

Supply chain efficiency and sourcing for scaling your gene therapy operation

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Scale-up for clinical and commercial gene therapy manufacturing impacts both process and operations. In the wake of SARS-CoV-2, supply chains have been significantly challenged and raw materials are in short supply. As the potential of gene therapies is being realized, long-term sustainable manufacture needs to be considered.

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Manufacturers of viral vector-based gene therapies implemented a single-use strategy early when setting up new manufacturing facilities. However, format, packaging, shipment, and storage are all key elements to ensure efficient operations and mitigate supply chain disruption risk moving forward. Moving from standard media and single-use technologies to configurable solutions will help future sourcing and increase operations performance.

Thermo Fisher Scientific offers a number of configurable packaging and mixing technologies, alongside various cell culture media formats. These configurable solutions solve many problems in manufacture scale-up, such as logistical space management challenges.

CONFIGURABLE PACKAGING

There are many BPC design options including varied tubing, connectors, and clamps. BPC totes (Figure 1) are important for ease-of-use and handling. Reusable outer support containers hold liquid-filled BPCs. Thermo Fisher Scientific has the largest and only truly networked single-use manufacturing organization in the world. The network approach consists of 5 networked sites, 7 regional assembly centers for manufacturing redundancy, and 3 Centers of

Figure 1. BPC totes.



Plastic totes for 10-20 L 2D BPCs
Stackable
Easy tube set access

Plastic cylindrical tanks for 50-250 L 3D BPCs
Shipping qualified
Options for top and bottom drain

Plastic 4-sided totes for 100-1000 L 3D BPCs
Shipping qualified
Options for top and bottom drain

Steel 4-sided totes for 100-3,000 L 3D BPCs
Lacklented totes, load cells, hoists optional
Options for top and bottom drain

Excellence. We work closely with our customers to troubleshoot or innovate to find a way to meet even the most unique requirements.

CELL CULTURE MEDIA

When it comes to media, choice of format is key to both increasing efficiency and de-risking the supply

chain. Pre-made liquids, Advanced Granulation Technology (AGT), and dry powder media each have their own pros and cons (Figure 2). However, dry formats are generally preferred for large-scale manufacture due to their smaller footprint. Gibco's AGT format offers the advantage over standard dry powder of a

Figure 2. Media format pros and cons.

Pre-made liquids & concentrates	Advanced granulation technology (AGT) format	Dry powder media
<ul style="list-style-type: none"> - Ready to use - Suitable for aseptic processing - 'Dry' facility 	<ul style="list-style-type: none"> - One-part media supporting large scale media preparation - Flexible choice of liquid container - Longer stability - Safety stock 	<ul style="list-style-type: none"> - Options for supply redundancy - Flexible choice of liquid container - Longer stability
<ul style="list-style-type: none"> - Higher storage footprint - Shorter stability - Cold shipment 	<ul style="list-style-type: none"> - Non aseptic - WF infrastructure - Higher control of QC/QA 	<ul style="list-style-type: none"> - pH/metallity adjustment required - Dust generation - Multiple part numbers

Figure 3. Thermo Scientific™ mixing technologies.



Thermo Scientific™ ImpULSE™ Single-Use Mixer (SUM):
bottom mounted - rolling diaphragm; water jacket; load cells; hoist & inflate options

Thermo Scientific™ HyPerforma™ Single-Use Mixer (SUM):
top mounted - marine impeller; water jacket; load cells; hoist options

Thermo Scientific™ HyPerforma™ DS 300 Single-Use Mixer (SUM):
decking; top mounted marine impeller

Thermo Scientific™ HyPerforma™ Mixtainer System:
stir bar impeller

simplified, one-part media formulation, as well as flexibility and stability benefits.

MIXING TECHNOLOGIES

Choice of mixer should be dependent on current and future process needs. Thermo Fisher caters to a variety of mixing needs (Figure 3). Considerations include BioProcess Container (BPC) deployment, room dimension, temperature control, cost-benefit, and scale-up volumes.

Your mission is our mission. As your supplier, we strive to exceed expectations and provide stability during disruption so you can keep pace with evolving market needs. This includes offering end-to-end supply chain resiliency by investing in capacity, capabilities, and quality systems.

Q&A

What if we cannot increase our storage space?

Celine Martin: When it comes to media, it depends on how your facility has been designed. If a buffer or media preparation area has been built-in, then going for dry format can save space. If it has not been built-in, we offer a GMP storage service that can help you increase your storage space while you develop other facilities.

Don Young: There is a program in place known as Forward PO, which is another way to maximize storage space on site. We do not build or deliver until right before it is needed. We work closely with the customer

to plan a delivery date. We build 30 days beforehand, and the product arrives 48 hours before it is needed in the production area cleanroom, ready for use.

How do you manage the shortage of single-use plastic for biopharmaceutical use?

Don Young: This challenge is COVID-related. The choice of materials and suppliers is critical – we encourage multiple sourcing. We encourage sourcing materials on a material construction basis rather than a specific part number. Rather than supplying a specific filter, we would encourage you to look at membrane-based options to give longer term flexibility in suppliers.