - Ideal for compounds with ΔRf of >0.1
  - Solution for silica sensitive compounds
  - Dramatic time and solvent savings

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Seamless Automation with CombiFlash NextGen

- .....Or you can load 2X up to 20%
  - Ideal for compounds with ΔRf of >0.1
  - Use smaller RediSep column
    - Saves time and solvent

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300 mL/min = More Capacity

- Run up to 150 gram material
  - Adaptor for 750 and 1500 gram columns
- Meet solvent safety limits for labs
  - Torrent at 1L/min available for process scale
- Built-in 80psi pressure bypass valve ensures safe operation.

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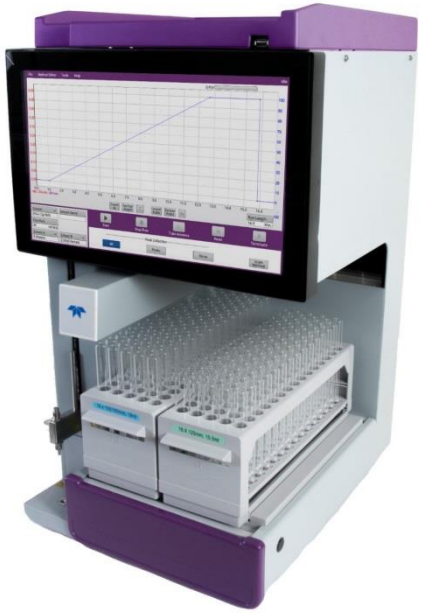
Chromatography Options

ACCQPrep HP125
Prep HPLC

EZPrep
Hybrid Prep/Flash LC



NextGen
Flash LC

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LC Comparisons

LC Method	Particle Size	Flow Rate Range	Back Pressure	Capacity
Flash	20-60 μ	>18 mL/min	10-50 PSI	mg-g
Prep HPLC	5-20 μ	3-100 mL/min	200 – 2000 PSI	10-500 mg
Analytical HPLC	5 u	1 mL/min	500- 6000 PSI	<5 mg
UHPLC	1.3-3 μ	0.1-0.5 mL/min	>6000 PSI	----

NextGen

EZPrep

ACCQPrep

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Thank You!

Guidelines & Tactics for Flash Chromatography

Free!!

www.teledyneisco.com/flashguid

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