CELL & GENE THERAPY – DESIGNING FOR FLEXIBILITY, SCALABILITY AND COST EFFECTIVENESS

November 14, 2018

Agenda

Overview of Cellular & Gene Therapy

Regulatory Guidance

Facility Strategy

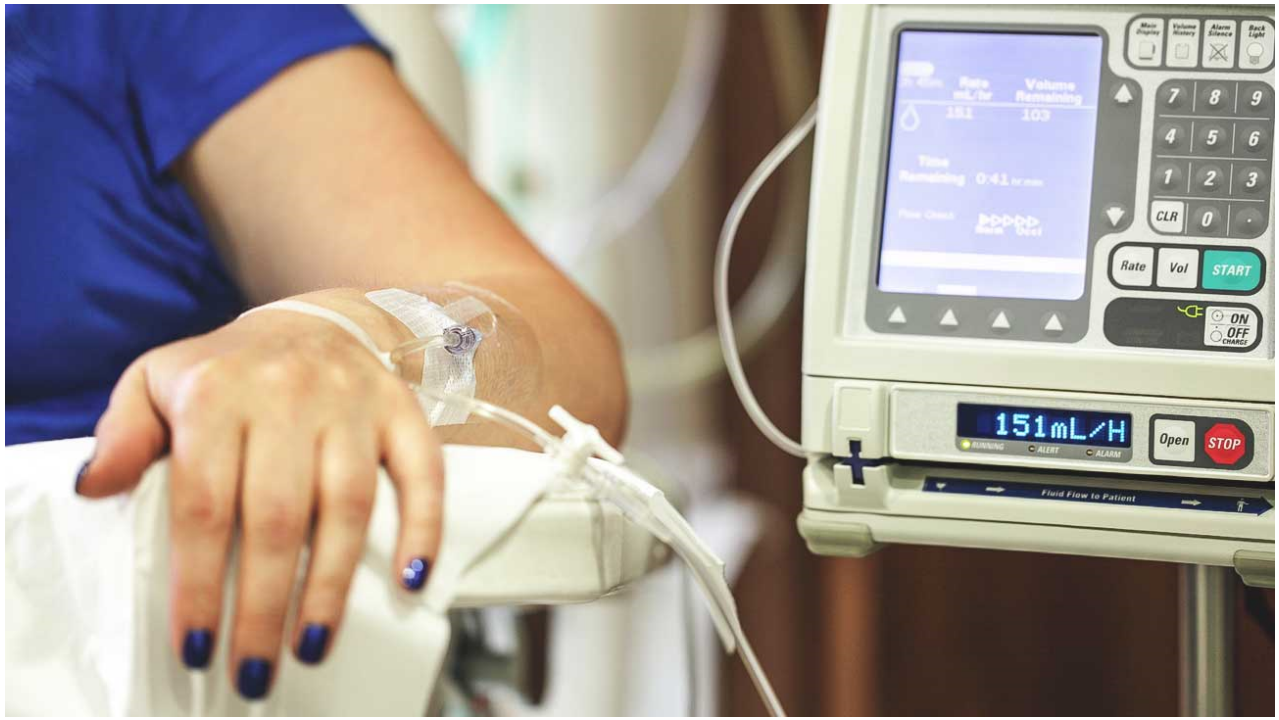
Enabling Technology

Summary

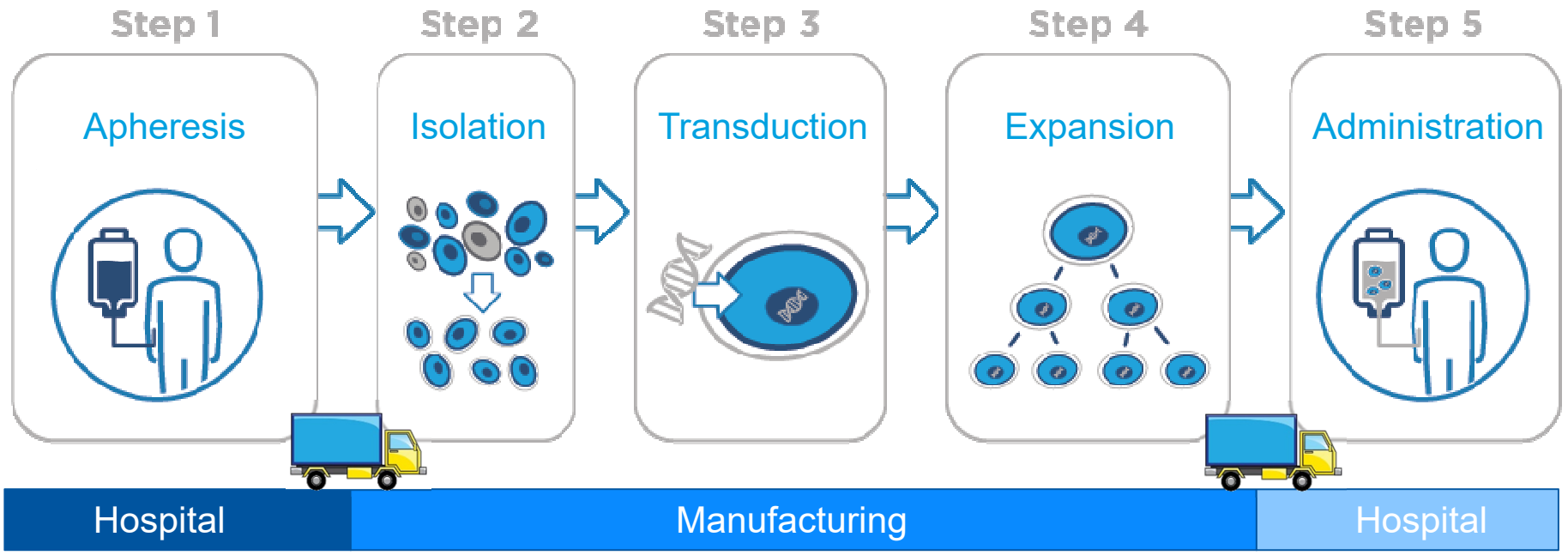
Q&A

OVERVIEW
CELLULAR AND GENE THERAPY

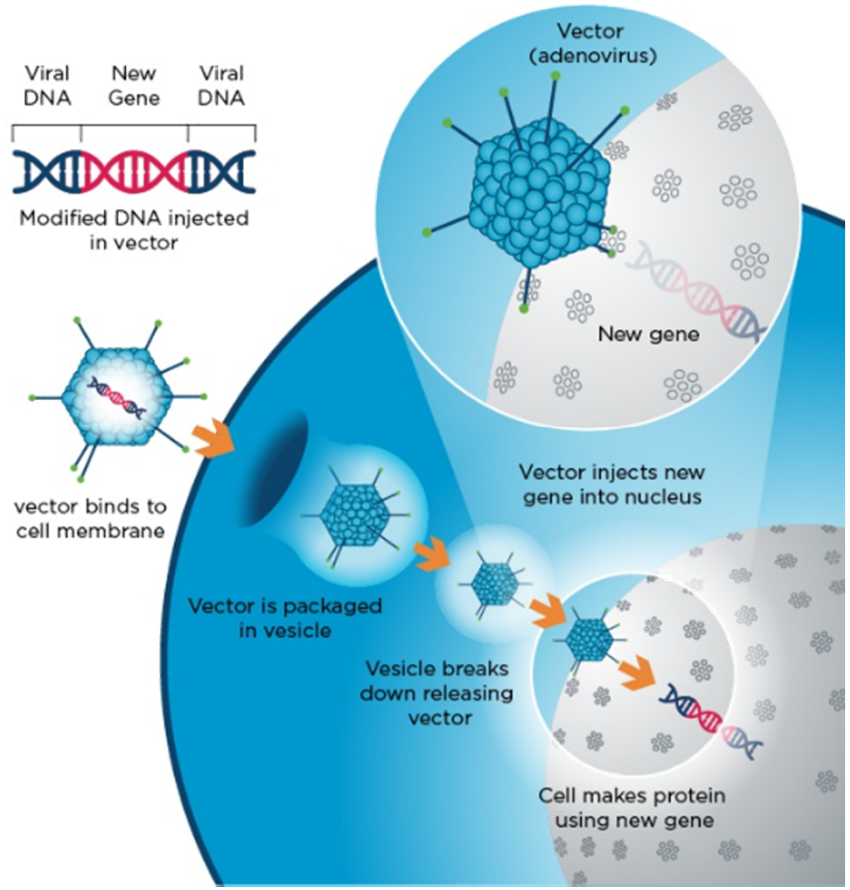
Cell Therapy



Cell Therapy



Gene Therapy – Viral Vectors



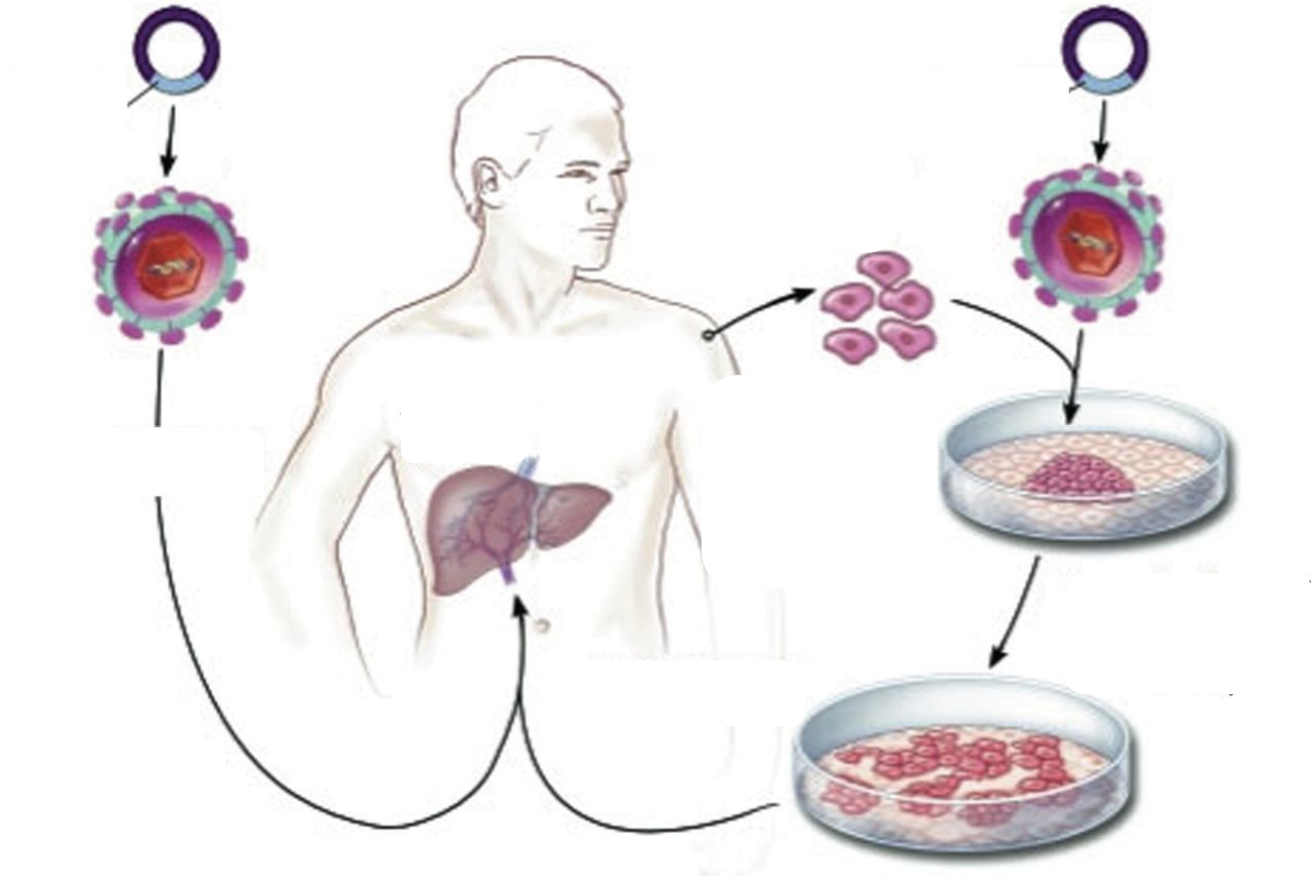
Gene Therapy

“in vivo”

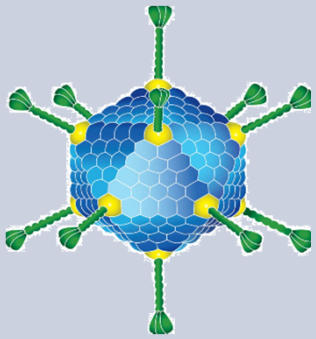
DIRECT DELIVERY

“ex vivo”

CELL-BASED DELIVERY



Manufacturing Types

Plasmid Manufacturing	Vector Manufacturing	Cell Therapy Manufacturing
		
Recombinant DNA Microbial Fermentation Separate Facility	Human Host Cell Line Cell Culture Biosafety Level 2	Patient Specific Cell Washing, Modification, and Expansion

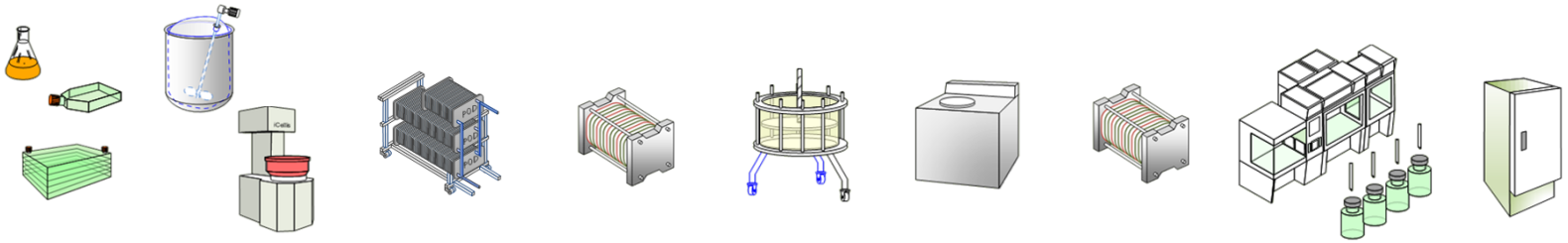
Manufacturing Comparison

mAb

Up to 20,000L

Cell Culture / Harvest	Purification	Bulk Fill

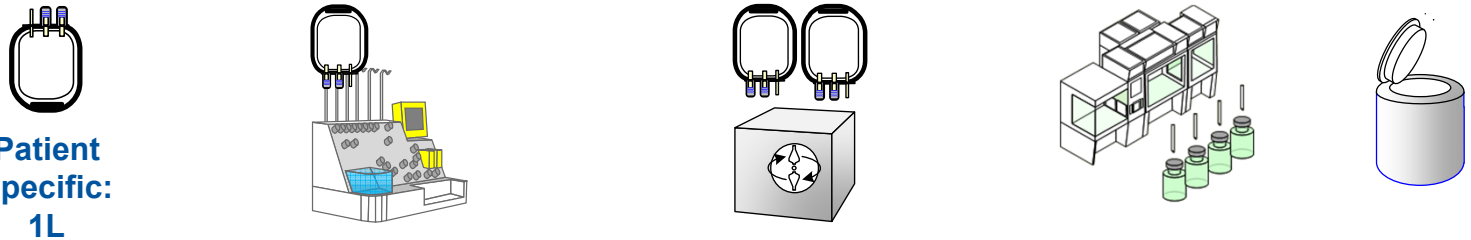
Viral Vector



200L – 2000L

Cell Culture / Harvest	Purification	Filling / Freezing

Cell Therapy



Patient Specific: 1L

Thaw	Cell Wash / Modify / Expand	Cell Harvest & Formulation	Filling / Cryo Freezing

REGULATORY
GUIDANCE

PIC/S

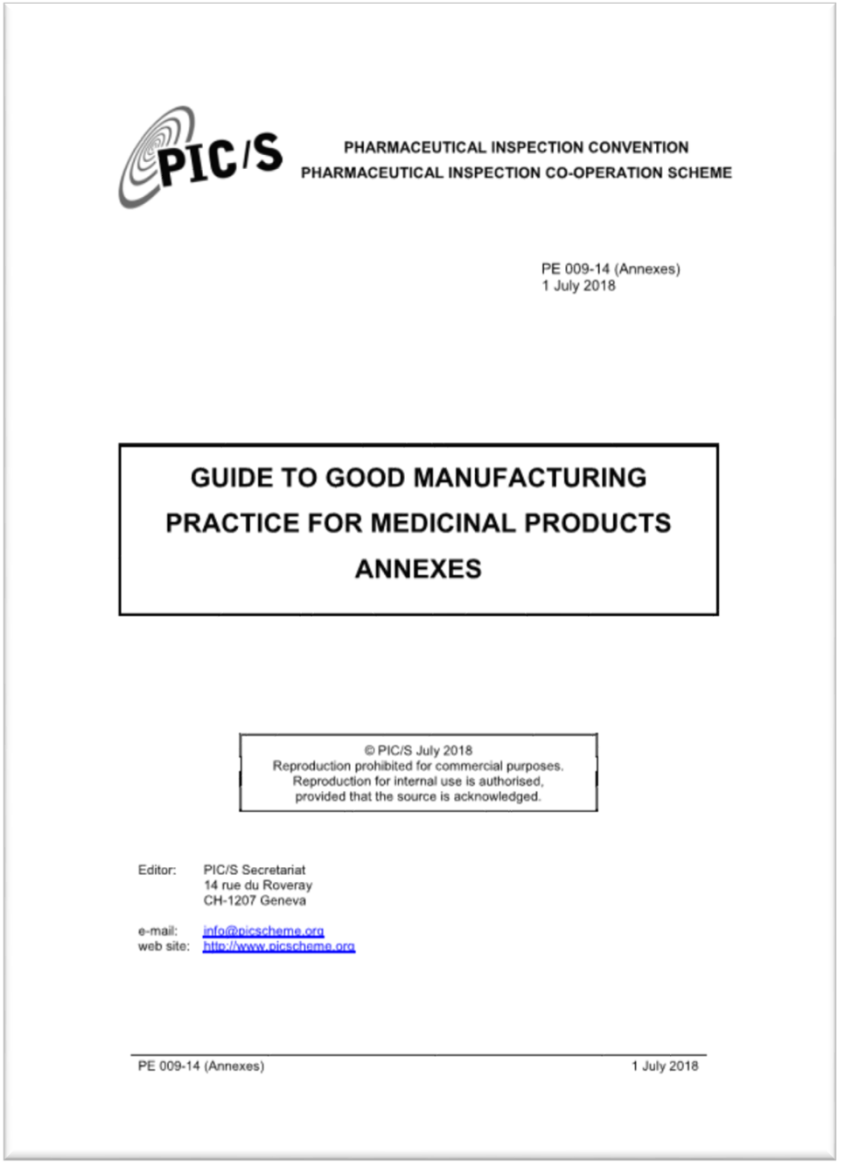
"Pharmaceutical Inspection Co-operation Scheme"

Annex 1

Manufacture of Sterile Medicinal Products

Annex 2

Manufacture of Biological Medicinal Substances and Products for Human Use



PIC/S

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PE 009-14 (Annexes)
1 July 2018

GUIDE TO GOOD MANUFACTURING PRACTICE FOR MEDICINAL PRODUCTS
ANNEXES

Editor: PIC/S Secretariat
14 rue du Roveray
CH-1207 Geneva

e-mail: info@picscheme.org
web site: http://www.picscheme.org

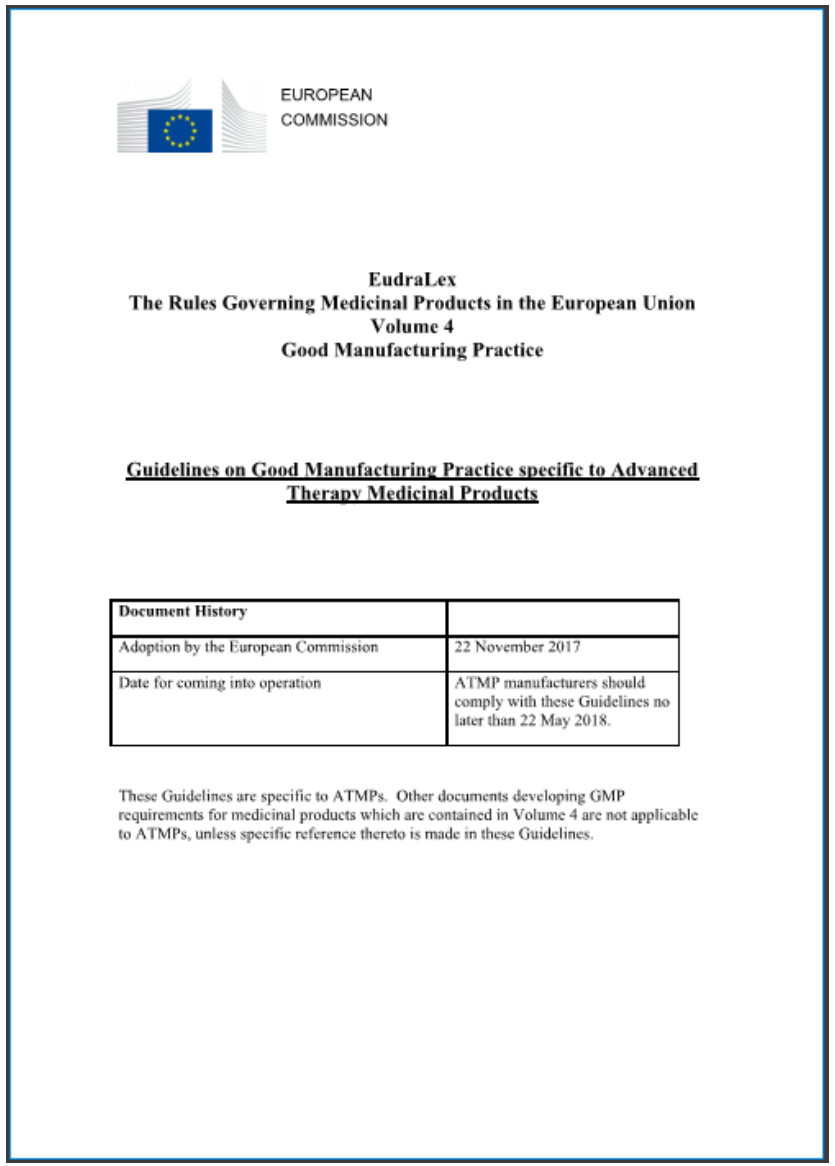
EudraLex Volume 4

"Guidelines on Good Manufacturing Practice Specific to Advanced Therapy Medicinal Products"

- Adopted 22Nov2017
- Compliance expected by 22May2018

Applies to:

- Gene Therapy
- Cell Therapy
- Engineered Tissue Therapy



EUROPEAN
COMMISSION

EudraLex
The Rules Governing Medicinal Products in the European Union
Volume 4
Good Manufacturing Practice

Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products

Document History	
Adoption by the European Commission	22 November 2017
Date for coming into operation	ATMP manufacturers should comply with these Guidelines no later than 22 May 2018.

These Guidelines are specific to ATMPs. Other documents developing GMP requirements for medicinal products which are contained in Volume 4 are not applicable to ATMPs, unless specific reference thereto is made in these Guidelines.

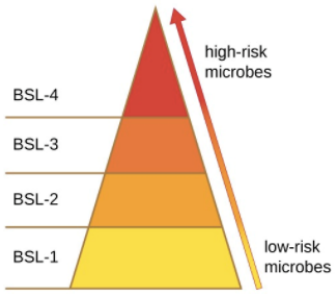
National Institutes of Health (NIH)

"NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)"

April 2016

Defines Requirements for:

Facility
Containment Equipment
Biosafety Procedures



NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (NIH GUIDELINES)

April 2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Visit the NIH OSP Web site at:
http://www.osp.od.nih.gov
For current information on Guidelines, Protocols, Principal Investigators, Meetings, and information about upcoming Gene Therapy Policy Conferences

NIH OFFICE OF SCIENCE POLICY CONTACT INFORMATION:

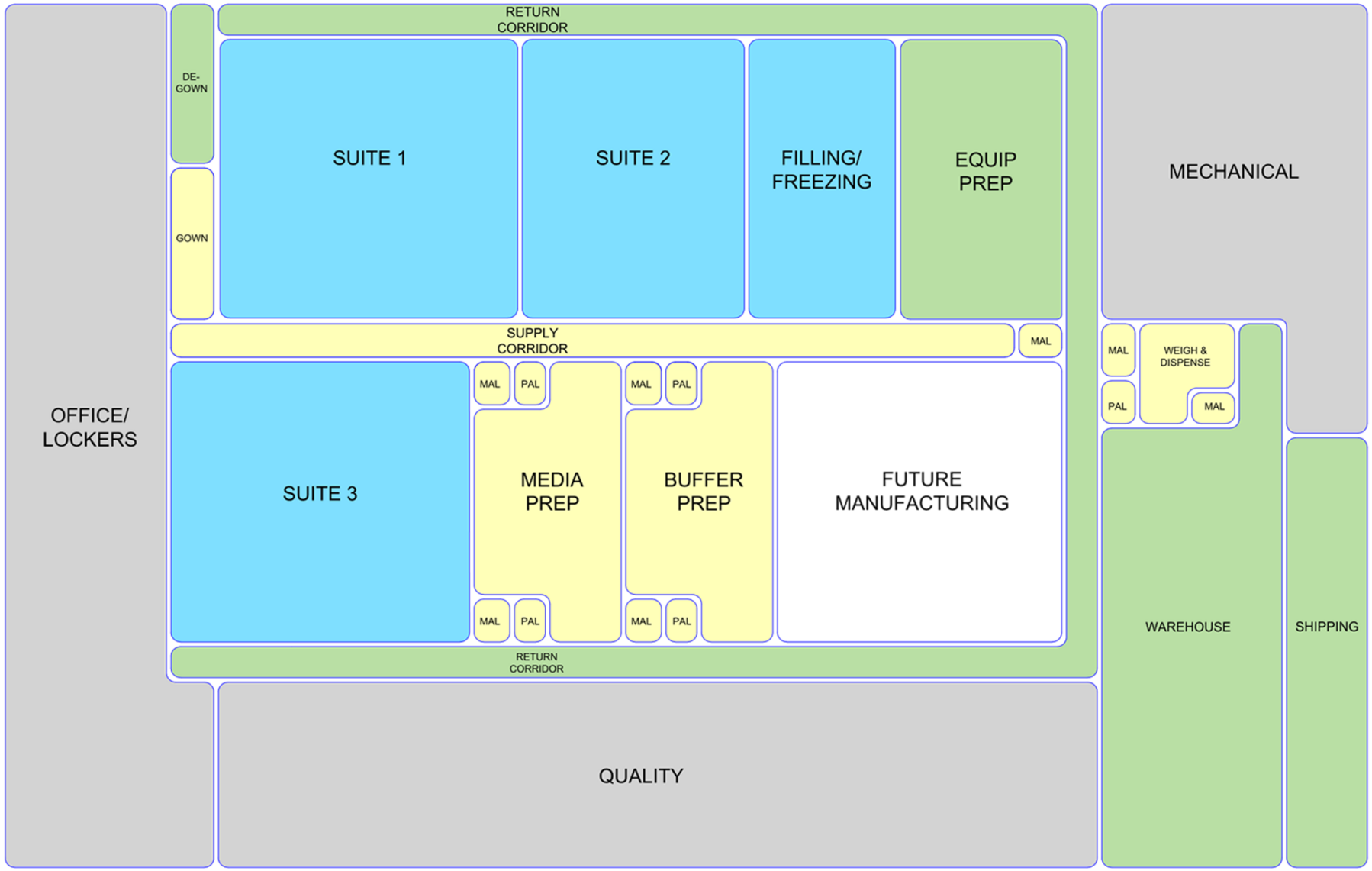
Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892-7985 (20817 for non-USPS mail), (301) 496-9838; (301) 496-9839 (fax).

For inquiries, information requests, and report submissions: NIHGuidelines@od.nih.gov
Human gene transfer protocol submissions: HGTprotocols@mail.nih.gov

These *NIH Guidelines* shall supersede all earlier versions until further notice.

FACILITY
STRATEGIES

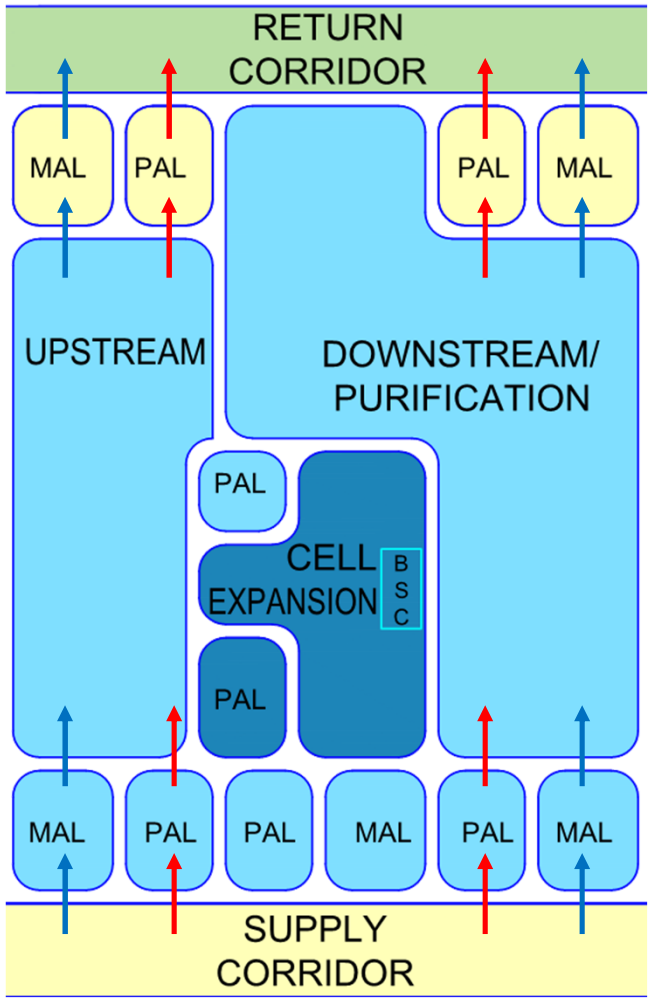
Impacted Facility Spaces



Facility Strategies: Unidirectional Flows

"Personnel (including QC and maintenance staff) and material flows…should be controlled…where possible utilizing unidirectional flows."

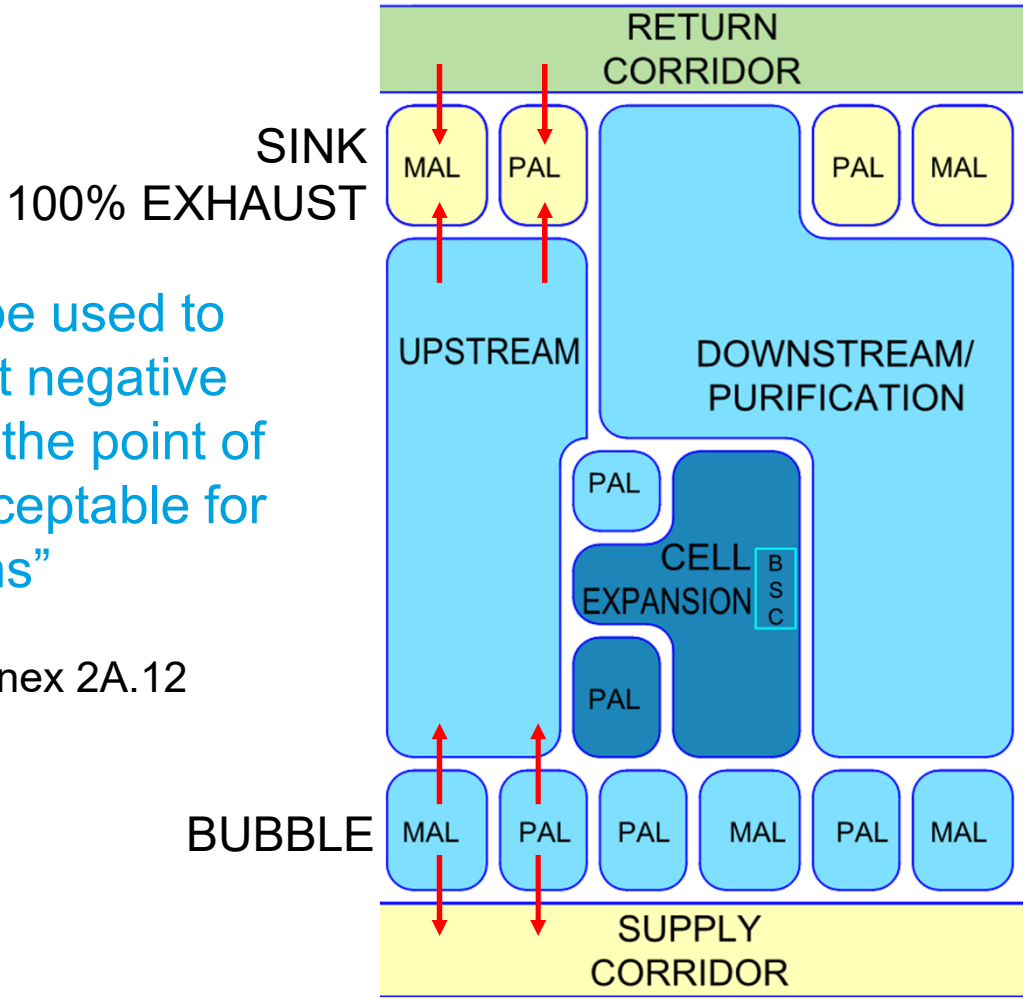
PIC/S PE 009-14 01Jul2018 Annex 2B9.4



Facility Strategies: Room Pressurization

"Positive pressure should be used to process sterile products but negative pressure in specific areas at the point of exposure of pathogens is acceptable for containment reasons"

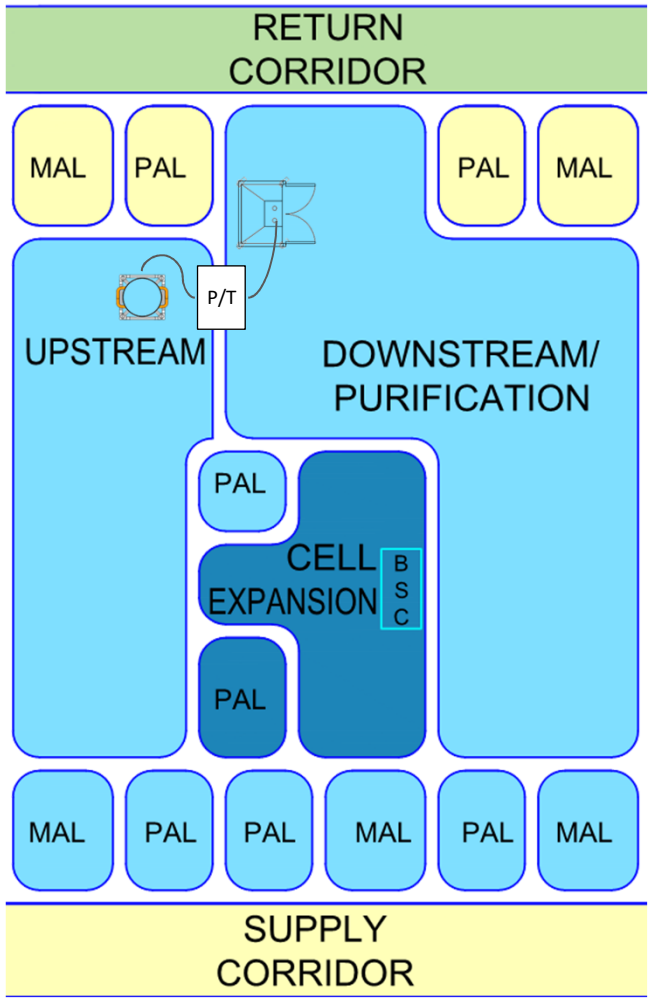
PIC/S PE 009-14 01Jul2018 Annex 2A.12



Facility Strategies: Pass-Through Transfers

"Products, equipment, ancillary equipment and disposable items are only moved within and removed from such areas in a manner that prevents contamination of other areas"

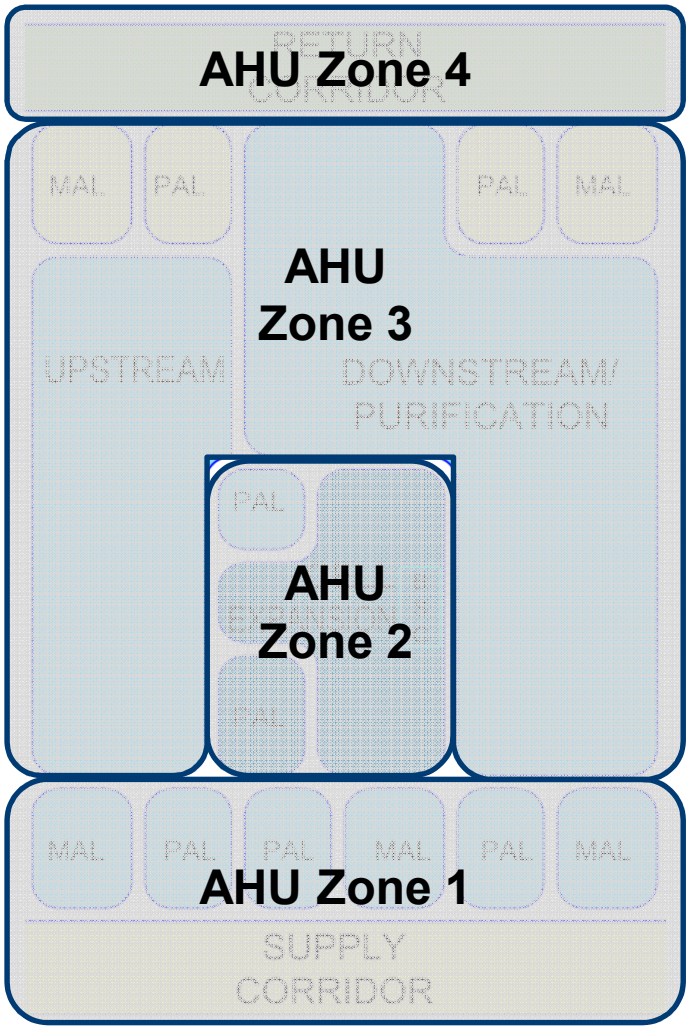
PIC/S PE 009-14 01Jul2018 Annex 2A.8e



Facility Strategies: Product Specific Airflow

"Air handling units should be designed, constructed and maintained to minimize the risk of cross-contamination between different manufacturing areas and may need to be specific for an area."

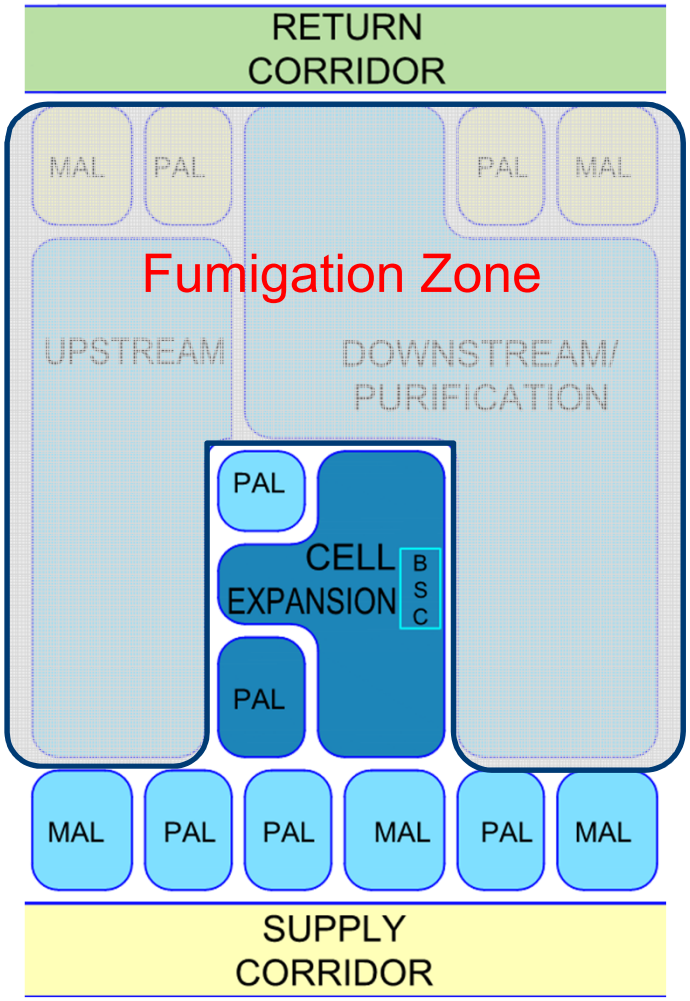
PIC/S PE 009-14 01Jul2018 Annex 2A.11



Facility Strategies: Fumigation

"Concurrent manufacture of different viral gene therapy vectors in the same area is not acceptable. "

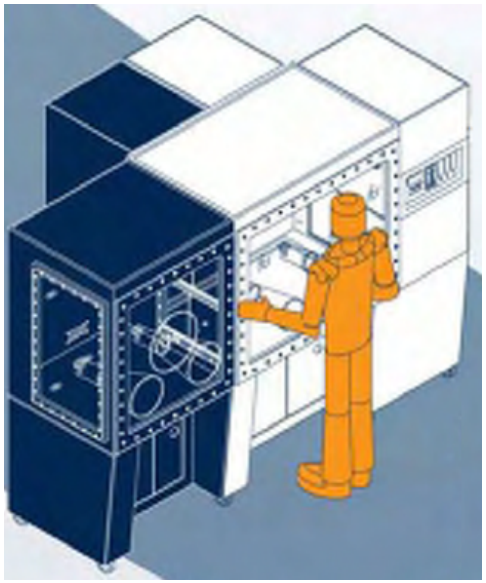
PIC/S PE 009-14 01Jul2018 Annex 2B9.



ENABLING
TECHNOLOGIES

Isolators

"The use of more than one closed isolator (or other closed systems) in the same room at the same time is acceptable"



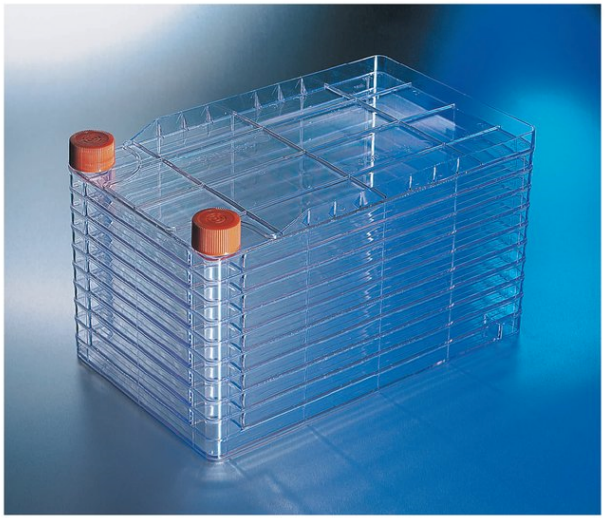
Xvivo system by BioSpherix

"When two isolators are used to process different viral vectors within the same room there should be 100% air exhaustion from the room and the facility"

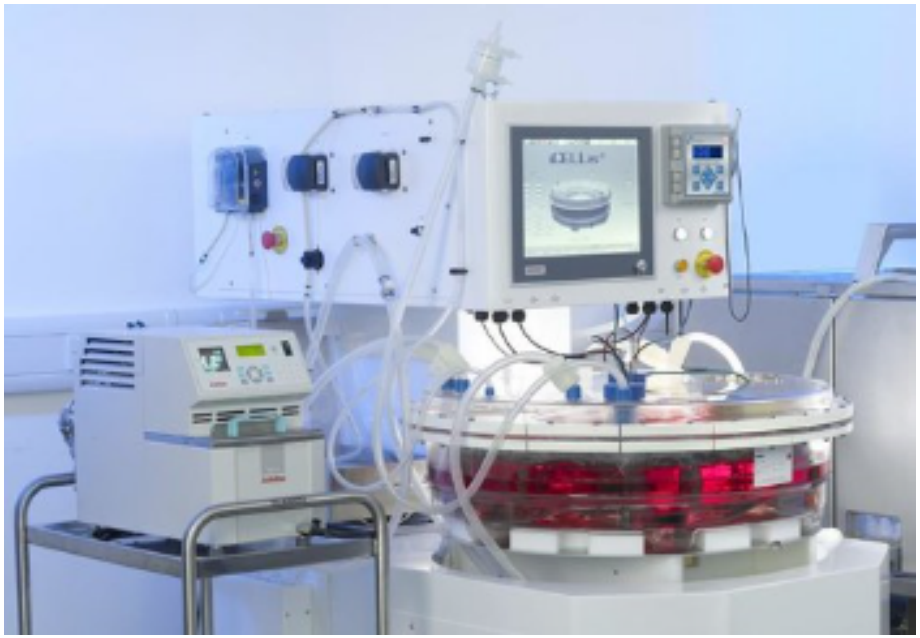
EudraLex Guidelines on GMPs for ATMPs
22Nov2017 4.19

Adherent Technology

- Anchorage dependent cells
- Growth is limited by surface area
- Cells must be removed either mechanically or chemically



CellSTACK® Chambers by Corning

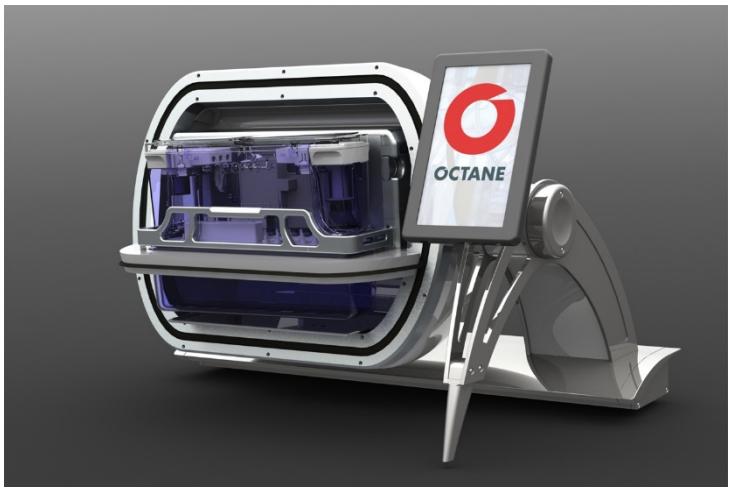


iCellis® 500 System Bioreactor by Pall

Cell Therapy Technology

CliniMacs Prodigy® by Miltenyi Biotec

Sepax Cell Separation System



Octane Cocoon™ by Octane Biotech

HEPA Filtered Pass-Throughs

"Pass through hatches without active filtered air supply should be avoided"

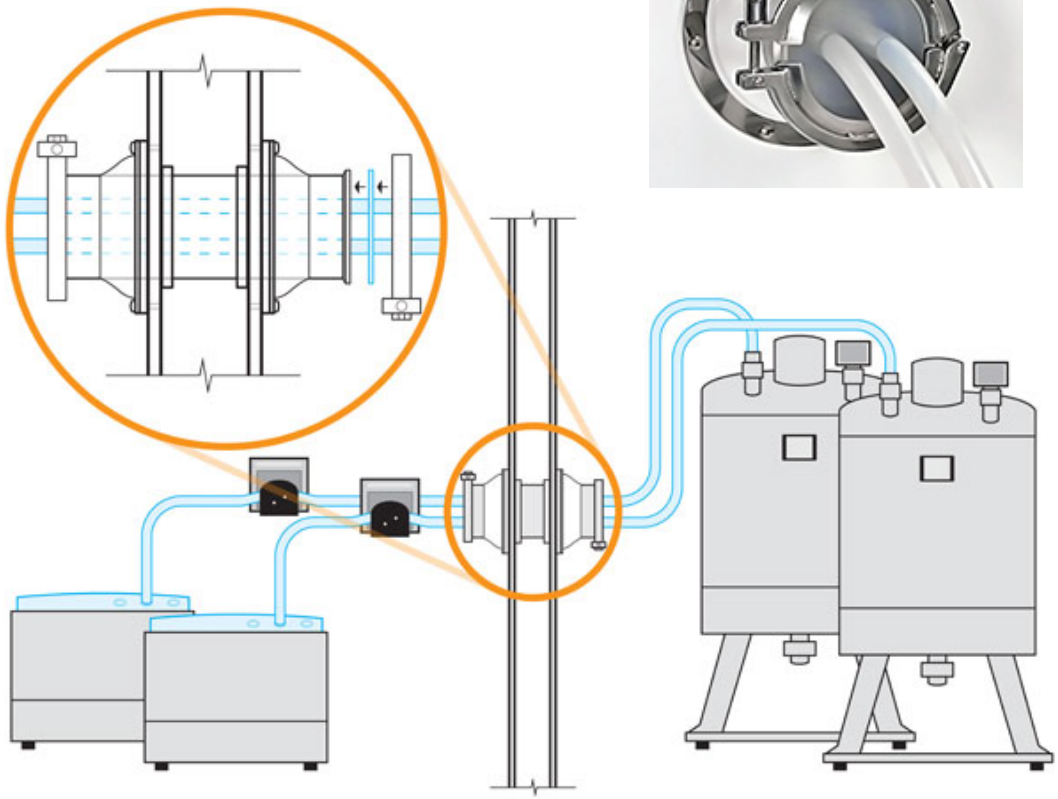
EudraLex 2017 Consultation Document Annex 1 5.9.b.i

Recirculating HEPA-filtered pass-through by Terra Universal

Tubing Pass-Throughs

"Pass through hatches without active filtered air supply should be avoided"

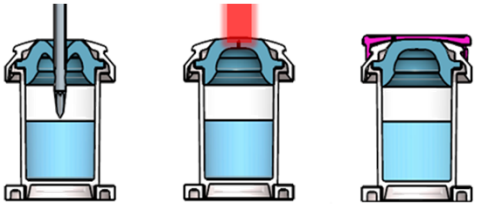
EudraLex 2017 Consultation Document Annex 1 5.9.b.i



AdvantaPass by AdvantaPure

Filling Line Technology

Crystal® PX Filling Line



AT-Closed Vials®

GENiSYS® Aseptic Filling System by AST

SUMMARY

Industry Guidance

BioPhorum Operations Group
Connect · Collaborate · Accelerate

CMaT
NSF Engineering Research Center for Cell Manufacturing Technologies

NIST National Institute of Standards and Technology U.S. Department of Commerce AMTECH
Georgia Research Alliance
Georgia Institute of Technology
Prepared by NEXIGHT GROUP

Summary

Facility Design

- Unidirectional Flow
- Cross-Contamination Prevention
- BSL-2 Design

Process Design

- Single-Use Technology
- Reduced Scale
- Aseptic Processing
- Specialized Equipment

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