

# Simulated Moving Bed Chromatography (SMB)

**KNAUER**



# *SMB*

*The next step in chromatography*

# Simulated Moving Bed Chromatography (SMB)

## SMB Pilot Unit CSEP® C9116

**System for the production of up to 100 kg of pure compounds per year!**

The SMB System CSEP® C9116 is used for the extraction of pure substances in a semi-preparative scale. Similar to the "big" system, CSEP® C9812, the pilot facility enables continuous operation with high efficiency.

The system operates with a thermostat and can hold up to 16 SMB columns of equal type. The patented Multi-Port Valve with 64 ports guarantees a compact design that maintains an incredibly small total dead volume.

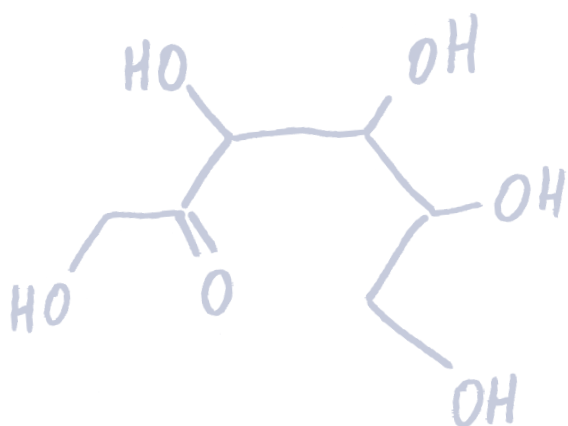
The continuous product feed covers almost all of the surface of the stationary phase. Thus, the extraction yields maximum results.

There is no need for small particle sizes or large plate numbers. This keeps the column packing inexpensive!

Software for process simulation and optimization is available. Refer to next page for more details.

### Important

Due to the individual requirements, columns are excluded from the standard delivery. We will gladly suggest appropriate columns and packing materials to suit your particular needs.



Order No.	Article	Quantity
A28701	<b>SMB Pilot Unit CSEP® C9116</b>	1
	Consisting of:	
	WellChrom HPLC Pump K-501 with 10 ml or 50 ml pump head, inert, with ceramic inlays, stainless steel	1
	64-Port Multi-Function Valve, Hastelloy (stainless steel), 1/16" connectors, pressure stability 80 bar, for up to 16 equal SMB columns with either max. length of 300 mm, max. OD 22 mm or max. weight of 20 kg	4
	Column Thermostat (up to 60°C)	1
	Rack on castors, 30 x 35 cm	1
	Set of capillaries, fittings, and accessories (1/16")	1
	PC including pre-configured ValveChrom software	1

# SMB Production Unit CSEP® C9812

**System for the production of up to 1,000 kg of pure compounds per year!**

The SMB System CSEP® C9812 stands out for its continuous operation and high productivity. The continuous delivery of feed and desorbent enables the permanent extraction of two fractions at high concentrations.

The thermostated system can hold up to 12 SMB columns of similar type in terms of column packing, column dimensions etc. The patented Multi-Port Valve with its 48 ports plays the role of the "heart" in the system. The compact design of CSEP® C9812 dramatically reduces the total dead volume compared to other available SMB concepts.

The product covers almost the complete surface of the stationary phase. Thus, the system is highly efficient. When peak recycling is practiced, one can save up to 90% of eluent consumption! With column packing another savings of up to 80% can be achieved.

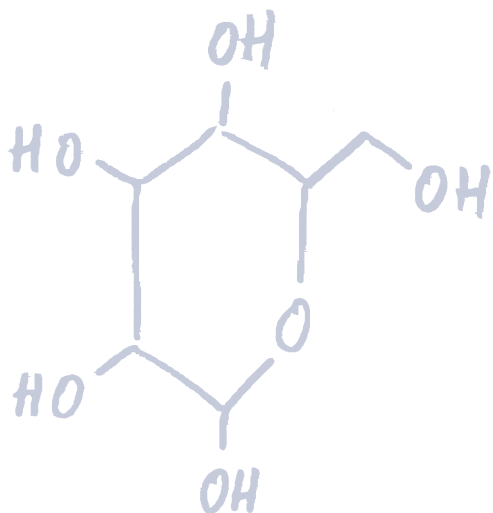
How? It's simple:

There is no need for small particle sizes or large plate numbers. This keeps the column packing inexpensive!

Software for process simulation and optimization is available. Refer to next page for more details.

## Important

Due to the individual requirements, columns are excluded from the standard delivery. We will gladly suggest appropriate columns and packing materials to suit your particular needs.



Order No.	Article	Quantity
A28706	<b>SMB Production Unit CSEP® C9812</b>	1
	Consisting of:	
	WellChrom Preparative Pump K-1800, with 100 ml, 250 ml, or 1,000 ml pump head, stainless steel	1
	48-Port Multi-Function Valve, Hastelloy, 1/8" connectors, pressure stability of 50 bar, for up to 12 equal SMB columns with either max. length of 1,000 mm or max. weight of 120 kg	4
	Column Thermostat (up to 60°C)	1
	Rack on castors 50x50 cm	1
	Set of capillaries, fittings, and accessories (1/8")	1
	PC including pre-configured ValveChrom software	1

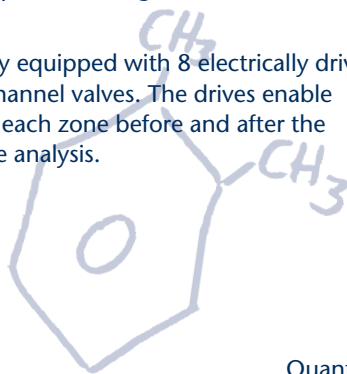
# Pilot SMB System CSEP® C9116S

**System for the production of up to 100 kg of pure substance extraction each year!**

The Pilot SMB System CSEP® C9116S, a modification of the CSEP® C9116 system, is designed for the extraction of pure substances out of a two component mixture in the semi-preparative range.

The system works thermostatically and can be operated with up to 16 SMB separating columns of the same type. The patented multifunctional valve drastically reduces the dead volume and provides for the compact design. The system is very efficient due to the continuously fed product being distributed over the entire stationary phase.

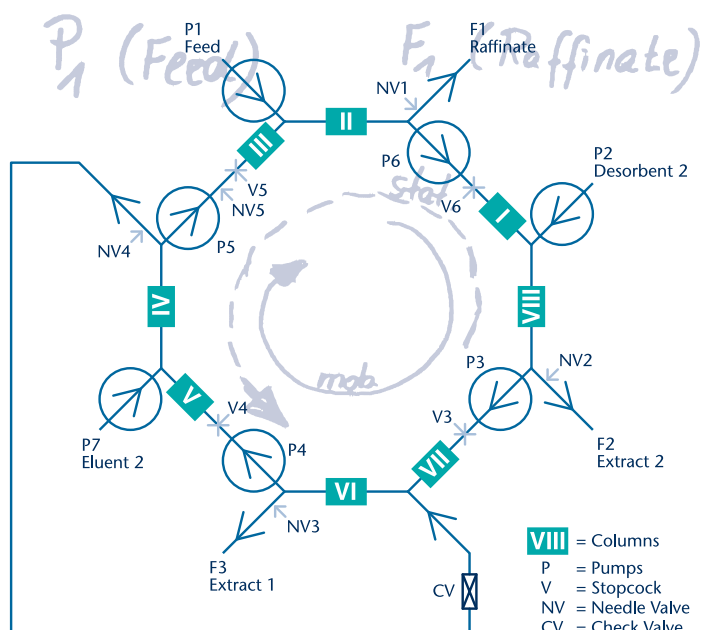
CSEP® C9116S is additionally equipped with 8 electrically driven valve drives with 6-port/3-channel valves. The drives enable samples to be withdrawn in each zone before and after the separation column for offline analysis.



Order No.	Article	Quantity
A28707	<b>Pilot SMB System CSEP® 9116S</b> with 8 WellChrom electrical valve drives K-6, with a 6-Port/3-Channel Switching Valve (A1484), maximum 16 columns, up to 80 bar, 1/16"	1



# Pilot SMB System CSEP® C91168



**The System is optimized for three component separation.**

The Pilot SMB System CSEP® C91168, a modification of the CSEP® C9116 system, is designed for the extraction of pure substances out of a three component mixture in the semi-preparative range.

The system works thermostatically and can be operated with up to 16 SMB separating columns of the same type. The patented multifunctional valve drastically reduces the dead volume and provides for the compact design. CSEP® C91168 has been modified so that an 8 zone SMB process can be less expensively simulated in comparison to the classical 4 zone. Therefore, three component separations are possible with only one SMB system.

Order No.	Article	Quantity
A28708	<b>Pilot SMB System CSEP® C91168</b> eight zone configuration, for maximum 16 columns, up to 80 bar, 1/16"	1

# Simulated Moving Bed Chromatographie (SMB)

## SMB\_Guide® for Windows

With the design and simulation software, SMB\_Guide® for Windows, it is possible to simulate and optimize an isocratic separation and SMB process PC based within the shortest amount of time. The calculations refer to the rapid and established algorithms from Prof. Guiochon (University of Tennessee, USA) and Prof. Seidel-Morgenstern (Max-Planck-Institute for dynamically complex technical systems, Germany). The calculations have made the long and empirical series of tests finally expendable.

The SMB\_Guide® helps you to thoroughly understand the inner process of a SMB system. This is due to the clear representation of the internal and external concentration profiles in the software.

It is only necessary to specify the system configuration and the feed current, the SMB\_Guide® will calculate all of the process parameters that have to be set. Then analyze the desired SMB configurations in reference to the number of columns, the dimensions, as well as distribution in the various SMB separation zones.

The optional eluent recycling or a solid regeneration are more features adding further flexibility to the SMB\_Guide®. Another helpful characteristic is the outstanding visual aid (i.e. assists in employee training).

The SMB\_Guide® will help you to get your SMB system up and running in the shortest amount of time!

## IsothermFit® for Windows

Since knowledge of the thermodynamic functions is the most essential prerequisite for optimizing preparative separations, the determination of non-linear adsorption isotherms in high concentration ranges have been simplified with IsothermFit®.

The software is able to apply different measurement methods (i.e. ECP, perturbation method) and evaluates the parameters of various single and competitive isotherm equations to non-linear regression methods. The competitive behavior is described by extensions of the Langmuir equation such as linear isotherm, Langmuir isotherm, and bi-Langmuir isotherm; or by the theory of the ideal adsorbed solution (IAS).

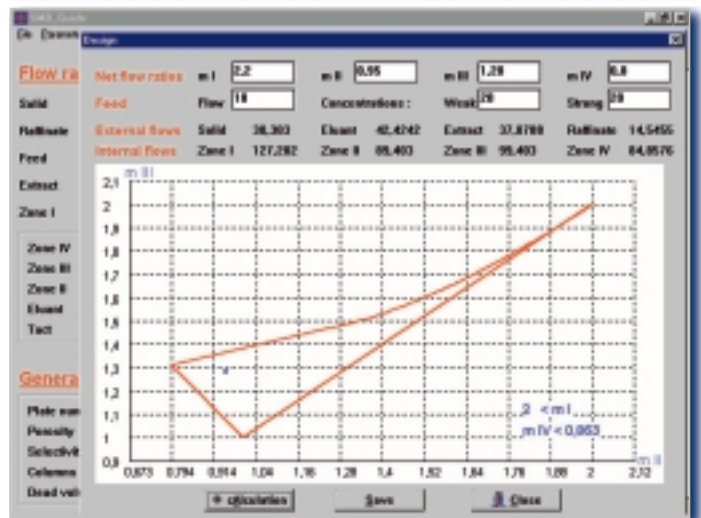
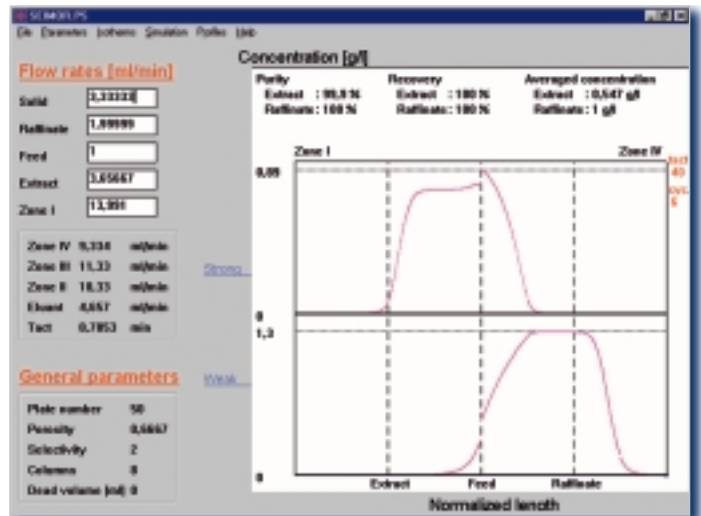
IsothermFit® supports the following four most suitable methods:

- Linear Isotherm Method (Retention Time Method)
- Adsorption Desorption Method (ADM)
- "Elution by a Characteristic Point" Method (ECP)
- Minor Disturbance Method (MDM, Perturbation Method)

The results are essential input parameters for the simulation of elution profiles, recycling chromatography, and for setting up SMB processes that can be simulated using the powerful ChromSim® and SMB\_Guide® software.

## ChromSim® for Windows

Over several years a detailed theoretical analysis of non-linear and preparative chromatography was performed by well known scientists such as Prof. Guiochon and his numerous co-workers. The presented theory has made the calculation of the migration concentration dependence velocities in chromatographic columns possible. ChromSim® reduces the experimental work



Screenshot taken from the SMB\_Guide® software

generally required to find optimal conditions such as flow rates or the proper injection amount.

The powerful ChromSim® software ...

- Reveals the consequences if chromatographic columns are overloaded
- Simulates how peak profiles and separation performance are affected after relevant parameters have been altered
- Implements various peak recycling modes with and without peak-sharing
- Calculates the cut times for fraction collection systems with respect to the predefined purity requirements
- Evaluates and compares the standard elution mode with other modes such as frontal chromatography

## Ordering information

Order No.	Article	Quantity
A2865	SMB_Guide® for Windows™. Software for simulation and optimization of SMB separations	1
A2867	IsothermFit® for Windows™ Software for determination of non-linear adsorption isotherms when working with high concentrations	1
A2866	ChromSim® for Windows™. Simulation software for peak recycling and fraction collection	1

## Why SMB?

Preparative chromatography (Simulated Moving Bed chromatography) is increasingly applied as a separation technique in the pharmaceutical industry, production of fine chemicals, and in the field of bioengineering. Simulated Moving Bed is a method in process chromatography that enables substance mixtures to be continuously separated and extracted in two fractions. By repeated use of the SMB process each partial fraction can be separated into a further fraction – up to binary substance mixtures. Typically, the SMB process is set up in advance for a two component mixture. Following this, both substances can be immediately extracted in pure form – up to 1,000 kg per year.

## Where can a SMB separation be used?

The SMB principle for continuous extraction of pure substances on a preparative scale is successfully used in several areas of chemistry and biochemistry. The yearly production of the offered systems is between 100 and 1,000 kg of pure substance.

Range of application	Separation and extraction of...
<b>Pharmaceutical chemistry</b>	Chiral compound (i.e. cis-trans phytol, steroids, peptides, antibiotics)
<b>Food chemistry</b>	Fatty acids, carbohydrate mixture (i.e. sucrose/molasses or fructose/glucose)
<b>Biochemistry</b>	Citric acid, phenylalanine
<b>Petrochemistry</b>	Cg-Hydrocarbon (i.e. xylene/toluene)

## When is a suitable time to set up a SMB process?

The extraction of pure substances (valuable substances) using a SMB system is offered after the required amount of a respective substance has been reached. Furthermore, the application of a SMB process is linked to the following prerequisites:

- Two-component mixture (binary mixture)
- Good solubility in the liquid phase
- It must be possible to carry out an isocratic separation
- Retention time of the substance must be under 20 min.
- Knowledge of the adsorption isotherms
- Selectivity of  $2.0 > d > 1.2$

## Advantages of SMB technology compared to classical batch chromatography

- The entire stationary phase is continuously covered with the mixture to be separated which produces a much higher productivity.
- A 90% reduction in the demand for solvent due to solvent recycling.
- High plate counts or particle sizes are no longer required, reducing packing material costs by 80%.
- Extract and raffinate are extracted in high concentration which make it easier to remove solvent.
- The patented multi-function valve enables an extremely small dead volume.

## Operation scheme for interpreting and carrying out a SMB separation

1. Determine the phase volume ratio or porosity between the stationary and mobile phase.
2. Determine the adsorption isotherms for each component based on the overload chromatogram from each component or the mixture.
3. Determine the isotherm parameters using the IsothermFit® software.
4. Definition of the process (hardware).
5. Simulation of the process and optimization of the interpretation using the SMB\_Guide® simulation software.
6. Carry out a continuous "SMB separation".
7. Optimize the productivity.

## Comparison between a SMB and a preparative HPLC system

Parameters	Preparative System	SMB System
Separation process	Batch method	Continuous, higher productivity
Stationary phase	Only effective to a fractional part	Maximum charge
Mobile phase	Higher consumption	90% less consumption by solvent recycling
Separation	Several components	2–3 components
Fractionation	Individual substances	Separation of a fraction from a mixture (can even be a mixture again)
Operating mode	Isocratic or gradient operation	Isocratic operation
Process simulation	Feasible	Feasible

## KNAUER SMB Systems "in use" – References

- Schering Plough Corp.**, New Jersey, USA (since 2002)
- Merck Rahway**, New Jersey, USA (since 2001)
- Dow Chemicals** Midland, Michigan, USA (since 2001)
- EISAI Research Institute**, Massachusetts, USA (since 2001)
- Pfizer**, Holland, Michigan, USA (since 2001)
- Wuxi University**, Wuxi, China (since 2000)
- Roche Diagnostics** Mannheim, Germany (since 1999)
- Max-Planck-Institut** Magdeburg, Germany (since 1999)
- Goedecke Parke Davis (Pfizer)** Freiburg, Germany (since 1998)

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