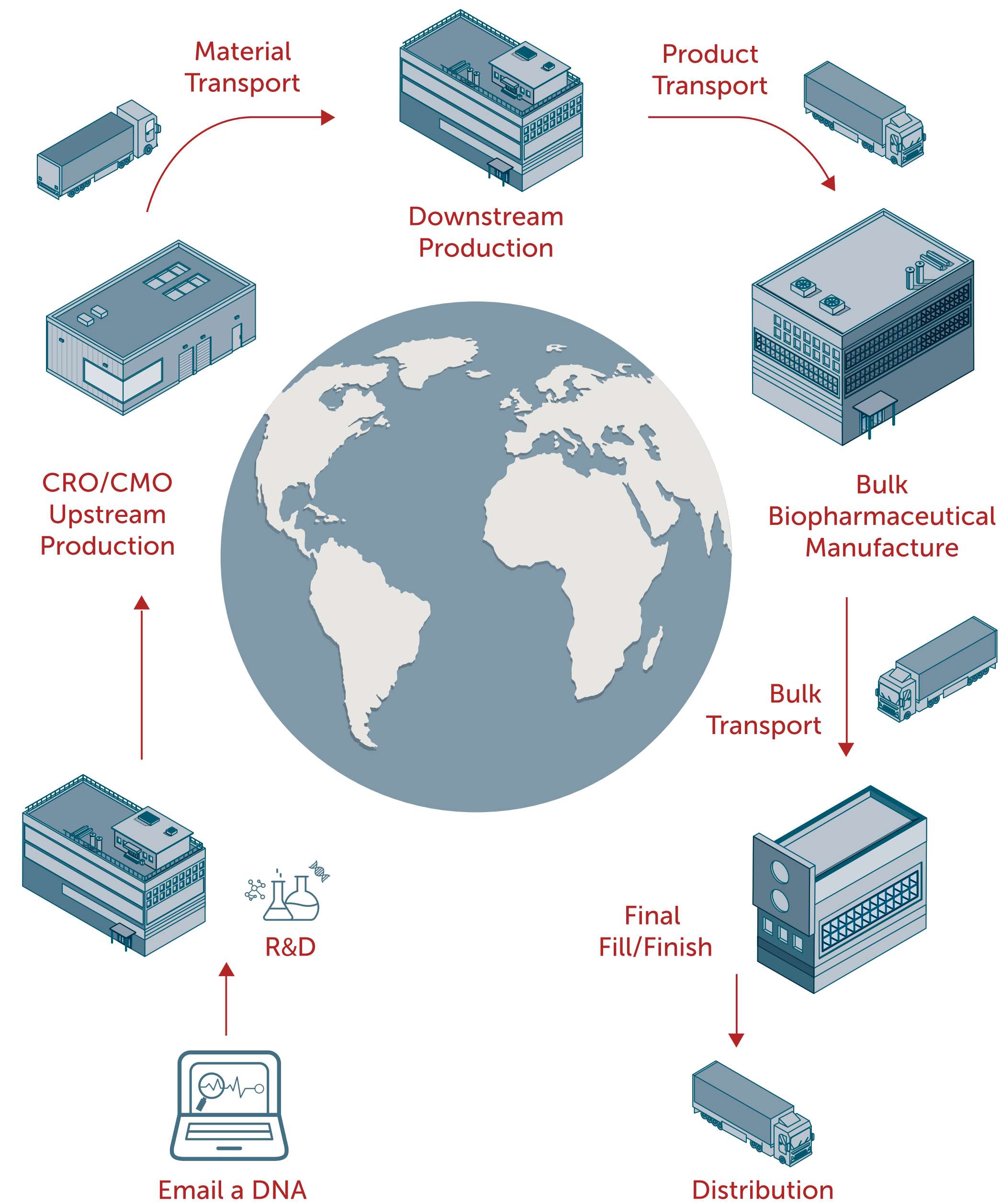


## ABSTRACT

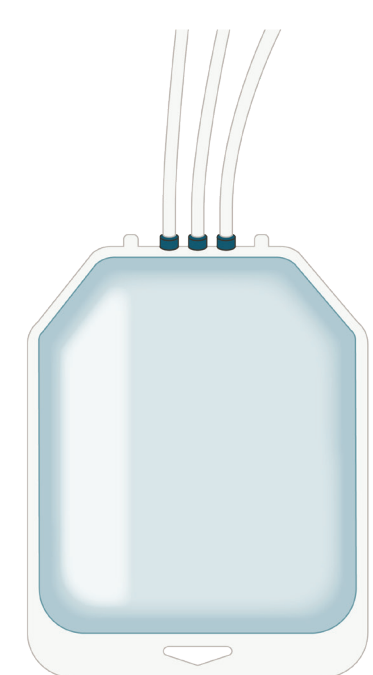
Disposable solutions are now widely accepted as the gold standard in the biopharmaceutical industry covering every single step of drug manufacturing. From early-stage small scale R&D projects, upstream production with several thousand-liter bioreactors, downstream process, API formulation up to critical fill/finish and transport applications, the industry is shifting from traditional processes to take advantage of single-use technology benefits.



## MATERIAL AND METHODS

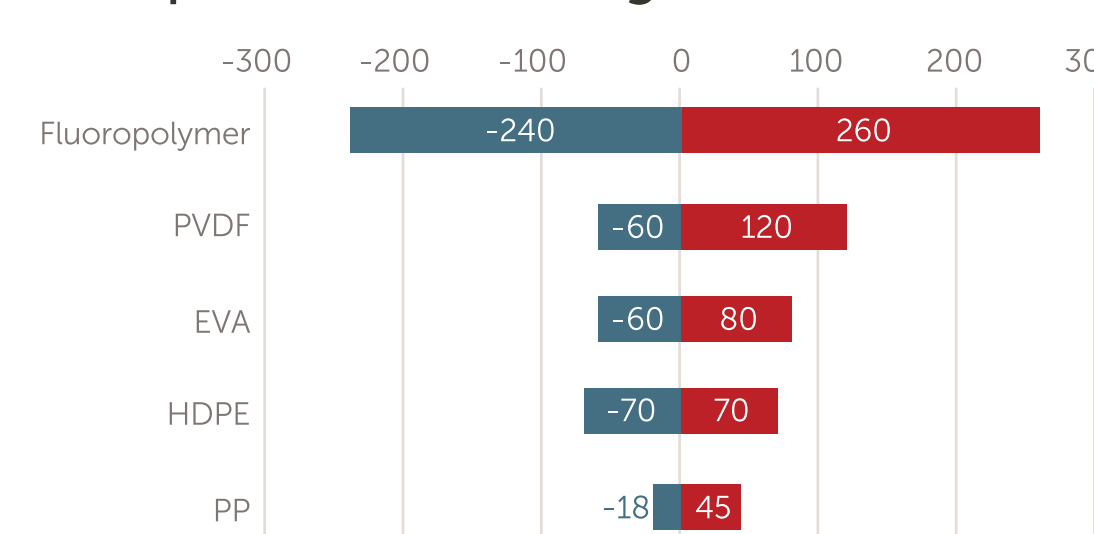
Entegris' commercially available gamma stable, fluoropolymer film has been used to support various applications such as large-scale bioprocessing/banking of mammalian cells (intensification), bulk drug substance (BDS), cell and gene therapy (adenovirus), critical vaccinology program (mRNA-LNP/liposomes), as well as protein-based therapeutics at large, industrial scales worldwide.

### Aramus™ Fluoropolymer Bag

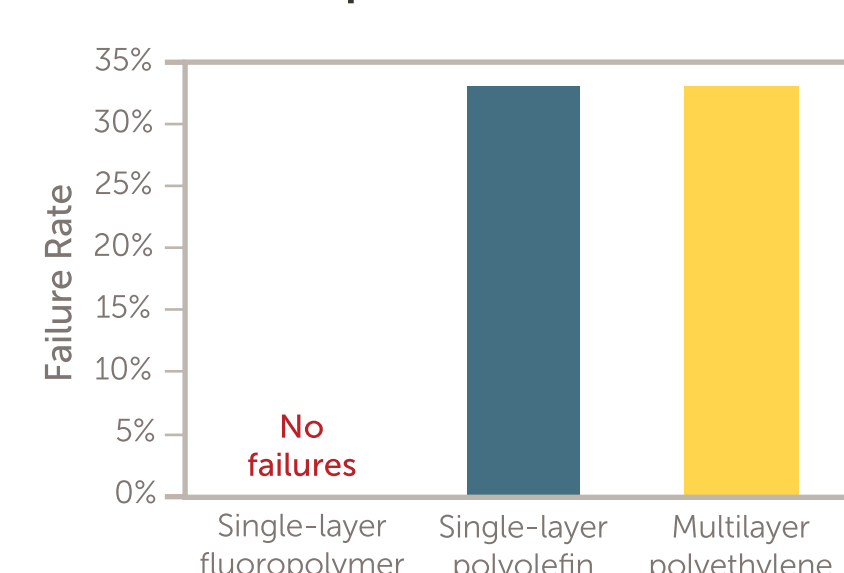


- No polymer additives
- No adhesives
- No catalysts
- Single layer fluoropolymer contact
- Extremely low E&L profile
- Inert
- Gamma stable
- No glass transition

### Temperature Use Range (°C)



### Frozen Drop Performance



### Chemical Compatibility

Chemical	PE	EVA	Fluoropolymer
Dimethyl sulfoxide (DMSO)	Go	Go	Go
Hydrofluoric acid	Go	Go	Go
Sodium citrate	Go	Go	Go
Polyethylene glycol	Go	Go	Go
Ethanol	Go	Go	Go

Legend: Go (Blue), Caution (Yellow), Stay (Red), Data not found (Grey)

### Film Summary

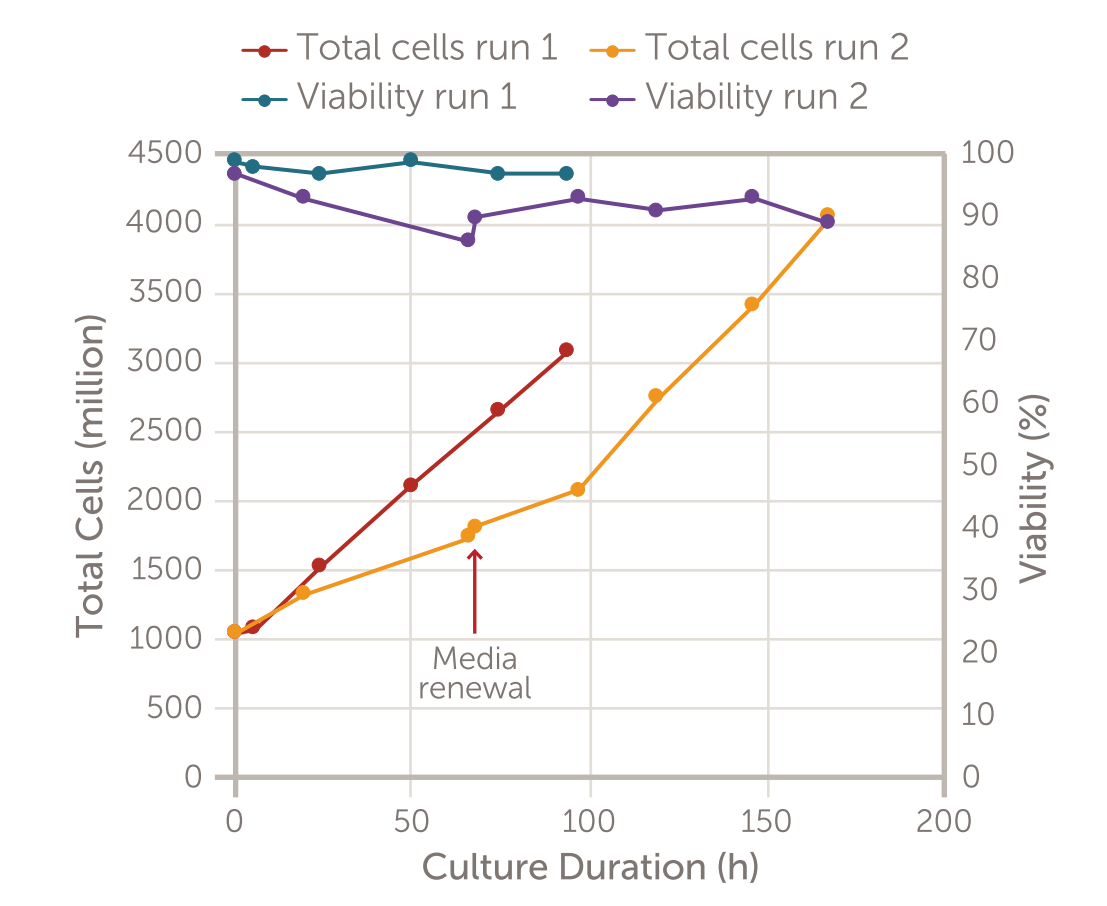
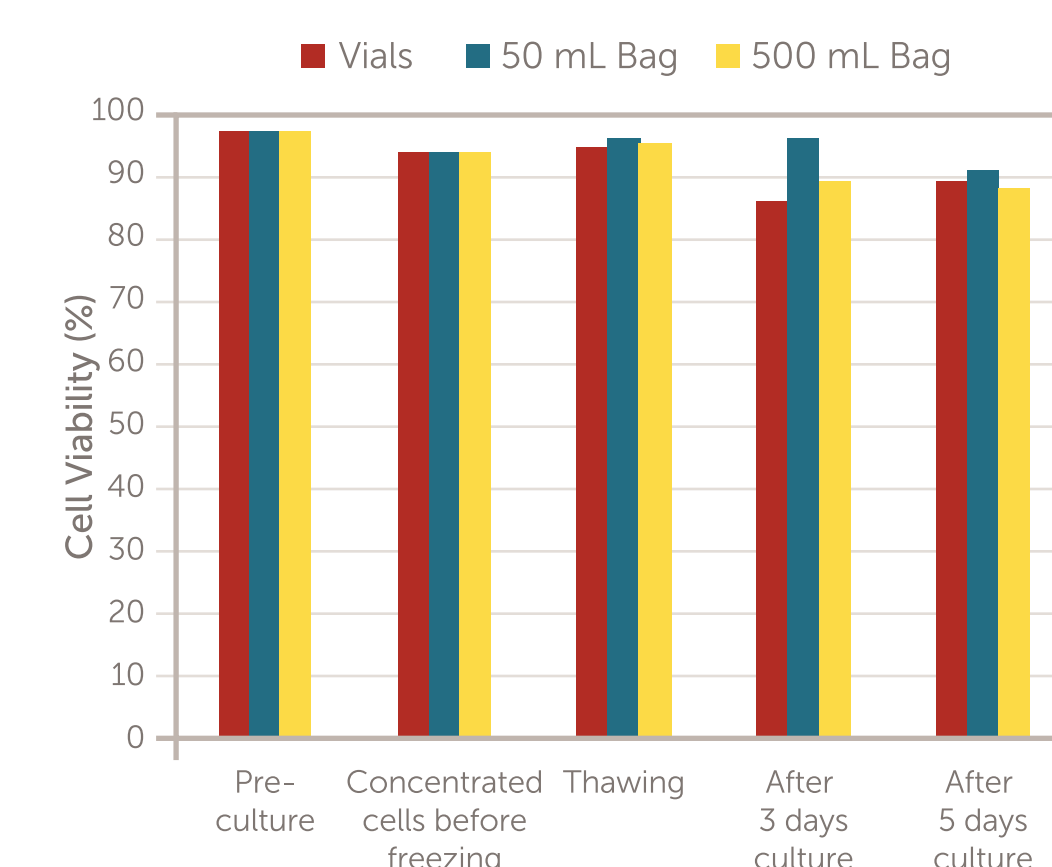
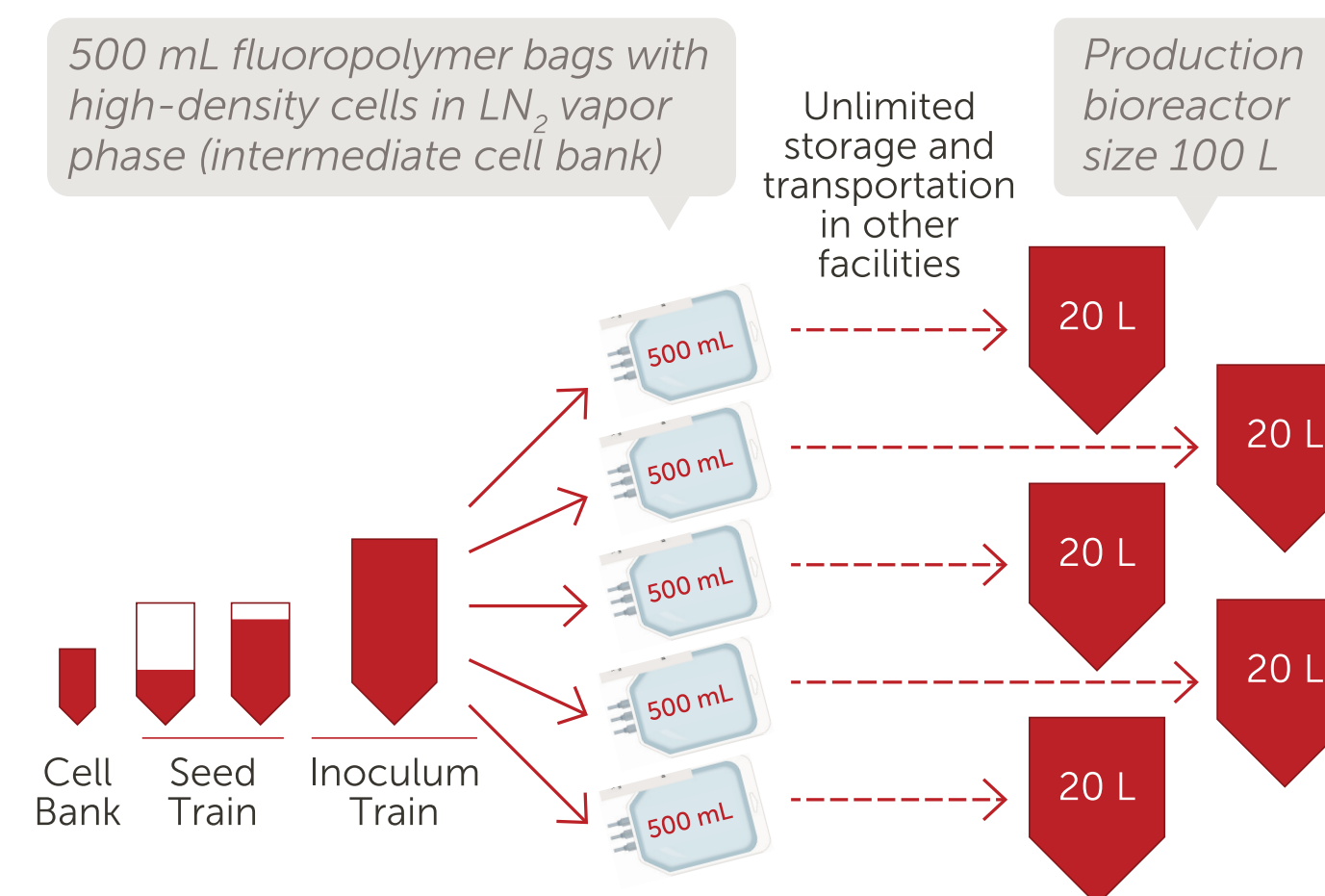
Polymeric Film	Regulatory	Temp. range	Chemical inertness	Glass transition	E&L	-80°C performance	Gamma irradiation
Aramus™ Fluoropolymer	Go	Go	Go	Go	Go	Go	Go
EVA	Go	Go	Go	Go	Go	Go	Go
PE/EVOH/PE	Go	Go	Go	Go	Go	Go	Go

Legend: Go (Blue), Caution (Yellow), Not recommended (Red)

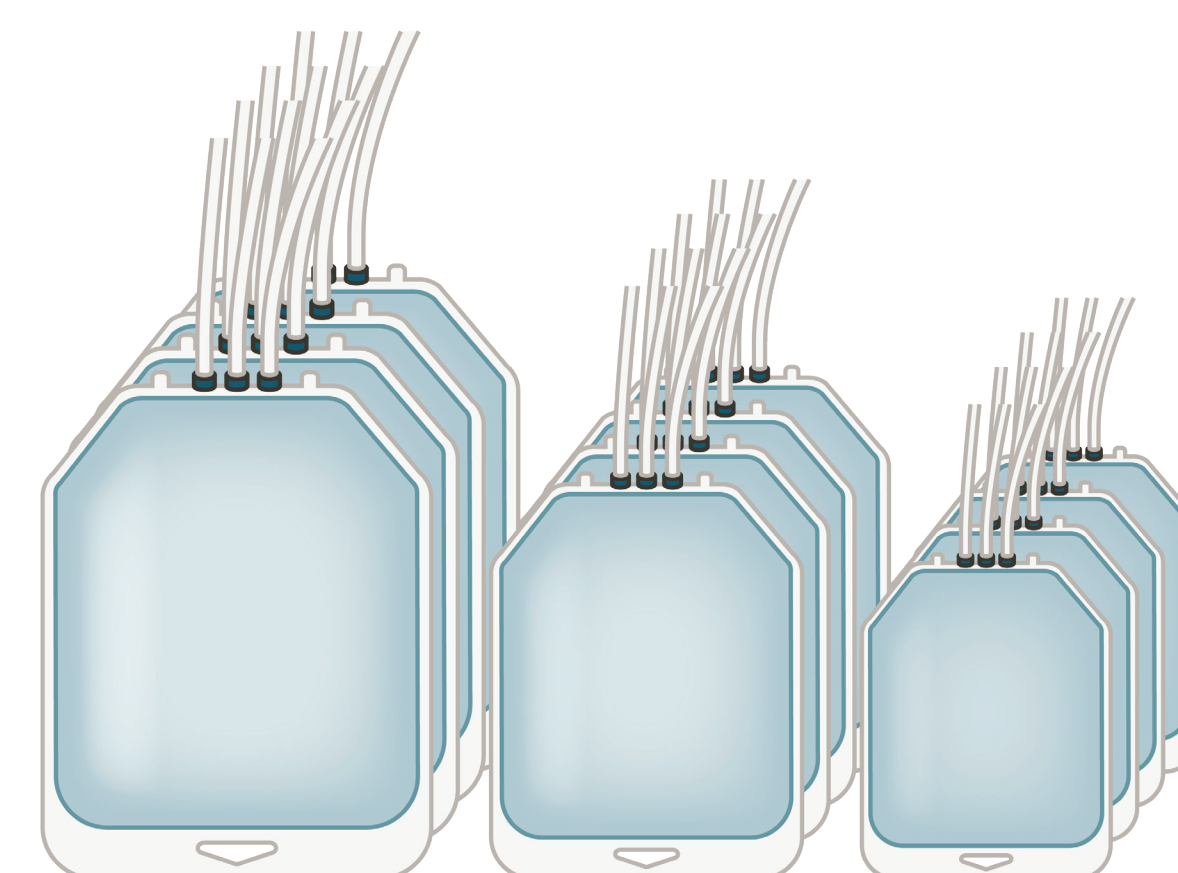
## RESULTS

Bypassing traditional biomanufacturing and disposable multilayered films

### High-Density Cell Banking

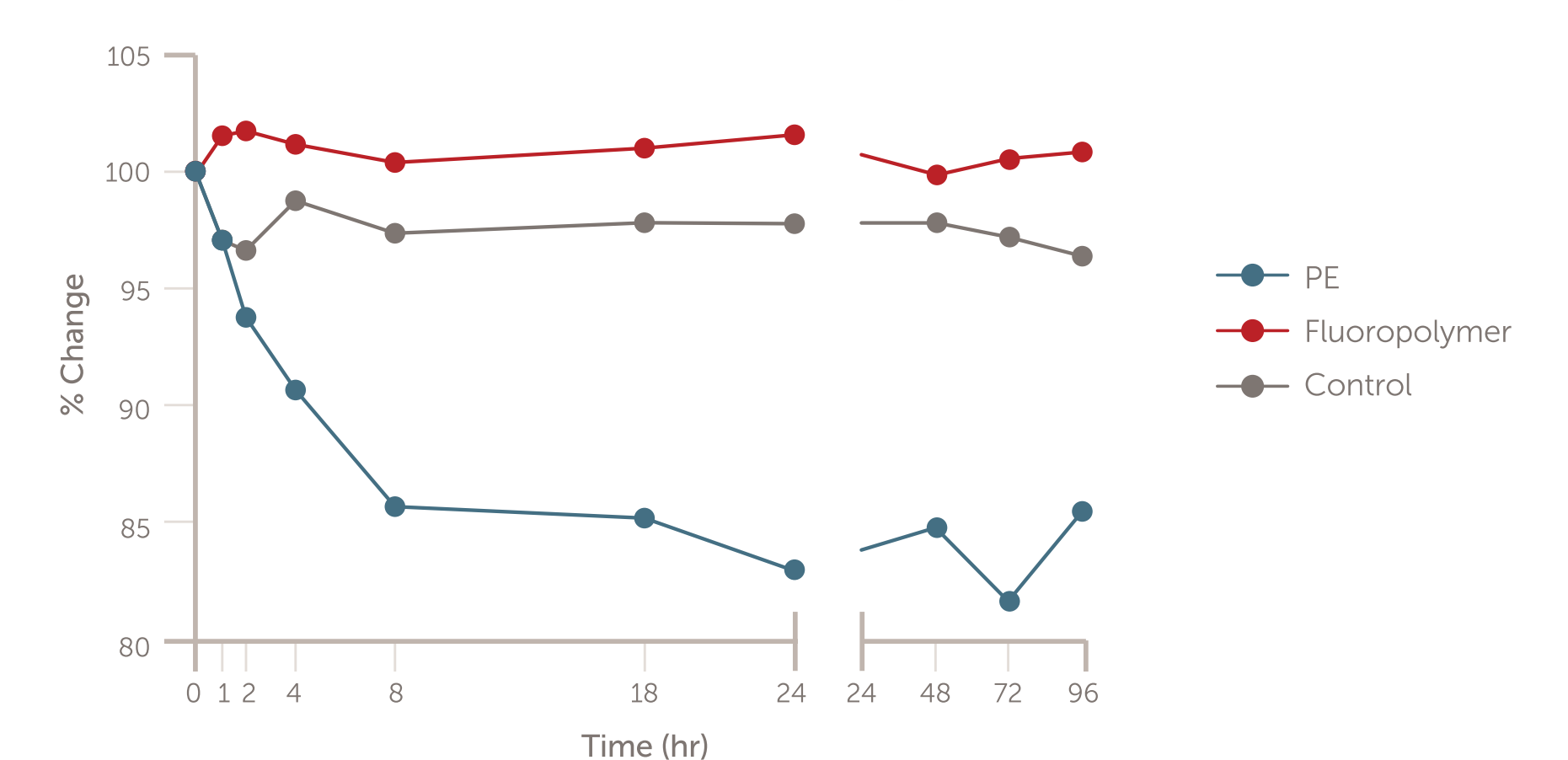


### COVID-19 Global Response/Vaccinology



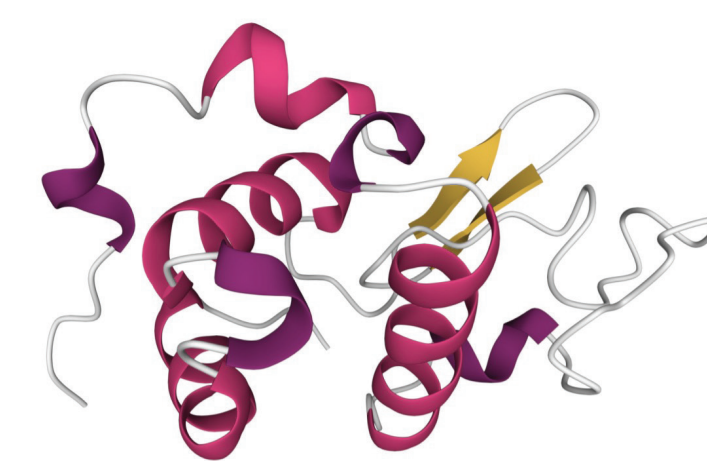
### Cell and Gene Therapy

#### Adeno Associated Virus (AAV) 5 Adsorption (HPLC)

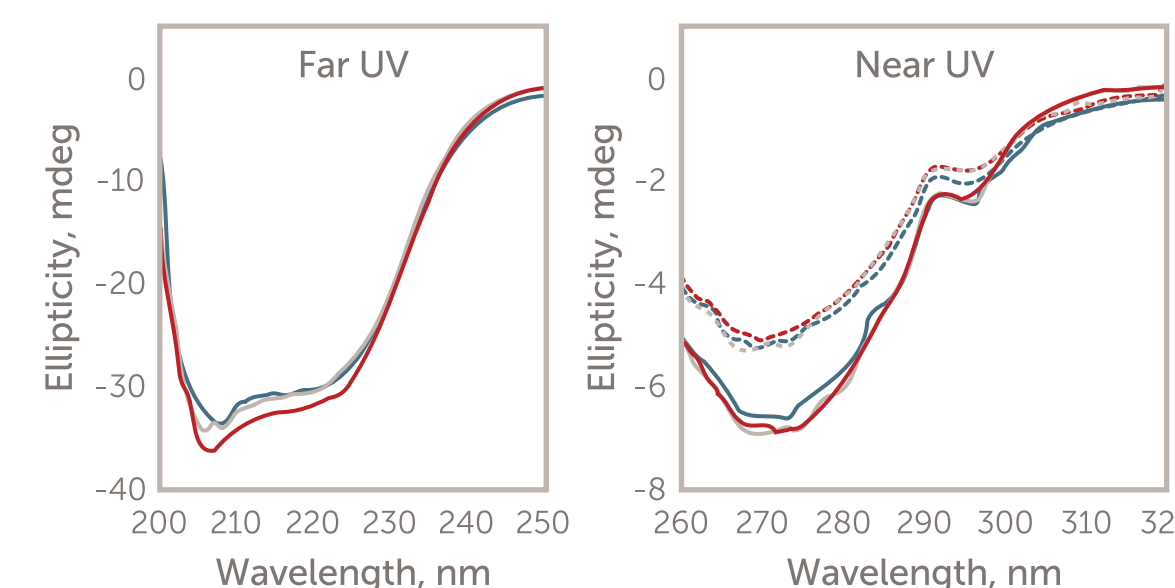


### Protein-Based Therapeutics

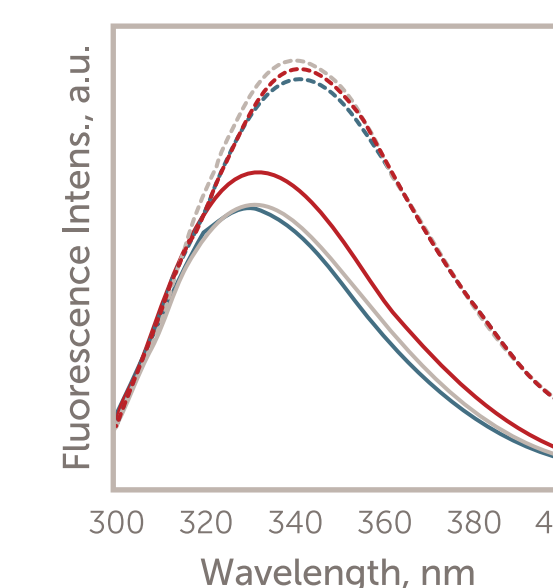
#### PDB ID: 1A4V



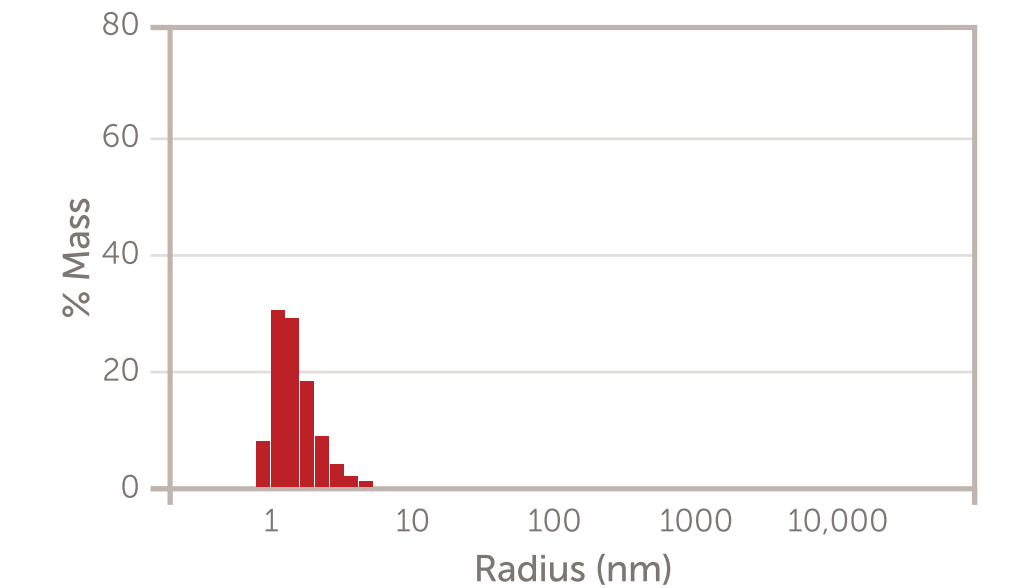
#### Circular Dichroism



#### Fluorescence



#### Particle Sizing (DLS)



- Aramus fluoropolymer bag demonstrates superior adsorption profile compared to regular multilayered PE films
- Seed train process has been redesigned, switching from vials and flasks to Aramus single-use fluoropolymer technology, which can be frozen and stored with the highest cell concentration and then used directly to inoculate a large-scale bioreactor
- Compared to PE material, fluoropolymer material demonstrates minimal AAV viral vector adsorption when held at room temperature for three days

- The Aramus bag assembly is a closed system, which reduces contamination risks
- No significant aggregation detected in Aramus bag after one (short-term storage) and four freeze/thaw cycles (long-term storage)
- No degradation/chemical modifications during storage in Aramus bag assembly

## CONCLUSIONS AND PERSPECTIVES

- Confirmation of protein/virus/cells integrity with our commercially available gamma-stable fluoropolymer
- Fluoropolymer layer is inert and smooth, has low surface energy, and has universal chemical resistance
- No impact on conformation and chemical integrity of protein at small and large scale
- Use of SPOS and DLS particle sizing technology is routine to screen and monitor aggregations
- Combine with single-use sensors and digital twin for Industry 4.0
- Used from high-density cell banking, gene therapy, to the transport of biologic/therapeutic compounds
- Validation of new applications (cell culture, other molecular scaffolds of biotechnological interest, personalized medicine)



\*Corresponding author, Julien Muzard, julien.muzard@entegris.com