Production Chemical
Custom Packaging Services
Simplify process liquid and buffer manufacturing

Thermo Fisher Scientific
Process liquid and buffer manufacturing workflow

Process liquid and buffer manufacturing for upstream and downstream bioprocessing requires weighing, dispensing, and hydrating (formulation) a wide range of chemicals to support all aspects of bioproduction unit operations. In-house process liquid manufacturing requires significant investments in dedicated cGMP space, equipment, and resources to execute the workflow, including regulatory oversight and quality management.

Weigh-Dispense-Hydration Steps

- **Transfer Order**
  QA released raw materials are requested in the Enterprise Resource Planning (ERP) system via a Transfer Order to be delivered from the warehouse to the production area.

- **Kitting & Staging**
  Raw material containers are cleaned and moved into the the clean staging/storage area within the cGMP manufacturing space. Detailed labeling, organizing, and kitting of raw materials to support specific formulations or production runs are conducted.

- **Weigh & Dispense**
  Raw materials are weighed and dispensed into secondary containers. Problematic raw materials often require extra handling (de-clumping). Changeovers require extensive cleaning to prevent contamination.

- **Hydration (Formulation)**
  Pre-weighed chemicals are mixed with a hydrating solution in a formulation tank. Tank time bottlenecks due to the demand for process liquids vs. production must be effectively managed in order to meet manufacturing demands.

- **Production Jobs**
  Cell Culture, Harvest, Purification, and Fill/Finish of the final drug product.
Challenges in the workflow
Resources focused on non-core, non-value-added activities

Operational Inefficiencies

• Time and resources required to execute the workflow and for changeover
• Extra time associated with problematic materials
• Unnecessarily rejected raw materials based on operator variability
• Poor stability and/or short shelf life for mixed liquid solutions

Financial Burdens

• Cost of resources dedicated to non-core manufacturing activities
• cGMP space requirements to support weigh, dispense, and hydration (WDH) workflow vs. core manufacturing
• Ongoing CapEx and OpEx requirements for building and maintaining WDH capacity to support core manufacturing

Risks

• Environmental, Health and Safety (EH&S) related restrictions and requirements (e.g., chemical handling, ergonomics, and safety)
• Manufacturing risk due to operator errors (e.g., contamination, mis-formulation, etc.)
Production Chemical Custom Packaging Services
Solving process liquid challenges together

Production Chemical Custom Packaging Services offered by Thermo Fisher Scientific is a service designed to help biologic manufacturers accelerate innovation and improve productivity. By supplying ready-to-hydrate (dry powders) and ready-to-use (pre-made liquids) chemicals, the process liquid manufacturing workflow can be simplified through the reduction or elimination of previously resource-intensive steps.

Open Architecture
Dry powder and liquids solutions customized to specifically meet your bioprocessing requirements—any chemical (specification, brand, format) and any container (specification, brand, type).

Manufacturing Network Flexibility
Global manufacturing network with broad chemical dry powder and liquid manufacturing capabilities and capacities to efficiently address your unique needs.

Expertise & Experience
Years of dry powder and liquid manufacturing experience combined with bioprocessing container expertise to simplify your workflow.

Tailored solutions for your unique needs
Through a collaborative engagement, leveraging Lean tools, Thermo Fisher will work with you to uncover areas of waste and risk within your weigh, dispense, and hydration (formulation) workflow. This process driven approach is designed to ensure a fit-for-purpose solution.
Chemical format flexibility

The unique challenges within your workflow will determine whether trusted-weight dry powders or pre-made liquid solutions are required. Often a hybrid approach, involving both trusted-weight dry powders and pre-made liquid solutions, results in the most effective workflow solution.

Comparison: liquids vs. powders
Outsourcing advantages over in-house manufacturing

<table>
<thead>
<tr>
<th></th>
<th>Pre-made liquids</th>
<th>Trusted-weight dry powders</th>
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<tbody>
<tr>
<td><strong>Operational Efficiency Optimization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time and resources for weigh-dispense steps</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Time and resources for hydration steps</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Chemical raw material rejection variability</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Product stability and shelf life</td>
<td>–</td>
<td>N/A</td>
</tr>
<tr>
<td>Equipment cleaning between chemical components</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Raw material transportation and inventory handling costs</td>
<td>–</td>
<td>N/A</td>
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<tr>
<th><strong>Expenditure Avoidance</strong></th>
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<tbody>
<tr>
<td>WFI system investment and maintenance</td>
<td>+++</td>
<td>N/A</td>
</tr>
<tr>
<td>Manufacturing space and equipment for weigh-dispense</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Manufacturing space and equipment for hydration</td>
<td>+++</td>
<td>N/A</td>
</tr>
<tr>
<td>Operating resources for non-core manufacturing activities</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Material waste and disposal fees</td>
<td>+++</td>
<td>+++</td>
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<tr>
<th><strong>Risk Mitigation</strong></th>
<th></th>
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<tbody>
<tr>
<td>EH&amp;S ergonomics and safety</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>EH&amp;S chemical handling</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Operator errors (misformulations, contamination, etc.)</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
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Key: + Advantage, – Disadvantage, N/A Not Applicable

Maximize your workflow efficiencies with a fit-for-purpose solution.
Bioprocessing workflow: chemicals commonly used (monoclonal antibody production)

### Process liquids and buffers are

<table>
<thead>
<tr>
<th>Process Liquid Examples</th>
<th>Media Hydration and Supplementation</th>
<th>Harvest and collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell line specific pre-mixed media (e.g., CHO, Insect, Bacterial, etc.), Cell line specific feed solutions (e.g., CHO, Insect, Hybridoma, etc.), Glucose Solutions, Sodium Bicarbonate, DMSO (for cell banks)</td>
<td>Amino Acids, Biological Buffers, Buffering Salts, Cell Culture Media &amp; Supplements, Carbohydrates, Glucose Solutions, Minerals &amp; Vitamins, WFI</td>
<td>Biological Buffers, Buffering Salts, Denaturants, Detergents, WFI</td>
</tr>
<tr>
<td>Tris HCl 20-50 mM, Triton X-100, Tween, 5M Sodium Chloride, Phosphate Buffered Saline (PBS)</td>
<td>Tris HCl 20-50 mM, Triton X-100, Tween, 5M Sodium Chloride, Phosphate Buffered Saline (PBS)</td>
<td>Buffers (e.g., Tris HCl 20-50 mM), Phosphate Buffered Saline (PBS)</td>
</tr>
</tbody>
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### Questions to consider

- How are bioproduction manufacturing demands impacting your weigh, dispense, and hydration (formulation) workflow?
- What chemicals or solutions are presenting the biggest challenges to your workflow?
- What strategies are you pursing to improve and streamline your process liquid manufacturing processes?
Collaborate with us to design a solution

Engage with your Thermo Fisher bioproduction sales representative to conduct a site assessment consisting of a Process Walk or Gemba Walk to help identify potential areas of waste or risk within your current workflow. Together, we will identify and design solutions that meet your workflow needs.

<table>
<thead>
<tr>
<th>CHEMICALS</th>
<th>CONTAINER</th>
<th>FORMAT</th>
<th>YOUR SOLUTION</th>
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</thead>
<tbody>
<tr>
<td>Any specification</td>
<td>Any specification</td>
<td>Any weight</td>
<td>Any formulation</td>
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Eliminate non-core, non-value-added manufacturing activities

When you outsource all – or a portion – of your weigh, dispense, and hydration process to Thermo Fisher through our Production Chemical Custom Packaging Services, you can simplify your process liquid manufacturing and make core manufacturing a priority.

How to get started

1. Contact your Thermo Fisher bioproduction sales representative for a workflow assessment. Coordinate a Process Walk or Gemba Walk to identify potential areas of waste and risk within your current workflow.

2. Determine your workflow challenges. Analyze current state process flow waste and risk and identify future state process flows that can improve productivity, reduce total cost, and/or mitigate risks.

3. Design your solution. Collaborate with Thermo Fisher to create a custom – fit for purpose – solution based on your unique specifications and needs.

Increase Productivity

Reduce Costs

Minimize Risks

Increase Productivity

Reduce Costs

Minimize Risks