



Lentivirus (LV) Suspension Platform AcceleratorSM Integrated Solutions

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Illustrations and recommendations are based upon a typical process and may be subject to change based upon your individual process requirements.



LV Drug Products

An introduction to today's LV manufacture

In recent years we've witnessed promising results from gene-modified cell therapy products, some of which are based on CAR-T cells. We look forward to seeing their progress and impact on patient health. CAR-T cells are T-cells that have been modified with a viral vector. These are commonly lentiviral vectors (LV), as they offer unique advantages over other gene delivery systems, namely the ability to integrate transgenes into the genomes of both dividing and nondividing cells. The large packaging capability of the LV allows the *in-vivo* or *in-vitro* transfer of large encoding sequences (genes) that are not possible with other commonly used vectors such as adeno-associated virus (AAV). Gene therapies represent a new medical paradigm, derived from decades of research, acquired best practices, and hard lessons learned. Despite an increasing number of gene therapy drugs in development and clinical trials every year, this part of the biotech industry is still in its early stages. While there is a lot of experience from the field of recombinant antibody and that can be bridged to this evolving industry, manufacturers are facing differences and challenges today in various stages of the drug marketing journey, from development and manufacture, to the regulatory approval of LV for *in-vivo* and *in-vitro* use.

Plan for Speed in LV Development

In process development, speed-to-market and cost are critical considerations. Selecting the most suitable production system that results in fast production, high yields, and high potency of LV is key. Several producers are currently entering the market using the approach of transfection with adherent cells because it enables a relatively fast route to market. There are, however, limitations to transfection-based manufacture as typical LV titers currently plateau around 10^6 to 10^7 Transduction Units (TU) per cm^2 in adherent systems. For products that require higher yield and lower cost, developing suspension cells or stable producer may offer long-term benefits of improved yield and scalability.

Increase Capacity and Quality in LV Manufacture

The manufacturing capacity of viral vectors is estimated to be 1–2 orders of magnitude lower than that needed to support commercial supply requirements. Academics and industry are therefore putting focus on measures for the most durable capacity increase; improving manufacturing practices to increase productivity through engineering cell lines, refining plasmid constructs, and enhancing process recovery in downstream processing. Current downstream recovery yields are a paltry 15%. Maximizing yield while meeting both product and impurity specifications are significant challenges in downstream processing. Lentivirus is extremely sensitive, making downstream processing a race against the clock. Although yields at bench scale can be higher, techniques such as ultracentrifugation are not scalable. Alternative techniques such as filtration, chromatography, and tangential flow filtration can be used, enabling manufacturers to work quickly, protecting the product and maximizing yields.

Gain Regulatory Approval for LV Drug Products

Moving LV products into the highly regulated GMP production environment puts a spotlight on the rising expectations in drug reviews, as the understanding in industry and regulatory bodies builds. This much-needed regulatory framework is rapidly developing and is supported through multiple guidance documents that have been published recently. Part of the challenge of obtaining regulatory approval is paired with the constraints of the available analytics: viral titer, quality and impurity assays require lengthy off-line processes and can come with limited sensitivity. This burden is lighter for LV used as raw material for gene modified cell therapies, but remains important for applications with *in-vivo* use. A series of next generation analytical tools are being developed at rapid pace and promise real-time monitoring and process analytical technologies (PAT) implementation.

With several approved gene therapies and hundreds of products in the pipeline, the industry knowledge is building rapidly. At the same time, the regulatory framework is developing which is increasing confidence in interpreting guidelines and builds regulatory maturity in both industry and regulatory bodies. The continued connection of academic research, industry investment, and regulatory commitment comes with great potential for streamlining LV manufacturing and allows new, high-quality LV therapeutics and gene-modified cell therapies to reach patients.

1. Cell Seeding

Additional
resources 

Scaling up suspension cell cultures, from PD to clinical production and from seedbank to final production bioreactor, requires well characterized and controllable technology that works as well on its own as it does as part of the seed train.

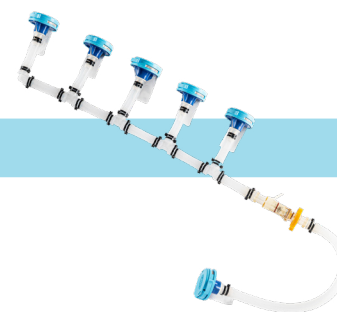
Equipment

Allegro™ STR Single-Use Stirred Tank Bioreactor

The Allegro STR bioreactor family combines Pall's bioprocess engineering expertise, cell culture know-how and our drive for quality into a series of single-use bioreactors that deliver consistent and scalable cell culture performance across the range.

Part Number (PN): STR200-230W, STR200-JC-FAT

[Discover more](#)



Input

Allegro® 2D Standard Systems
PN: 7190-1397U, 7190-1397M,
7190-1397P

Allegro 3D Standard Systems
PN: 7190-1376R

Allegro Bioprocessing Workstations
PN: LGRTBDC, LGRTSDC, LGRTPE20L,
LGRTLPE20L, LGRTDRC,
LGRTTBSC, LGRPTE50L,
LGRPTE200L, LGRPTRL200L

Allegro XRS 25 Bioreactor System
PN: XRS25BRS, XRS25FAT, 609-40A

mPath™ Benchtop Bioreactor
Control Tower
PN: MPATHLINK

2 L Bottle
PN: 7414-0972X

Allegro Ready Transfer Sets
PN: 7292-1381X

Output

Allegro Ready Transfer Sets
PN: 7292-1381A



Supporting

Allegro STR Bioreactor
Biocontainer Bags
PN: 6412-0473Q



When viewing on desktop roll over product name to view more

2. Clarification

Additional resources 

The clarification step removes cells, cell debris, and other impurities to reduce biological burden and filtration offers a versatile, scalable solution that can be quickly optimized to deliver high throughput and high yield of infectious particles. Our experienced technical team can help you find the best filter technologies to optimize performance and maximize vector yield. Contact us for assistance in determining the best filter technology for your process.

Equipment

HDC® II Membrane in Kleenpak™ Nova Capsules

HDC II all-polypropylene filters incorporate proprietary tapered-pore polypropylene depth media. With removal ratings from 0.6 µm to 700 µm, HDC II filters are well-suited to a broad range of prefiltration applications in biological and chemical API manufacturing facilities where purity, economy and reliability are critical.

PN: NT8J100P1G

[Discover more](#)



Input

Allegro 2D Standard Systems
PN: 7190-1397S, 7190-1374W

Allegro Bioprocessing Workstations
PN: LGRKPCBKHD, LGRUFBK,
LGRTPE20L, LGRTLPE20L, LGTRDC

LevMixer® System
PN: 7403-1351N, LM400NCMA-B4N,
LMG403

Allegro Ready Transfer Sets
PN: 7292-1381A, 7292-1381X

Output

Allegro Bioprocessing Workstations
PN: LGRTTBSC, LGRPTTE50L

LevMixer System
PN: 7403-1351N, LM400NCMA-B4N,
LMG403

Allegro Ready Transfer Sets
PN: 7292-1381A

Supporting

Allegro MVP Single-Use System
PN: LGRMVPAPPE, 9430-1688M, 7430-1507C

Supor® EAV Membrane in Kleenpak™ Capsules
PN: 7090-1688N, 7090-1685C, 7090-1685D,
7090-1685E

Allegro Ready Transfer Sets
PN: 7421-1685M, 7421-1685L



When viewing on desktop roll over product name to view more

3. Purification (Chromatography)

Additional resources 

Purification by ion exchange chromatography can be optimized to reduce empty, broken or partially filled capsids, DNA and host cell proteins (HCP). Adsorptive membrane technology, coupled with optimized elution conditions, offer an efficient and effective option for this step and, as a scalable single-use solution, can be quickly integrated into any manufacturing process.

Equipment

ÄKTA ready† Single-Use System

ÄKTA ready is a single-use liquid chromatography system built for process scale-up and manufacturing. The system uses disposable flow paths and pre-packed columns that enable flexibility and speed in bioprocessing.



Input

Allegro 2D Standard Systems
PN: 7190-1397N, 7190-1397U,
7190-1397S

Allegro Bioprocessing Workstations
PN: LGRTBDC, LGRTPE20L,
LGRTLPE20L, LGRTDC, LGRTSDC

LevMixer System
PN: LMG403, LM400NCMA-B4N,
7403-1352N

Allegro Plastic Totes
PN: LGRPTE200L, LGRPTEW200L

Allegro Ready Transfer Sets
PN: 7292-1381L

Output

Allegro 3D Standard Systems
PN: 7190-1376T, 7190-1374Y

Allegro Plastic Totes
PN: LGRPTE500L, LGRPTRL500L,
LGRPTEL500L

Allegro Ready Transfer Sets
PN: 7292-1381L



Supporting

Allegro Ready Transfer Sets
PN: 7291-1399Y

UNICORN† Workstation License

ÄKTA ready Flow Kit

Mustang® Q XT Ion Exchange
Chromatography Capsules
PN: XT450MSTGQP05



When viewing on desktop roll over product name to view more

4. Concentration

Timely reductions in post-elution salt concentration by diafiltration and subsequent concentration by ultrafiltration further concentrates the target molecule and exchanges buffers to assure optimal infectivity. Minimizing shear affects and maximizing recovery is a common challenge, but our technical experts can work with you to optimize your process and system design based on years of experience and thorough testing.

Equipment

ÄKTA readyflux[†] Filtration System

The automated system uses gamma irradiated single-use flow kits including single-use flow path, pumps and sensors for pressure, conductivity, temperature, flow and pH. These allow a wide variety of control modes and help users to tailor the filtration controls to different processing requirements.



Input

Allegro 2D Standard Systems
PN: 7190-1397M, 7190-1397N

Allegro 3D Standard System
PN: 7190-1374Y

Allegro Bioprocessing Workstations
PN: LGRTBDC, LGRTSDC, LGTRTDC,
LGRTPE20L, LGRTLPE20L

Allegro Ready Transfer Sets
PN: 7292-1381A



Output

Allegro 2D Standard Systems
PN: 7190-1397P

Allegro Plastic Totes
PN: LGRPTE200L, LGRPTEW200L

Allegro Ready Transfer Sets
PN: 7292-1381A

Supporting

Allegro 2D Standard Systems
PN: 7190-1397S

Cadence® Single-Use Tangential
Flow Filtration (TFF) Modules
PN: CSUM100T010, 7443-1437P

Allegro Ready Transfer Sets
PN: 7292-1381A

ÄKTA readyflux Flow Kit TriClamp

Bagkart[†] Bag Trolley

C10 Manifold with TriClamp Ready for
ÄKTA readyflux

UNICORN Workstation License

5. Bulk Filtration

Additional resources 

Manufacturing clinical material requires the production of highly pure and biologically active vectors that meet regulatory requirements. As part of this, a final sterilizing grade (0.2 µm) filtration step contributes to sterility assurance and maintains product safety while the product is sent for final filling.

Equipment

Palltronic® Flowstar V Filter Integrity Test Instrument

The Palltronic Flowstar V integrity test instrument ensures accurate filter integrity testing with a further reduction in test time, full compliance with 21 CFR Part 11, advanced automation capabilities, and simplified network integration saving the user time while improving process efficiency.

PN: FFS05

Discover more



Input

Allegro 2D Standard Systems
PN: 7190-1397M, 7190-1397P

Allegro Bioprocessing Workstations
PN: LGRTBDC, LGRTPE20L,
LGRTLPE20L, LGRTRDC,
LGRKPCBKHD, LGRUSFBK

Allegro Ready Transfer Sets
PN: 7292-1382M



Supporting

Fluorodyne® EX EDF Cartridges
PN: 7090-1681M

Supor EKV Sterilizing-Grade Filter Cartridges

Emflon® II Membrane in Mini Kleenpak Capsules



When viewing on desktop roll over product name to view more

Additional Resources

Process Description	Format	Title	Link
Cell Seeding	Whitepaper	Choice of Upstream Bioreactor Technologies for Industrial Scale Viral Manufacturing	▶
Cell Seeding	Webinar	Gene Therapy Upstream Processing: Adherent v Suspension Cost Modelling and Perspectives	▶
Clarification	Poster	Single-Use Platform for Scalable Purification of a VSV-G Lentiviral Vector	▶
Clarification	Poster	Optimizing the Clarification of Viral Vector Culture for Gene Therapy	▶
Purification (Chromatography)	Poster	Single-Use Platform for Scalable Purification of a VSV-G Lentiviral Vector	▶
Purification (Chromatography)	White Paper	Mustang Membrane Chromatography for Gene Therapy Purification: A Robust and Scalable Solution	▶
Concentration	White Paper	Understanding Single-Pass Tangential Flow Filtration and the New Era of Bioprocessing	▶
Concentration	Poster	Single-Use Platform for Scalable Purification of a VSV-G Lentiviral Vector	▶
Bulk Filtration	Poster	Single-Use Platform for Scalable Purification of a VSV-G Lentiviral Vector	▶

Equipment List

Step No.	Process Description	Product	Part Number	Link
1	Cell Seeding	2 L Bottle	7414-0972X	
1	Cell Seeding	Allegro 2D Standard Systems	7190-1397U, 7190-1397M, 7190-1397P	▶
1	Cell Seeding	Allegro Bioprocessing Workstations	LGRTBDC, LGRTSDC, LGRTPE20L, LGRTLPE20L, LGRTDRC, LGRTTBSC, LGRPTTE50L, LGRPTTE200L, LGRPTRL200L	▶
1	Cell Seeding	Allegro Ready Transfer Sets	7292-1381X, 7292-1381A	▶
1	Cell Seeding	Allegro STR Single-Use Stirred Tank Bioreactor	STR200-230W, STR200-JC-FAT	▶
1	Cell Seeding	Allegro STR Bioreactor Biocontainer Bags	6412-0473Q	▶
1	Cell Seeding	Allegro XRS 25 Bioreactor System	XRS25BRS, XRS25FAT, 609-40A	▶
1	Cell Seeding	mPath Benchtop Bioreactor Control Tower	MPATHLINK	▶
1	Cell Seeding	Allegro 3D Standard Systems	7190-1376R	▶
2	Clarification	Allegro 2D Standard Systems	7190-1397S, 7190-1374W	▶
2	Clarification	Allegro Bioprocessing Workstations	LGRKPCBKHD, LGRUFBK, LGRTPE20L, LGRTLPE20L, LGRTDRC	▶
2	Clarification	LevMixer System	7403-1351N, LM400NCMA-B4N, LMG403	▶
2	Clarification	Allegro Ready Transfer Sets	7292-1381A, 7292-1381X, 7421-1685M, 7421-1685L	▶
2	Clarification	HDC II Membrane in Kleenpak Nova Capsules	NT8J100PIC	▶
2	Clarification	Allegro Bioprocessing Workstations	LGRTTBSC, LGRPTTE50L	▶
2	Clarification	Allegro MVP Single-Use System	LGRMVPAPE, 9430-1688M, 7430-1507C	▶
2	Clarification	Supor EAV Membrane in Kleenpak Capsules	7090-1688N, 7090-1685C, 7090-1685D, 7090-1685E	▶
3	Purification (Chromatography)	Allegro 2D Standard Systems	7190-1397N, 7190-1397U, 7190-1397S	▶
3	Purification (Chromatography)	Allegro Bioprocessing Workstations	LGRTBDC, LGRTPE20L, LGRTLPE20L, LGRTDRC, LGRTSDC	▶
3	Purification (Chromatography)	LevMixer System	LMG403, LM400NCMA-B4N, 7403-1352N	▶
3	Purification (Chromatography)	Allegro Ready Transfer Sets	7292-1381L, 7291-1399Y	▶
3	Purification (Chromatography)	Allegro Plastic Totes	LGRPTTE200L, LGRPTTEW200L, LGRPTTE500L, LGRPTRL500L, LGRPTTEL500L	▶
3	Purification (Chromatography)	ÄKTA ready Single-Use System	29032038 (gradient system), 28906261	

Equipment List

Step No.	Process Description	Product	Part Number	Link
3	Purification (Chromatography)	Allegro 3D Standard Systems	7190-1376T, 7190-1374Y	▶
3	Purification (Chromatography)	Mustang Q XT Ion Exchange Chromatography Capsules	XT450MSTGQP05	▶
3	Purification (Chromatography)	UNICORN Workstation License	29128116	
3	Purification (Chromatography)	ÄKTA ready Flow Kit	28930182	
4	Concentration	Allegro 2D Standard Systems	7190-1397M, 7190-1397N, 7190-1397P, 7190-1397S	▶
4	Concentration	Allegro Bioprocessing Workstations	LGRTBDC, LGRTSDC, LGRTDRC, LGRTPE20L, LGRTLPE20L	▶
4	Concentration	Allegro Ready Transfer Sets	7292-1381A	▶
4	Concentration	Allegro 3D Standard System	7190-1374Y	▶
4	Concentration	ÄKTA readyflux Filtration System	29151000	
4	Concentration	Allegro Plastic Totes	LGRPTTE200L, LGRPTTEW200L	▶
4	Concentration	ÄKTA readyflux Flow Kit TriClamp	29151600	
4	Concentration	Bagkart Bag Trolley	29151500	
4	Concentration	C10 Manifold with TriClamp ready for ÄKTA readyflux	7443-1437S	
4	Concentration	Cadence Single-Use Tangential Flow Filtration (TFF) Modules	CSUM100T010, 7443-1437P	▶
4	Concentration	UNICORN Workstation License	29128116	
5	Bulk Filtration	Allegro 2D Standard Systems	7190-1397M, 7190-1397P	▶
5	Bulk Filtration	Allegro Ready Transfer Sets	7292-1382M	▶
5	Bulk Filtration	Palltronic Flowstar V Filter Integrity Test Instrument	FFS05	▶
5	Bulk Filtration	Supor EKV Sterilizing-Grade Filter Cartridges		▶
5	Bulk Filtration	Emflon II Membrane in Mini Kleenpak Capsules		▶
5	Bulk Filtration	Fluorodyne EX EDF Cartridges	7090-1681M	▶
5	Bulk Filtration	Allegro Bioprocessing Workstations	LGRTBDC, LGRTPE20L, LGRTLPE20L, LGRTDRC, LGRKPCBKHD, LGRUSFBK	▶

Scientific and Laboratory Services

The scientific and regulatory knowledge that supports the selection, adoption and ongoing use of critical process technology, coupled with analytical, imaging and measurement capabilities, creates a versatile and practical resource ready to respond to an ever-changing industry. Pall duplicates these laboratories across the globe and leverages their cumulative knowledge to deliver practical scientific and regulatory support to all process technologies to keep you moving forward.

Technical Services

The accessibility of local technical support networks minimize delays in your journey at all points. From the early stage of process development to on-site support for mature processes, Pall's technical support groups are there to help remove barriers to progress and to make your journey as rapid and stress free as possible. Our knowledge of the technology and the process can be applied to everything from training to trouble-shooting and consultancy. Our global team of technology experts are on hand to respond to your changing needs.

Advanced Separation Systems

Operating within the defined design space demands the monitoring and control of critical process parameters to assure product quality. Systems that control critical unit operations and that communicate with your existing process components can control process risks and maximize productivity by reducing operator involvement for many processes, Pall applies strong engineering and regulatory understanding to deliver compliant and qualified systems that safeguard and simplify your journey.

Process Development Services

Prior knowledge is a rare and valuable commodity, especially when preparing to take a new direction or when under pressure to deliver to a tight deadline. Take advantage of Pall's experience, process knowledge and technical know-how to help you achieve your goals. From the optimization of an end-to-end continuous process to establishing the right parameters for a single unit operation, our teams of scientists are ready to work with you and to generate the data you need to make the critical decisions necessary for success.

Validation Services

Arriving at your destination counts for nothing without the necessary paperwork to proceed to the next stage. Pall's Validation Services are committed to delivering the supporting data packages and analysis required to quantify process risk and to support regulatory submission. Our strengths include critical filtration technologies such as the performance validation of sterilizing grade filtration, and we are at the forefront of the evolving needs in the area of extractables and leachables for all product contact components. We combine the generation of data with interpretation and consultancy to deliver data packages that are ready for regulatory scrutiny and to ensure there are no barriers to progress.

Servicing and Maintenance

Our range of service packages keeps your equipment protected and well maintained, and includes itemized pay-as-you-go services, start-up care and training packages and a variety of post-warranty service plans that include priority response times, discounts for emergency repairs and flexible payment options. Pall service plans provide total peace of mind and worry-free support throughout the coverage period.



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