





# FlowStar LB 513 HERM LB 500

Radioactivity flow detectors for HPLC

## Radioactivity flow detector for HPLC

Flow monitoring of radiolabelled compounds separated by chromatographic techniques has been established as one of the most powerful tools in many biochemistry related areas.

Radiolabelled compounds for drug and pesticide, metabolism or pharmacokinetic studies provide exceptional high sensitivity and specificity that is not available with mass detection, UV, fluorescence or conductivity measurements.

Berthold Technologies first produced a Radio HPLC detector nearly 50 years ago. Improvements have been made over the years in performance of the instrument resulting in the latest "state of the art" detector.

FlowStar represents the latest enhancements in flow detectors for Radio HPLC. It combines the latest technology such as a touch screen for easy operation and optimised detector for ultimate sensitivity.

FlowStar can be externally controlled by the RadioStar software. A control library to implement FlowStar into other software packages is available on request.

The instrument can also be operated in stand-alone mode and can be interfaced with all HPLC systems currently on the market.





#### FlowStar Features

- High sensitivity detection unit with random coincidence counting and luminescence subtraction for ultimate performance.
- Touch screen for easy operation and data display.
- Automatic cell type detection and parameter definition.
- Automatic HV shutdown for system safety.
- Built-in leak detection to prevent the measuring damage caused by aggressive liquids. The system shuts down automatically in the event of cell leakage.
- Integrated multi channel analyzer for improved optimisation of detector setup for each isotope and ease of troubleshooting.
- Onboard system performance tests with instrument based history function to ensure instrument performance validation.







- Multi user access control with security password to protect instrument from unauthorized use.
- Integrated A/D converter to record signals from external instruments (e.g. UV-detector) without using additional hardware.
- Dual analogue output interfaces FlowStar into an existing HPLC data system.
- USB or Ethernet (option) to control FlowStar externally using RadioStar or other HPLC control software (e.g. CHROMELEON).
- Extensive isotope library with predefined energy windows settings (¹⁴C, ³H, ³²P, ³³P, ³⁵S, ¹²⁵I, ¹¹¹In, ⁴9mTc).
- Capability to perform dual label measurements.
- Automated internal system performance tests using specific test cells.

### **Applications**

#### ■ Metabolic research

Many applications in metabolic research require the use of HPLC radioflow detectors. Labelled compound studies in urine or plasma for drug metabolism is a common application.

#### ■ Pesticide research

The detection of pesticide residues in plant research demands high sensitivity detectors. Using FlowStar even lowest concentrations of pesticides can be detected in plant extracts.

#### ■ Labelling of antibodies and proteins

When antibodies or proteins are labelled with radioactive isotopes, quality control is possible to ensure regulatory compliance using FlowStar.

## ■ Development, production and quality control of radio-chemicals

Manufacturers of radio-chemicals have to ensure the product quality for regulatory purposes. This is realised through HPLC separation and FlowStar.

### New Technologies

#### ■ Fast Liquid Chromatography (UPLC™)

A new generation of measuring cells are designed with regard to upcoming new technologies such as UPLC<sup>™</sup>. These new cells together with the latest HPLC technology open a new chapter in HPLC radioflow detection.

#### ■ LC/MS

Mass spectrometry in liquid chromatography is often used in pharmacokinetics. The use of a radioactivity flow detector improves compound identification and traceability. Special cells are available to provide sensitive detection of radio peaks in LC/MS.

#### ■ LC/NMR

Analytical techniques combining mass spectrometry and chromatography are well established laboratory tools. The combination of chromatography and NMR is an emerging technique fully supported by FlowStar.

#### ■ PET

High positron efficiency flow cells with low gamma response providing unique detection capabilities for PET isotope studies.

## Radioactivity flow detector for HPLC

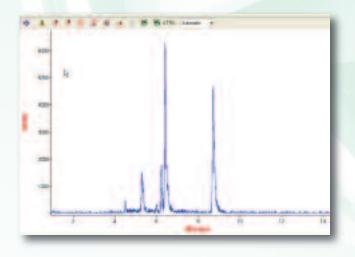
### Measuring cells

A wide range of highly sensitive measuring cells for all types of applications are available. All cells are equipped with "smart chip" to automatically call up all cell related parameters. This prevents the user from measuring with incorrect system parameters. In addition the system automatically shuts down, when a cell is removed from the detector to avoid damage.



## **Cell Types**

- Liquid Scintillation (admixture) Cells
- Solid Scintillator Cells
- Microbore Cells
- LC/MS Cells
- Fast LSC Cells (UPLC<sup>TM</sup>,UHPLC, RLC)
- Preparative SFC Cells
- Cherenkov Cells for High Energy Beta Emitters
- Gamma Isotopes and Positron Emitter (PET) Cells
- Special Iodine Cells
- GLP/GMP Validation Test Cells
- Customized Cells



### **Order Information**

Order IIII	ormation	
Standard Solid	d Cells	Order Number
YG-150-S5D	150µL	50158
YG-150-U5D	150µL	50157
YG-400-S5D	400µL	50138
YG-400-U5D	400µL	50137
YG-600-S5	600µL	50139
YG-600-U5	600µL	50136
Standard Adm	ixture Cells	
Z-100-5	100µL	50148
Z-200-5	200µL	50151
Z-500-5	500µL	50154
Z-1000-5	1000µL	50153
Microbore Soli		
YG-10-S6M	10µL	55215
YG-10-U6M	10µL	55216
YG-40-S6M	40µL	53262
YG-40-U6M	40µL	53263
YG-75-S6M	75µL	53259
YG-75-U6M	75μL	53261
Microbore Adn		
Z-100-6M	100µL	54672
Z-200-6M	200µL	54415
Z-500-6M	500µL	55196
Preparative Sc		
YG-50-S5P	50µL	50152
Gamma Cells		
MX-100-5	100µL	50456
MX-200-5	200µL	50457
MX-500-5	500µL	50458
	variable	80080
BGO-X 5,30	),150µL	51114
a.,		

Other scintillators or cell volumes on request.





## LB 513 FlowStar Cell Configuration Finder

LB 51.	3 FIOW	Star Cell Configuration	Finder
H-3	*Liquid-Cell Z-500	<b>Standard flow rate and activity</b> For lower flow rate or higher activity use Z-200 For higher flow rate or lower activity use Z-1000	<ul><li>General</li><li>Tritium labelled samples</li></ul>
	Solid-Cell YG-150	Standard flow rate and higher activities	<ul> <li>Preparative  Quality control samples samples (high-est activity)</li> <li>Purification samples</li> </ul>
	*Liquid-Cell Z-500	<b>Standard flow rate and activity</b> For lower flow rate or higher activity use Z-200 For higher flow rate or lower activity use Z-1000	■ Peptides, proteins, ■ Phenolic high molecular compounds weight lipids
C-14	Solid-Cell YG-150	<b>Standard flow rate and activity</b> Samples with sticking problems use YG-150 silanised For higher flow rate or lower activity use YG-150	<ul> <li>Urine, blood, liver, bile etc. extracts</li> <li>Plant and soil extracts</li> </ul> Metabolides of fungicides, herbicides and pesticides
S-35	Solid-Cell GT-200	Standard flow rate and activity For higher flow rate or lower activity use GT-400	All preparative samples which can be measured with solid cells.
P-33	Microbore- Solid-Cell YG-75	Flow rate less than 0.7 mL/min and normal activity For very low flow rate or higher activity use YG-40 or 10	<ul> <li>Urine, blood, liver, bile etc. extracts</li> <li>Plant and soil extracts</li> </ul> Metabolides of fungicides, herbicides and pesticides
	Solid-Prep Cell YG-50	For preparative samples with higher activity or flowrates higher than 3 mL/min	All preparative samples which can be measured with solid cells.
			*All liquid-cell applications require a liquid scintillation pump LB 5036
P-32	Solid-Cell YG-150	Sometimes it could be better to measure with standard cells, depending on the application	MATERIAL AND
	Cerenkov- Cell Z-500	Standard flow rate and higher activity	100
J-125	Cell J-XXX	For all I-125 applications Cell volume can be varied, depending on the activity	
OY	Cell BGO-X	For all gamma applications Cell volume can be varied (5,30 or 150 $\mu$ L), depending on the activity	
PET	Cell MX-100	For all PET isotopes with extremely low background Selectable cell volume (100 or 200 $\mu$ L, other volumes on request), depending on the activity	
		3	

## Radioactivity flow detector for HPLC

#### Solid scintillation cell

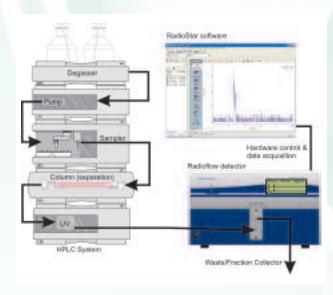
These cells consist of a very thin teflon hose filled with fine scintillator grains. The cells have been specially designed to withstand backpressure due to eluate viscosity and flow rate. The YG cells offer exceptional efficiency yields and are very inert. Surface treated (YG-S type) cells are also available to minimise memory effects seen when analyses stick to the scintillator.

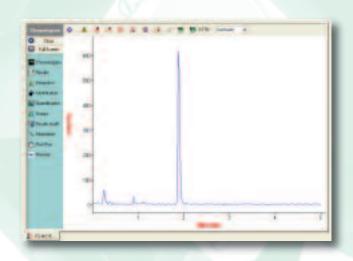
#### Microbore Cells

Microbore cells are designed to fulfill the demands of the microbore technology. They have lower volumes and minimal dead volumes. This increases the peak quality and resolution dramatically.







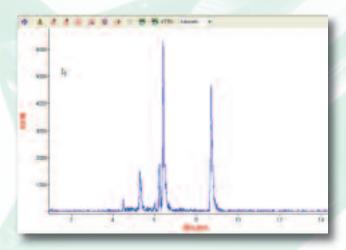


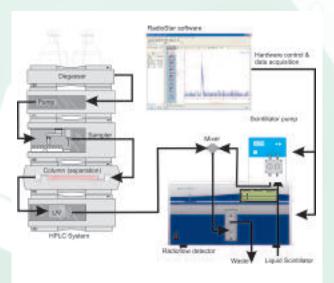




## Liquid scintillation cells

These cells are made for use with the homogeneous method. Liquid scintillator is added externally using a scintillation pump. The benefits of the homogeneous method are improved peak shape, best signal to noise ratio and no sticking problems. In addition it makes tritium measurements possible with highest efficiency. Liquid scintillation cells are available for all applications including standard HPLC, LC/MS microbore and UPLC $^{\text{TM}}$  applications.





#### Gamma Cells

The BGO-X cell is a specific measuring cell for all gamma isotopes. It consists of a 40 mm BGO crystal offering a high efficiency even for higher energy isotopes. A selection of different cartridges is available to cover a wide range of volumes.

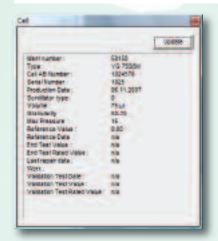
An optimized cell especially for \$^{125}I\$ offers best efficiency while having an extra low background.

The MX cell is specially designed to measure all types of PET isotopes such as <sup>18</sup>F. This unique design offers highest positron efficiency with extremely low background, even in high ambient gamma environments, resulting in unsurpassed signal to noise ratio and peak resolution.



#### Typical background for measuring cells:

Solid Cells (YG)	12-15cpm
Liquid Cells (Z)	5-7cpm
MX Cells	6-10 cpm
BGO-X Cells	90-120 cpm



## Radioactivity flow detector for HPLC

#### Test Cells

Several test cells are available to perform periodic system performance tests. These cells have been developed with regard to GLP/GMP compliance to guarantee a continuous system performance.

Specific validation functions are implemented in the instrument firmware to check the system performance using the test cells. Since all required parameters are already stored in the test cell "smart chip", these tests run automatically.

All results are saved in the instruments memory for further inspection. Inspection intervals can be assigned to automatically remind the user to run a system performance test.



### Static Mixer

Mixing the eluate with the liquid scintillator is one of the key issues in radio HPLC. If mixing is not optimal the results can be compromised. To improve the mixing a static mixer is available. The mixer consists of a solid housing combining a T-piece and a housing for a mixing cartridge. Two cartridges are available with a dead volume of  $50\mu L$  or  $150\mu L$ .



### Splitters and waste valve

Splitting of the eluate before mixing with scintillator is achieved by using valveless splitters, allowing part of the eluate to be diverted to a fraction collector. As only part of the eluate is radioactive, a waste valve diverts the radioactive peak to a fraction collector and the non radioactive waste to a low activity waste container.



## The Scintillator Pump

For admixture applications, where a liquid scintillator is continuously mixed with the column eluate, a mixing pump is required. The pump is separated from the main detector to eliminate the possibility of scintillator leaking into the detector and associated electronics. It is also possible to split the eluate stream prior to mixing.

The pump is completely controlled by the FlowStar ensuring the flow rates start and stop signals are handled automatically. In addition the FlowStar uses a specific ramp function. The wide flow rate range (0.001-10mL/min) offers many applications without exchanging the pump head.





## Flow Plus Liquid Scintillator

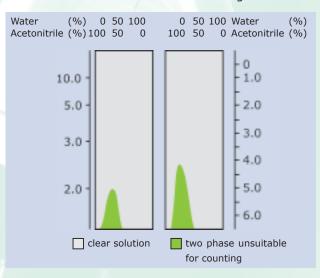
Flow Plus has been formulated to meet the special requirements of radio HPLC and in particular the counting of solvent/water gradients when using a Z-cell of the FlowStar. Flow Plus prevents the formation of gels or high viscosity liquid stream. In addition to solvent/water gradients Flow Plus formulation is balanced for water and lower ionic strength aqueous solutions.

- Low viscosity, non-gelling
- Suitable for solvent/water gradients
- Buffer gradient capability for HPLC



## **Applications**

The formulation of Flow Plus is based on the requirement for counting aqueous/solvent gradients from 100% water to 100% solvent at high sample to scintillator ratios in flow cell applications. Flow Plus is also recommended for water and dilute aqueous solutions and buffers. Flow Plus can be used in vials as well as in flow counting.



### Flow Safe 2 Liquid Scintillator

Flow Safe 2 is a scintillation cocktail for use in flow counting, especially in combination with Z-cells. It comprises selected solvents and surfactants chosen to give rapid mixing with eluates, high counting efficiency and to be non toxic, non flammable and of low odour.

Non-toxic solvent

- High flash point (105°C)
- Rapid mixing
- Compatible with polar solvents
- Low odour



Sample Ratio Capacity		
Water	2:1	33%
Acetonitrile	1:1	100%
Methanol	1:1	100%
Sodium chloride 0.15M	2:1	40%
Potassium phosphate 0.2M	3:1	33%
Ammonium formate 2M	3:1	25%
Acetonitrile 50% water 50%	2:1	33%
Methanol 50% water 50%	3:1	33%
Acetonitrile 50% 0.05M		
K2HPO4 50%	2:1	40%

Sample			
Water	23%	21%	19%
Acetonitrile 50% 0.05M			
K2HPO4 50%	20%	18%	16%
Methanol 50% water 50%	20%	19%	11%
Sodium chloride 0.15M	21%	20%	-
Ammonium formate 2M	-	21%	-

Order Information	Order Number
Flow Plus (2 x 5L)	43036
Flow Safe 2 (2 x 5L)	43037

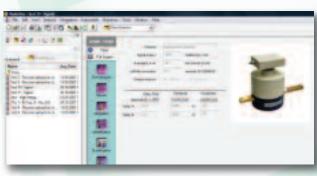
## HERM LB 500

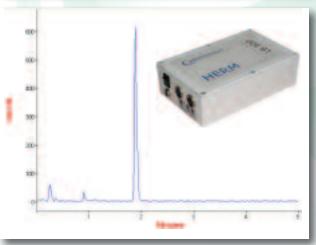
## High Energy Radio Monitor

#### HERM LB 500

The HERM is an additional product in the detector range of Berthold Technologies for flow through measurements. The high sensivity Sodium lodine Crystal enables, in conjunction with a lead shielding and Twin-Cell-Changer, to detect different Gamma emitting nuclides.

- Detection of Gamma nuclides for flow analysis
- High sensitivity NaI counter including optimised lead shielding and Twin-Cell-changer
- Control and evaluation software providing easy connection to external evaluation systems
- Choice of analogue output (0-1 V, sampling rate 10 Hz) or digital via RS232 PC connection
- Stand alone mode (setup via terminal program) or connection to PC
- Microprocessor controlled with internal Flash RAM for simple upgrade and fast data processing
- Luminescence flow through detection (optional)







## Key features

- Half life correction and background subtraction are available via digital connection.
- The HERM permits a setting of threshold values to control external devices (also time-delayed) such as separation valves or fraction collectors.
- For validating (GLP) and function control of HERM a built-in oscillator is present as a reference source.
- In connection with the Berthold WinTerm software a simple data transfer via terminal function and/or via OLE transport to EXCEL is possible.
- A special RadioStar software package driver for complete parameter control and digital data acquisition is available.

## **Applications**

■ Development, production and quality control of radio-labelled pharmaceuticals

Manufacturers of radio-chemicals especially for Positron Emission Tomography (PET) have to ensure the product quality for regulatory purposes. This is realised through HPLC separation and HERM connected.

■ Quality control in isotope production

The quality of radio isotopes must be monitored at the production site. HERM is used to measure the isotopes in quality control departments.





### RadioStar

RadioStar combines the ability to run sophisticated measurements with the ease of a simple user interface.

Acquisition and integration of the chromatogram is supported by RadioStar with the added benefit of a unique RadioStar menu bar and help wizard with short video clips explaining each function.

RadioStar has been designed especially for radio HPLC applications, controlling instruments or evaluating and integrating measured data.

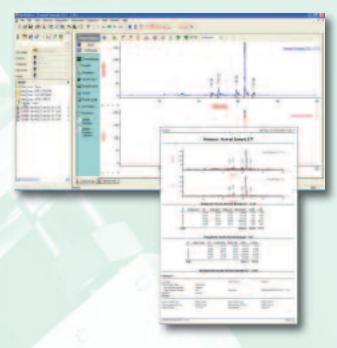
The flexible context definition allows user specific definitions of data structures.

Recording the four different measuring channels, provides the user with a high degree of flexibility in their applications, such as radioactive and non radioactive measurements.

A built-in half live correction function enables applications with short lived isotopes to be processed online.

Individually designed reports are generated through the built-in report generator. This allows user specific layouts to comply with company specific reporting rules.

A powerful conversion engine recalculates the raw data into different units such as cpm, dpm, Bq etc. The export to standard HPLC data formats (ANDI etc.) is realised through sophisticated export features.



## **Key Features**

- Digital acquisition of radio channels.
- 21CFR part 11 compliance.
- Analogue signal acquisition through built-in FlowStar A/D converters or external devices to integrate other HPLC detectors such as UV, RI or fluorescence detectors.
- Batch integration functions to handle large sample throughput.



## FlowStar LB 513 & HERM LB 500

# Technical Specification and Order Information

#### FlowStar LB 513

Detection Unit	State-of-the-art ultra sensitive PMT detection system with random coincidence counting and luminescence subtraction
Display	Graphical touch screen with
ызыцу	320 x 240 pixel resolution
Communication	USB port (B-Type)
Inputs	Start, Stop and Ready signals
Tiputs	
	(TTL) 2 analogue inputs (24 bit)
	variable voltage (bipolar)
Outputs	Scintillator pump control
	2 analogue signal outputs 0-1 V
	(3 times oversampling)
	waste valve and fraction collector
	control output (relay)
MCA	1024 channel analyzer for system
	testing and calibration
Software	built-in software operated with
	touch screen or external control and
	evaluation via RadioStar software
Power supply	90-265 VAC, 50/60 Hz
Temp. range	Storage: 5-40 °C
, 5	Operation: 15-35 °C
Humidity	10-90% non condensing
Dimensions	420 x 210 x 390 mm (WxHxD)
Weight	22 kg
	-

Order Information	Order Number
FlowStar Detector LB 513	47953
RadioStar software for LB 513	36627-06
RadioStar software process version	
(evaluation only)	36627-03
Scintillator pump LB 5036	53748
Static mixer housing	33762
Cartridge 50µL for static mixer	33763
Cartridge 150µL for static mixer	33764
Static micro mixer housing	on request
Micro mixer cartridge 25 μL	on request
Micro mixer cartridge 10 μL	on request
Waste valve, complete	15681
Analytical splitters AS-X	
complete set (15%, 25%, 33%, 50%	6) 24822
Test cell H³ for system test	49927
Test cell C <sup>14</sup> for system test	49926
Test cell background for system test	51086
Test cell set (H <sup>3</sup> , C <sup>14</sup> and background	51087

#### HERM LB 500

Detection Unit	State-of-the-art ultra sensitive PMT coupled NaI detector	
Communication	RS-232 serial port	
Inputs	Start signal (TTL)	
inputs	Signal input (TTL)	
Outputs	TTL signal output	
Outputs	-	uto 0 1 \/
	analogue signal outp	
-	2 programmable rela	· · · · · · · · · · · · · · · · · · ·
Power supply	6 V (via wide range m	
Weight	electronics box: 1 kg	
	detector: 1 kg	
	shielding: 25 kg	
Dimensions	electronics: 210 x 60	x 120 mm
(WxHxD)	detector: 140 x 180 x 100 mm	
	shielding: 150 x 350 x 180 mm	
Order Information Order Number		
HERM LB 500 with NaI detector		35144-01
HERM LB 500 NaI detector only 810		81083
HERM LB 500 electronics unit 35144		
HERM LB 500 luminescence detector on request		
		36627-08
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