Gibco Bulk Process Liquid and Buffer Capabilities

Becky Moore, PhD
Senior Product Manager, Large Volume Liquids

May, 2019
Global BioProduction Manufacturing Facilities

**Logan, Utah**
- BioProcess Containers
- Single-use technologies
- Class 10,000/ISO 7 clean room

**Matamoros, Mexico**
- BioProcess Containers
- Single-use technologies
- ISO 13485
- cGMP standards

**Bedford and Framingham, MA**
- Chromatography resins
- ISO 13485

**Grand Island, NY**
- Cell culture media, reagents
- Sera
- ISO 13485
- GMP 21 CFR 820

**Paisley, Scotland**
- Cell culture media, reagents
- ISO 13485
- GMP 21 CFR 820

**Grand Island, NY**
- Cell culture media, reagents
- Sera
- ISO 13485
- GMP 21 CFR 820

**Lillestrom and Oslo, Norway**
- Invitrogen™ Dynabeads™ Magnetic Beads
- ISO 9001– and ISO 13485–certified

**Warrington, UK**
- Analytics kits

**Naarden, the Netherlands**
- Affinity ligands
- ISO 9001–certified

**Millersburg, PA**
- BioProcess Containers
- Single-use technologies
- ISO 13485
- cGMP standards

**Matamoros, Mexico**
- BioProcess Containers
- Single-use technologies
- ISO 13485
- cGMP standards
Gibco Media Network

US manufacturing
Grand Island, New York

EMEA manufacturing
Paisley, Scotland

Dry powder media
AGT media
1X media/buffer
Concentrated media/buffers

Serving over 110 commercial therapies worldwide
Benefits to Outsourcing Bioprocess Liquid Manufacturing

### Advantages

- Better product consistency
- Improved cell culture performance
- Suppliers of liquids are knowledgeable and experienced
- Fewer contamination risks
- Eliminate need for mixing tanks
- Time and labor-intensive steps eliminated:
  - QC of salts, liquid preparation, filtration, quarantine, finished good testing, documentation, procedures, validation
- Improved safety due to less handling
- Just-in-time logistics solutions
  - Doe & Ingalls™ cGMP warehousing (in US and Ireland)

### Customer benefit

- Decreased capital and operating costs
- Improved quality and compliance
- Increased productivity

Bulk process liquids and buffers help increase **biopharmaceutical process efficiency** and reduce risk by **simplifying and standardizing workflows**
Critical Attributes Help Ensure Product Integrity and Performance

Characteristics that determine whether a flexible container will **maintain product integrity** and perform as expected during specific bioprocess operations:

- Biological compatibility
- Tensile properties
- Puncture resistance
- Glass transition temperature
- Transportability
- Clarity
- Permeability
- pH stability
- Extractable profile
- Cell culture growth performance
- Stability
- Standard & custom designs
Expanded Choice of Secondary Packaging

1, 5, 10, and 20 L bioprocess containers
- Corrugate cases
- Returnable plastic crates

50, 100, and 200 L bioprocess containers
- Option to ship in different drum designs
- Bottom- or top-emptying
- Nestable
- Single-trip
- Hazardous material handling

100, 200, 500, and 1,000 L bioprocess containers
- ALLpaQ (Arca/Auer) plastic returnable systems
- Bottom- or top-emptying
- 100 and 200 L returnable containers available in EU
# Liquid Production Network

## Research

## Bioproduction

<table>
<thead>
<tr>
<th>Bottled liquids (10 mL–1 L)</th>
<th>Grand Island, USA</th>
<th>Paisley, Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bagged liquids (1–1,000 L)</th>
<th>Grand Island, USA</th>
<th>Paisley, Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Batch sizes (10–10,000 L)</th>
<th>Grand Island, USA</th>
<th>Paisley, Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Corrosive solutions (10–5,000 L)</th>
<th>Grand Island, USA</th>
<th>Paisley, Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td></td>
<td>Under development</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alcohols (up to 20% v/v ethanol) (400–2,500 L)</th>
<th>Grand Island, USA</th>
<th>Paisley, Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td></td>
<td>Under development</td>
</tr>
</tbody>
</table>

## Formulation

## Filtration

## Fill and finish

## Delivery

## Order management

## Dispensing

## Formulation

## Filtration

## Fill and finish

## Delivery
Grand Island Liquid Facility Investments

**Facility footprint**
- 15,000 ft² manufacturing over two floors
- 12,400 ft² finished goods warehouse space
- Clean room, gowning, storage, formulation, staging

**Equipment deployed**
- Multiple 10,000 liter tanks
- 5,000 liter tank
- 2,500 liter tank

**Support systems**
- WFI still
- HVAC
- Clean steam generation
- Electronic batch records

$21.8M investment to increase liquid manufacturing (5 million liters)

Additional capabilities added to include an alcohol suite to manage hazardous solutions

Grand Island facility expansion for Annex 1 compliant Animal Origin-Free bulk liquids
Design Criteria and Quality Standards

To meet current and future customer requirements for insourcing bulk liquids, our Grand Island manufacturing facility is built to and compliant with the following standards:

<table>
<thead>
<tr>
<th>Design criteria</th>
<th>Value</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO 13485</td>
<td>Internationally recognized standard on the requirements for a quality management system for medical devices</td>
<td>Industry standard</td>
</tr>
<tr>
<td>21 CFR 820–compliant</td>
<td>FDA current Good Manufacturing Practice (cGMP) quality system regulation for medical devices</td>
<td>Industry standard</td>
</tr>
<tr>
<td>Annex 1 standard</td>
<td>cGMP guidelines to harmonize US/EU controls and procedures to manufacture sterile medicinal products</td>
<td>Differentiator</td>
</tr>
<tr>
<td>Animal origin–free (AOF)</td>
<td>All raw materials are free of animal-derived components; dedicated AOF equipment</td>
<td>Differentiator</td>
</tr>
<tr>
<td>Grade C and grade D controlled spaces</td>
<td>Monitored and controlled temperature, pressure, air change rate for formulation and filtration</td>
<td>Differentiator</td>
</tr>
<tr>
<td>Single material flow</td>
<td>One-way raw material flow with no return to inventory; dedicated AO/AOF raw materials for manufacturing</td>
<td>Differentiator</td>
</tr>
<tr>
<td>Proximity to raw material and finished goods warehouse</td>
<td>Segregated AO/AOF raw material sampling booths; close proximity to manufacturing and distribution</td>
<td>Differentiator</td>
</tr>
<tr>
<td>2nd floor formulation</td>
<td>Gravity transfer to fill and filtration for ergonomic workflow; separate formulation suites for each tank</td>
<td>Differentiator</td>
</tr>
<tr>
<td>Manifold filling</td>
<td>Semiautomated closed manifold system</td>
<td>Differentiator</td>
</tr>
</tbody>
</table>
Examples of Customer Liquid Projects

Total liquid volume in 2018
- 12.4M liters of catalog and custom liquid products
- 8.4M liters Grand Island, NY, USA
- 4.1M liters Inchinnan, Scotland

<table>
<thead>
<tr>
<th>Liquid type</th>
<th>Gibco™ product and annual volume examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell culture media</td>
<td>GMEM: [66,000 L] 330 x 200 L bag</td>
</tr>
<tr>
<td></td>
<td>Custom media formulation: [462,500 L] 925 x 500 L bag</td>
</tr>
<tr>
<td></td>
<td>AIM V T cell Medium: 15,000 x 1 L bag</td>
</tr>
<tr>
<td>Feeds and additives</td>
<td>10% antifoam: [13,000 L] 2,600 x 5 L bag</td>
</tr>
<tr>
<td></td>
<td>CHO CD EfficientFeed™ A supplement: [3,800 L] 760 x 5 L bag</td>
</tr>
<tr>
<td></td>
<td>BME: 8,130 x 1 L bottle</td>
</tr>
<tr>
<td>Bioprocess liquids</td>
<td>Sodium citrate: [90,000 L] 450 x 200 L bag</td>
</tr>
<tr>
<td></td>
<td>PBS: [32,000 L] 1,600 x 20 L bag</td>
</tr>
<tr>
<td></td>
<td>WFI: [28,000 L] 2,800 x 10 L bag</td>
</tr>
<tr>
<td></td>
<td>HEPES: [29,000L] 29 x 1,000 L bag</td>
</tr>
<tr>
<td>Concentrates</td>
<td>CD CHO concentrate: [296, 400 L] 1,800 x 150 L bag + 1,320 x 20 L bag</td>
</tr>
<tr>
<td></td>
<td>1,000X CD lipids: [3,900 L] 1,950 x 2 L bottle</td>
</tr>
</tbody>
</table>

Gibco BioProduction services
- Media / buffer / concentrate development
- Process development
- Scale-up / technology transfer
Large Volume Powder Repacks

Single Component Goods
Finished in GMP controlled dispensing suites
- Available in Securitainers (≤ 1Kg)
- Available in Ropak buckets (1 – 10Kg)
- Dose specific weights offered
- Chemicals may include:
  - Tris
  - Sodium bicarbonate
  - Glucose

Multi-Component Buffers
Manufactured in GMP powder facility
- Available in Powdertainers (1 – 25Kg)
- Available in Securitainers (≤ 1Kg)
- Available in Ropak buckets (1 – 10Kg)
- Dose specific weights offered
- Includes custom formulations

Pre-Weighed Powders
- Eliminate labor intensive weighing steps with ready-to-use liquid or dry formats for catalog and custom formulations
- Custom packaging available to simplify connections at point-of-use
- Provide customers ease of shipping
## Case Study: 0.1 M NaOH buffer cost analysis

<table>
<thead>
<tr>
<th></th>
<th>In-house</th>
<th>ThermoFisher Scientific</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Batch size</strong></td>
<td>2,000 L</td>
<td>10,000 L</td>
</tr>
<tr>
<td><strong>Batches per year</strong></td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td><strong>QC releases</strong></td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td><strong>Prep time (2,000 L)</strong></td>
<td>4 hours</td>
<td>1 hour</td>
</tr>
<tr>
<td><strong>Annual prep time</strong></td>
<td>10 days</td>
<td>2.5 days</td>
</tr>
<tr>
<td><strong>Total batch cost</strong></td>
<td>$11,500</td>
<td>$35,000</td>
</tr>
<tr>
<td><strong>Per liter cost</strong></td>
<td>$5.75</td>
<td>$3.50</td>
</tr>
<tr>
<td><strong>Annual prep time</strong></td>
<td>$230,000</td>
<td>$140,000</td>
</tr>
</tbody>
</table>

- **$90,000** annual savings
- **75% reduction** in prep time
- **80% reduction** in lot testing
Buffer Economic Model

Buffer prep decisions require accurate economic cost models to evaluate options, including make vs. buy

Eric Langer, BioPlan Associates

- Interviewed 10 end-users to understand buffer prep costs
- Aggregated end-use supplied data ranges

Buffer prep data entry guide

- Identify ranges for unknown costs
- Clarify cost definitions
- Ranges based on actual data collection

Additional information

- Contract pharma: Economics of in-house buffer preparation
- BioProcess International: Outsourcing of buffer preparation activity is increasing

**Trend in Outsourcing Upstream Production Operations**

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>45.4%</td>
</tr>
<tr>
<td>2015</td>
<td>42.1%</td>
</tr>
<tr>
<td>2014</td>
<td>44.0%</td>
</tr>
<tr>
<td>2013</td>
<td>48.1%</td>
</tr>
<tr>
<td>2012</td>
<td>34.4%</td>
</tr>
<tr>
<td>2011</td>
<td>32.1%</td>
</tr>
<tr>
<td>2010</td>
<td>20.7%</td>
</tr>
</tbody>
</table>

**Trend in Outsourcing Downstream Production Operations**

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>45.4%</td>
</tr>
<tr>
<td>2015</td>
<td>38.9%</td>
</tr>
<tr>
<td>2014</td>
<td>39.6%</td>
</tr>
<tr>
<td>2013</td>
<td>51.9%</td>
</tr>
<tr>
<td>2012</td>
<td>33.3%</td>
</tr>
<tr>
<td>2011</td>
<td>30.7%</td>
</tr>
<tr>
<td>2010</td>
<td>27.9%</td>
</tr>
</tbody>
</table>
## Cost Analysis Model

### Start here: Input your facility's annual liters buffer production

250,000 liters

### Fixed expenses, buffer prep equipment

<table>
<thead>
<tr>
<th>Item</th>
<th>Calculated annual expenses</th>
<th>Your facility's cost: Input here</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital facility expenses, (Buffer Prep Bldg-excl. Equip/HVAC)</td>
<td>$184,936</td>
<td>$1,500,000</td>
</tr>
<tr>
<td>WFI (or RO) skid, tanks/piping (cost allocated to buffer prep-hardware)</td>
<td>$42,679</td>
<td>$190,000</td>
</tr>
<tr>
<td>Mixed buffer-only storage/holding tanks</td>
<td>$17,970</td>
<td>$80,000</td>
</tr>
<tr>
<td>Classified HVAC systems (allocated to buffers)</td>
<td>$73,975</td>
<td>$600,000</td>
</tr>
<tr>
<td>Refrigerated storage unit (allocated to buffers)</td>
<td>$36,304</td>
<td>$700,000</td>
</tr>
<tr>
<td>Warehousing, facility operations, annual</td>
<td>$10,000</td>
<td>$10,000</td>
</tr>
<tr>
<td>Utilities,  electric, gas, used in buffer prep areas</td>
<td>$80,000</td>
<td>$80,000</td>
</tr>
<tr>
<td>Other buffer prep equipment</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Other facilities construction</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Automation of equipment for mixing</td>
<td>$60,000</td>
<td>$60,000</td>
</tr>
<tr>
<td>Filtration (equip. only, excl filter cost)</td>
<td>$35,000</td>
<td>$35,000</td>
</tr>
<tr>
<td>Other equipment</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Fixed costs subtotal</td>
<td>$590,864</td>
<td>$3,264</td>
</tr>
</tbody>
</table>
| Fixed costs per liter                                                | $2.36                      |\n
### Variable/staffing expenses, buffer prep

<table>
<thead>
<tr>
<th>Item</th>
<th>Calculated annual expenses</th>
<th>Your facility's cost: Input here</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation/documentation, for buffers</td>
<td>$200,000</td>
<td>$200,000</td>
</tr>
<tr>
<td>Logistics, in-house</td>
<td>$40,000</td>
<td>$40,000</td>
</tr>
<tr>
<td>Quality control lab costs for buffers</td>
<td>$150,000</td>
<td>$150,000</td>
</tr>
<tr>
<td>IT system setup and GMP, related to buffers</td>
<td>$150,000</td>
<td>$150,000</td>
</tr>
<tr>
<td>Labor, annual, operations for buffer prep only</td>
<td>$300,000</td>
<td>$300,000</td>
</tr>
<tr>
<td>Regulatory, QA/documented, related to buffer prep</td>
<td>$75,000</td>
<td>$75,000</td>
</tr>
<tr>
<td>Repairs, labor buffer prep</td>
<td>$25,000</td>
<td>$25,000</td>
</tr>
<tr>
<td>Other G&amp;A Labor</td>
<td>$50,000</td>
<td>$50,000</td>
</tr>
<tr>
<td>Variable/staffing subtotal</td>
<td>$990,000</td>
<td>$990,000</td>
</tr>
</tbody>
</table>
| Variable/staffing costs per liter                                    | $3.96                      |\n
### Consumable expenses, buffer preparation

<table>
<thead>
<tr>
<th>Item</th>
<th>Calculated annual expenses</th>
<th>Your facility's cost: Input here</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer ingredient costs</td>
<td>$2,000,000</td>
<td>$2,000,000</td>
</tr>
<tr>
<td>Other ingredients/powders</td>
<td>$75,000</td>
<td>$75,000</td>
</tr>
<tr>
<td>Fibers and related consumables</td>
<td>$500,000</td>
<td>$500,000</td>
</tr>
<tr>
<td>Single-use devices (bags, tubing, connectors, manifolds)</td>
<td>$150,000</td>
<td>$150,000</td>
</tr>
<tr>
<td>WFI costs, consumables, not elsewhere noted</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Disposal expenses</td>
<td>$50,000</td>
<td>$50,000</td>
</tr>
<tr>
<td>Other consumables, expenses</td>
<td>$25,000</td>
<td>$25,000</td>
</tr>
</tbody>
</table>
| Consumables subtotal                                                 | $2,800,000                 |\n| Consumables cost per liter                                           | $11.20                     |\n| Your total annual cost                                               | $4,380,864                 |\n| Your total cost per liter                                           | $17.52                     |\n
Your current cost/liter for buffer production, including your all-in variable, fixed, and allocated costs.
Case Study: Cost Comparison from Economic Model and DSP Process Buffers

<table>
<thead>
<tr>
<th>DSP Buffer</th>
<th>Volume/ Batch</th>
<th>Unit Size (L)</th>
<th>Price/Unit</th>
<th>Price/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer 1</td>
<td>10950</td>
<td>200</td>
<td>$725.52</td>
<td>$3.63</td>
</tr>
<tr>
<td>Buffer 2</td>
<td>1300</td>
<td>200</td>
<td>$1,203.98</td>
<td>$6.02</td>
</tr>
<tr>
<td>Buffer 3</td>
<td>975</td>
<td>200</td>
<td>$1,489.92</td>
<td>$7.45</td>
</tr>
<tr>
<td>Buffer 4</td>
<td>500</td>
<td>200</td>
<td>$1,677.65</td>
<td>$8.39</td>
</tr>
<tr>
<td>Buffer 5</td>
<td>750</td>
<td>200</td>
<td>$1,678.26</td>
<td>$8.39</td>
</tr>
<tr>
<td>Buffer 6</td>
<td>200</td>
<td>200</td>
<td>$2,499.60</td>
<td>$12.50</td>
</tr>
<tr>
<td>Buffer 7</td>
<td>200</td>
<td>200</td>
<td>$5,021.47</td>
<td>$25.11</td>
</tr>
<tr>
<td>Buffer 8</td>
<td>600</td>
<td>200</td>
<td>$1,685.18</td>
<td>$8.43</td>
</tr>
<tr>
<td>Buffer 9</td>
<td>2400</td>
<td>200</td>
<td>$1,008.58</td>
<td>$5.04</td>
</tr>
<tr>
<td>Buffer 10</td>
<td>2400</td>
<td>200</td>
<td>$4,116.65</td>
<td>$20.58</td>
</tr>
<tr>
<td>Buffer 11</td>
<td>450</td>
<td>10</td>
<td>$160.21</td>
<td>$16.02</td>
</tr>
<tr>
<td>Buffer 12</td>
<td>1800</td>
<td>200</td>
<td>$988.44</td>
<td>$4.94</td>
</tr>
<tr>
<td>Buffer 13</td>
<td>500</td>
<td>200</td>
<td>$3,410.10</td>
<td>$17.05</td>
</tr>
<tr>
<td>Buffer 14</td>
<td>1600</td>
<td>10</td>
<td>$245.10</td>
<td>$24.51</td>
</tr>
</tbody>
</table>

Outsourcing downstream buffer manufacturing determined to be cost effective compared to modeled manufacturing costs.

<table>
<thead>
<tr>
<th>Modeled Cost/L @ 500,000L annual volume*</th>
</tr>
</thead>
<tbody>
<tr>
<td>$4.49  Modeled Fixed Cost</td>
</tr>
<tr>
<td>$4.11  Modeled Variable Cost</td>
</tr>
<tr>
<td>$9.69  Modeled Consumable Cost</td>
</tr>
<tr>
<td>$18.29 Total Cost/L</td>
</tr>
</tbody>
</table>

* Economic model developed by Eric Langer, BioPlan Associates
** Assumes 20 batches/Yr

$5,000,000 potential annual savings
One Consistent Bioprocessing Supply Chain Partner

Free up your capacity and resources with a GMP extension of your supply chain

**Raw Materials**
- Robust chemical supply chain for bio-manufacturing leveraging a breadth of suppliers and brands
- Emphasis on compliance, cost, and continuous supply

**Pre-Weighed Powders**
- Eliminate labor intensive weighing steps with ready-to-use liquid or dry formats for catalog and custom formulations
- Custom packaging available to simplify connections at point-of-use

**Fully-Hydrated Bioprocessing Liquids**
- Wide range of proven products, from buffers and bioprocessing liquids to time-tested Gibco™ media
- Designed to meet your specifications, including flexible BioProcess Containers (BPCs) in the size of your choice

---

**Warehouse and Supply Chain Management**, including:
- Order and logistics management
- Supplier and quality management
- Custom inventory
- QC sampling
- Material handling
- ISO and GMP storage solutions

---

*Currently available in US and Ireland*
**Customer Success Stories with Outsourcing Large Volume Liquids**

Focused on delivering more control and choice to receive dependable, high-quality products that are designed to meet your exact bulk liquid and buffer requirements

<table>
<thead>
<tr>
<th>Situation</th>
<th>Our response</th>
<th>Value delivered</th>
</tr>
</thead>
<tbody>
<tr>
<td>• A large biotech company decided to technology transfer from one site to another and identified a need for bulk liquids</td>
<td>• Reviewed process steps and suggested the use of premade buffers to simplify the workflow</td>
<td>• Custom bioprocess container to fit within workflow</td>
</tr>
</tbody>
</table>
| • Large biotech exceeding current capacity for downstream high-molarity NaCl and HEPES | • Designed custom BPCs  
• Local warehousing at a Doe & Ingalls facility | • Custom batch size and specifications  
• Delivery in 8 weeks |
| | | • Custom 1,000 L BPC design with attached tailgate samples—returnable containers  
• Stability and leachable studies initiated to support outsourcing justification  
• Specified raw material vendor and grade  
• JIT delivery |
More Choice and Control Through Manufacturing Flexibility

The right liquid format, container, and manufacturing process for each product

### Liquid format
- Process liquids for upstream and downstream applications
- Gibco™ media and feeds for cell culture processes
- 1X and concentrates

### Container type
- Bottles from 10 mL to 1 L
- Flexible bioprocess containers from 1 to 1,000 L
- Custom designs and sizing available

### Film choice
- Industry-standard CX5-14 film for general applications
- Aegis™ 5-14 film for critical applications
- Industry-standard ASI 26/77 film for general applications

### Manufacturing speed
- Non-GMP Gibco™ Media Express™ (GME) services
- Full GMP for scale-up

Streamlined management of order, manufacturing, testing, storage, and delivery

Feasibility assessment → Quotation provided → Order acknowledgement → Manufacturing → QC testing → CoA and shipping

Learn more at thermofisher.com/bioprocessliquids
EfficientFeed A+, B+, C+ Liquids

Available in two formats

• AGT format – 1, 10, and 100 L
• Liquid format – available in 1 L boxy bottle and in 10 L bioprocess container with Aegis Film

AGT format can be concentrated

Liquid formats are concentrated

• EfficientFeed A+ 3X
• EfficientFeed B+ 3X
• EfficientFeed C+ 2X
Liquid Manufacturing Process

- POMS weigh verification system
- Raw material weighing (800+ raw materials)
- Facility monitoring system: pressure/temp/RH
- Dedicated dust collection/HVAC
- ISO cleanroom classified manufacturing rooms
- Segregation: dedicated weigh rooms/booths with $\Delta P$
Liquid Manufacturing Process

- SS tank sizes of 200 L to 10,000 L, portable Nalgene tanks 10–400 L
- AOF 5,000 L and 10,000 L tanks and associated suites
- AOF 2,500 w/ alcohols, 5,000 and 10,000 L tanks in LVLM
- Facility monitoring system: pressure & temp monitoring
- ISO cleanroom classified manufacturing spaces
- Validated CIP/COP processes

Water For Injection
- TOC ≤ 500 ppb
- Bioburden ≤ 10 CFU/100 mL
- Endotoxin < 0.25 EU/mL
- Conductivity ≤ 1.2 uS/cm
- pH 5.0-7.0
Liquid Manufacturing Process

**Manual filling**
- Aseptic fill into irradiated bottles and bags
- Dedicated HVAC
- Qualified ISO 7 annually
- Qualified ISO 5 annually
- Environmental monitoring program
- Media fill validation program
- Facility monitoring system: temp/pressure

**Autofillers**
- Aseptic fill into irradiated bottles and bags
- Dedicated HVAC
- Qualified ISO 7 annually
- Qualified ISO 5 annually
- Environmental monitoring program
- Media fill validation program
- Facility monitoring system: temp/pressure

**Manifold Filling**
- Aseptic fill into irradiated BioProcess Containers (BPC)
- Steam In Place final filters and BPC connections
- Pressure hold test, followed by positive pressure test
- Filling room qualified Grade C per Annex 1
- Environmental monitoring program
- Media fill validation program
- Facility monitoring system: temp/pressure
Liquid Manufacturing Process

- Application of final bottle torque, bag seal, tamper-evident seal and labels
- Three automated packaging lines: 100 bottles/min
- Label verification and reconciliation

**Bottle features**
- Wide mouth/no drip spout/flat sides for easy handling
- Ultra-clear PET/virtually unbreakable
- Industry standard heat inactivation (HI)–compliant
- 100 mL, 500 mL, and 1,000 mL

**Media bag features**
- Easily customized (connections, in-line filtration, flow rates, tubing lengths, recirculation loops, etc.)
- 1 liter through 1000 liters