Ready to implement CIM® Monolith Technology

You can order CIMmultus™ Column and other CIM® products online at www.monoliths.com/product-listing or by contacting your local BIA Separations Sales representative.

Request a CIM® Technology Seminar?

To educate your entire organization about CIM® Technology and its capabilities in biomolecule purification, request a CIMinar™.
Just write to us at sales@biaseparations.com to begin solving your purification challenges.

For any additional information please contact us:

EUROPE

BIA Separations d. o. o.
Mirce 21
5270 Ajdovščina, Slovenia, EU
Tel.: +386 59 699 500
Fax: +386 59 699 599
sales@biaseparations.com
orders@monoliths.com
www.biaseparations.com

USA

BIA Separations, Inc.
1000 N. West St. Suite 1200
Wilmington, DE 19801, USA
Phone: +1 888 520 4CIM (4246)
Fax: +1 302 861 0362
sales@biaseparations.com
usorders@monoliths.com
tech-support@monoliths.com
www.biaseparations.com

Publication #: CIMmultus1405

BIA separations
Leaders in Monolith Chromatography

CIM Convective Interaction Media®

CIMmultus™ Disposable Monolithic Column

www.biaseparations.com

BIA Separations, an ISO-9001 certified company.

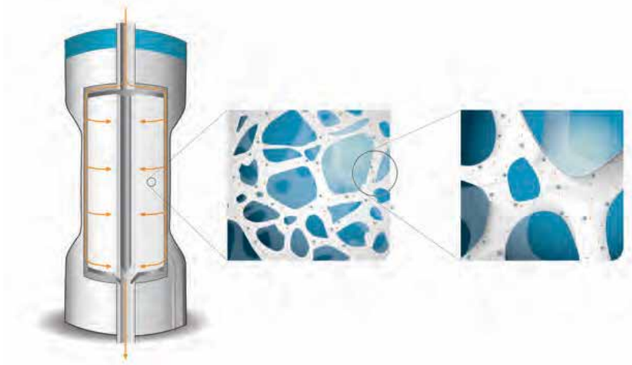
CIM® Monolithic Resin

CIM® (Convective Interaction Media) monoliths are highly cross linked, porous monolithic polymers with a well-defined channel size distribution. They are supplied readily packed in specially designed housings at a variety of chemistries and scales.

Polymers consist of:

> Poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) or
> Poly(butyl methacrylate-*co*-ethylene dimethacrylate)

The polymer composition of CIM® monoliths allows for exceptional mechanical and chemical stability. Incompressibility at extraordinary high flow rates and resistance to harsh chemical conditions during regeneration and sanitization are basic prerequisites of our material. Extensive reusability studies under real life conditions confirm the long-life cycle of CIM® monoliths.



Channel size

The channel dimensions of CIM® monoliths allow for convective mass transfer and combine excellent separation power with flow characteristics, enabling fast separation of large biomolecules and preserving their functionality.

The standardized channel size of CIMmultus™ Disposable monoliths lies in the range of 2 µm and allows for unhindered passage of most commonly used large biomolecules.

Figure 1: Radial flow and transport of biomolecules inside monolithic channels

Biomolecules are conveyed to the active groups located at the surface of the channels by the bulk flow rate of the mobile phase.

The transport between the mobile and the stationary phase is very fast because there is:
> No diffusion
> No dead-end pores
> No void volume
> No stagnant zones

Consequently, the chromatographic performance of CIM® monoliths is flow-rate independent.

Certain applications have special demands, and the use of bigger pore sizes might be beneficial. For this purpose, custom made monoliths with pore sizes in the range of 3 to 6 µm are provided on request. Using this approach, the advantages of CIM® monoliths can be fully capitalized even when working with particularly large biomolecules (e.g. Vaccinia virus).

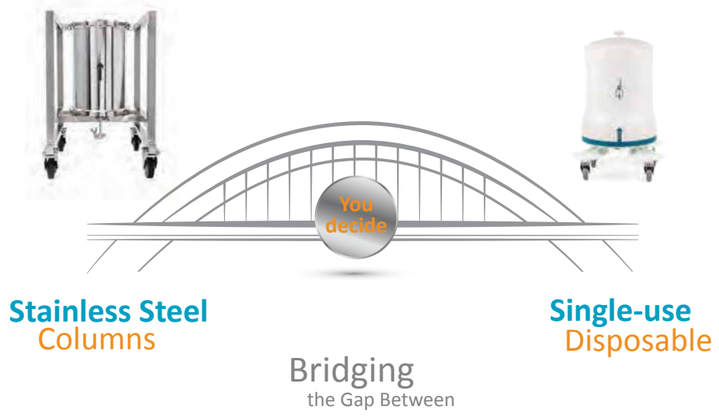
CIMmultus™ Disposable Columns

CIMmultus™ is a line of high throughput multiuse disposable columns that are designed for the purification of large biomolecules such as viruses, plasmids, large antibodes (IgM, IgG), and virus like particles (VLPs). CIMmultus™ puts bioprocess engineers in the driver's seat at all stages of process development – the choice of single or multi-use is up to you as the column has the characteristics of stainless steel with the benefits of a disposable column.

CIMmultus™ columns are suitable for cGMP production, research and development, and quality assurance.

Bridging the Gap

The reduction of production costs is a key driver for all biopharmaceutical companies and contract manufacturing organizations - whether based on stainless steel or disposable technology. When screening material for your new process, it is reassuring to know that you have built-in single or multi-use capability. CIMmultus™ columns meet all of your needs. It can be reusable through appropriate storage and sanitization or it can be a single use disposable. The choice depends exclusively on your policy and process requirements but not the column manufacturers' product line up. No matter what you decide, CIMmultus™ bridges the gap between the robustness of stainless steel and the disposability of single use columns.



CIMmultus™ IS THE COLUMN THAT FITS YOUR REQUIREMENTS - NOT OURS!

It is the next generation of monolithic columns that is decreasing time to market, production costs, and creating the competitive edge your company needs to bring lifesaving treatments to the market faster.

Our engineers designed CIMmultus™ with safety in mind. The column's structural integrity and leachable profile match medical grade stainless steel but has the process economics of a single or multi-use device. With the introduction of composite materials into an epoxy-based housing and the application of USP Class VI Parylene C coating to the entire column surface, CIMmultus™ offers:
> SAFETY
> cGMP COMPLIANCE
> VERSATILITY
> HIGH PERFORMANCE
> LOW WEIGHT BUT HIGH STRENGTH

Safety

Leachables and extractables are a concern to all manufacturers. This concern intensifies if you wish to use the column multiple times to make a process economically feasable. CIMmultus™ addresses this concern by applying Parylene C to the entire surface of the housing. Parylene C is an inert substance with a well-proven safety record as a coating for permanent medical implants.

CIMmultus™ has a layer of carbon fiber embedded in the epoxy thermoset walls well away from the contact surface. This layer gives the column the same structural strength of a stainless steel column ensuring maximum safety.

Versatility

CIMmultus™ is a highly versatile separation device. It is economical either as a single use device, or as a multi-use device (intra-batch or inter-batch use). Above all, it can be used at any step in your downstream processing:
> Capture of complex biomolecules
> Impurity removal (intermediate step or final polishing)
> Separation of complex samples

Performance - compatible to stainless steel

CIMmultus™ contains an improved CIM® monolithic technology, distinguished by 2 µm flow-through channels. They allow convective mass transfer of large biomolecules, making these columns a perfect choice for the purification of viruses, VLPs, plasmids, antibodies, PEGylated proteins and other big molecules. CIMmultus™ stands for:
> Convective mass transfer, reduced backpressure and minimal sample clogging
> Fast product isolation and concentration of diluted samples
> Efficient removal of high molecular mass impurities in polishing steps

	1 mL		8 mL		80 mL		800 mL		8000 mL	
Type of column	**CIM SS**	**CIMmultus™**	**CIM SS**	**CIMmultus™**	**CIM SS**	**CIMmultus™**	**CIM SS**	**CIMmultus™**	**CIM SS**	**CIMmultus™**
Max pressure	18 bar	18 bar	20 bar	20 bar	20 bar	20 bar	7 bar	14 bar	7 bar	14 bar
Recommended flow rates (mL/min)	1-5	1-5	8-60	8-60	80-240	80-240	200-1300	200-1300	2000-10000	2000-10000
Max. flow rate (mL/min)	16	16	100	100	400	400	2000	2000	10000	10000
Max. operating temperature	40 °C	40 °C	40 °C	40 °C	40 °C	40 °C	40 °C	40 °C	40 °C	40 °C
L-t storage conditions	20% ethanol									
Sanitization for IEX, C4 HLD	1 M NaOH for at least an hour									

Table 1: CIM® Stainless Steel Columns vs. CIMmultus™ Advanced Composite Columns - matching characteristics

Reasons to use CIMmultus™ Columns

Use CIMmultus™ as a Single-Use Disposable if:

> You want to avoid cleaning validation
> Your regulatory issues request it
> Your application does not allow multiple use (i.e. too strong binding)
> You want to avoid cross contamination between batches imperatively

CIMmultus™ is economical enough to use it as Single-Use Disposable. Due to the high binding capacity you are able to use a column that is 10 times smaller in size than conventional supports.

CIMmultus™ Cost Effective Alternative to purification:
> Low capital investment
> Reduction in buffer use (less buffer tanks)
> High capacities
> Fast method development

DECREASED TIME TO MARKET!

Use CIMmultus™ as a Multi-Use Column if:

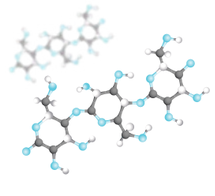
> Your economy issues allow it and cleaning validation is acceptable
> Your process allows for re-use of columns
> Your production cycle requires long-term column storage in between production campaigns
> You would like to decrease production costs by turning to disposable columns but don't want to sacrifice the level of safety your stainless steel columns are giving you

Available chemistries

> Quaternary amine (QA)
> Diethylamine (DEAE)
> Sulfonyl (SO3)
> Butyl (C4 HLD)
> Hydroxyl (OH)
> Other chemistries upon request

Applications

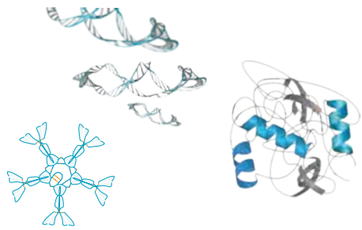
Large biomolecules
> VIRUSES:
- Adenovirus
- Lentivirus
- AAV
- Influenza A&B
- Bacteriophages (T4, T7, M13, VDX-10, lambda, etc)
- VLPs
- Rotavirus
- Baculovirus
- Rabies
- Rubella
- Measles virus
- Hepatitis
- Herpes virus
- Vaccinia
- Murine Leukemia Virus (MuLV)
- Parvovirus (Minute Virus of Mice, MVM)
- Plant viruses (Tomato Mosaic virus, Pepino Mosaic virus, Potatoe virus Y)



> pDNA

> PEGYLATED PROTEINS

> LARGE PROTEINS (IgM)



- concentration -
- purification -
- removal -

Molecules	Dynamic binding capacity
influenza	1.9 E+10 $TCID_{50}$/mL
T7 phage	1 E+13 pfu/mL
M13 phage	4.5 E+13 pfu/mL
lambda phage	1 E+13 pfu/mL
PRD1 phage	6 E+13 pfu/ml
S.aureus phage VDX-10	1.1 E+10 pfu/mL
adenoviruseses	2 E+12 vp/mL
baculovirus	2.4 E+11 pfu/ml
pDNA	8 mg/mL
genomic DNA	15 mg/mL
IgM	25 - 50 mg/mL
endotoxins	> 115 mg/mL

Table 2: Dinamic binding capacities for different target molecules (on different CIM chemistries)

Validation and Quality Control

To ensure safety and consistent performance of CIMmultus™ columns, each column undergoes thorough testing to ensure that the columns meet all requried specifications. The CIMmultus™ columns are designed, developed and manufactured according to ISO 9001 Quality Management System. Entire CIMmultus™ product line (1 mL, 8 mL, 80 mL, 800 mL, 8L) meets United States Pharmacopeia (USP) Class VI standard. In addition, CIMmultus™ 80 ml, 800 ml, 8L columns are cGMP compliant. Each column is supplied with the Certificate of Analysis which ensures the product meets production specifications.

CIMmultus™ Disposable Monolithic Columns

From development to GMP production!

- High binding capacity
- High throughput
- High resolution

Regardless of the flow rate applied to the columns.

Simple Scale-up

CIMmultus™ 1 mL

Recommended flow rates:
1 - 5 mL/min

CIMmultus™ 8 mL

Recommended flow rates:
8 - 60 mL/min

CIMmultus™ 80 mL

Recommended flow rates:
40 - 240 mL/min

CIMmultus™ 800 mL

Recommended flow rates:
200 - 1300 mL/min

CIMmultus™ 8000 mL

Recommended flow rates:
2000 - 10000 mL/min

Screening/Method Development

Preparative Scale

Large Scale Production