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# A Guide to Aseptic Manufacturing:

## What to Consider

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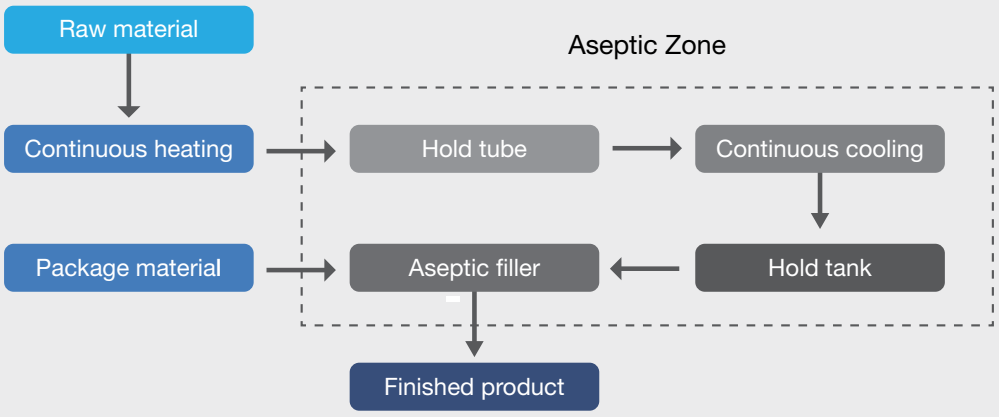
# Overview

Aseptic manufacturing is a complex process; understanding everything involved in the process is essential to providing the best finished product possible. Not only does it involve packaging decisions, plant and equipment selection, and layout and processing equipment, it requires a clear understanding of what type of processing is best suited for the final product. Options such as UHT vs ESL play a major role but final product testing is of critical importance to ensure final product is safe for consumption. Implementing rapid tests for final product release can assist in this process. This guide discusses aseptic manufacturing options, challenges, and testing solutions to overcome these challenges.

## What is aseptic manufacturing?

Aseptic manufacturing is the method used to commercially sterilize a product and fill and seal it into a sterile container under aseptic conditions. The final filled package is hermetically sealed to produce a final product that is impermeable to external contamination or spoilage organisms. Therefore, it can be stored at ambient conditions for extended periods of time. In addition, thermal processing of the food product takes place outside the packaging, allowing it to be rapid and controlled. This is followed by cooling, before packaging. This method allows the product to maintain its nutritional and sensory qualities (i.e., smell and taste).



# Advantages of Aseptic Manufacturing

**Precision Processes**

- Automated controlled filling provides reliable weight consistency
- Automatic tamper-proof sterilization assures quality confidence
- Integrated workflows offer fill-to-seal sterility

**Environmental Optimization**

- Steam sterilization eliminates chemical exposure and improves safety profile
- Lower transportation weight and storage needs reduces greenhouse emissions and logistics costs
- Elimination of refrigeration reduces energy use and expense

**Food Safety & Nutrition**

- Maximum nutrient content provides for more healthful foods
- Enhanced palatability creates greater appeal and higher consumption
- Extended shelf stability allows for longer dating and maximum safety

**Consumer Satisfaction**

- Natural mouth feel offers an enhanced consumer experience
- Bacterial and contaminant elimination delivers optimal consumer safety
- Dramatically reduced waste allows for good environmental stewardship

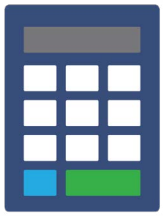
# Disadvantages of Aseptic Manufacturing

**Complexity**

- Extensive process validations impact workflow and add cost
- Skilled operators require expensive, time-consuming technical training
- Aseptic workflow requirements may impact existing product/brand quality and characteristics

**Cleaning**

- Clean room operations increase total costs
- Complex clean-in-place procedures introduce additional cost and contamination risk
- Specialized training increases cost and impacts productivity



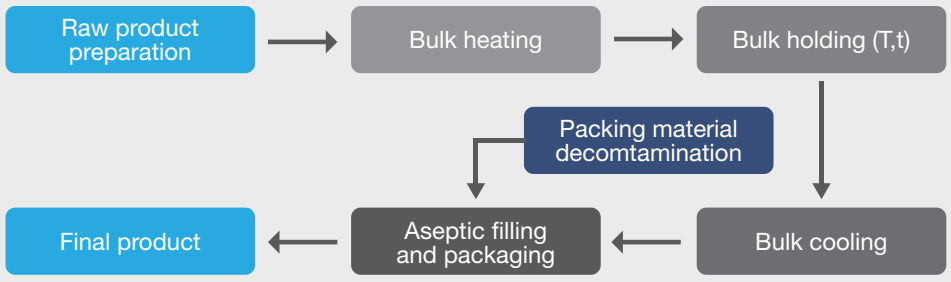
**Cost**

- Clean-in-place materials and solutions increase expenses
- Premium aseptic processing and packaging decrease profit
- A more skilled workforce commands higher wages

# Considerations Summary

1. **Complex operations**
   - Difficult to validate, clean and operate processing equipment.
   - Aseptic system validations takes the longest amount of time among shelf-life stable sterilization technologies.
   - Changeover to a new product involves time-consuming clean-in-place (CIP) processes.
2. **Requires highly technical operational training**
   - Operators and maintenance workers in a clean room environment must understand intricate control systems by undergoing detailed operator training.
3. **Challenges in cleaning processing systems**
   - CIP systems pose challenges with piping, proper cleaner selection/concentration, and the thermal and mechanical forces used within the piping system to ensure maximum cleaning without damage, along with optimizing temperature and contact time.
   - Each design/application will have a unique CIP procedure, adding complexity.
4. **Cost of cleaning in place procedures**
   - CIP circuit design can be single use with the cleaning solution discarded after CIP cycle completion or cleaning solutions can be reused/recovered for additional use.
   - Single use systems are the easiest to design and control – all cleaning, sanitizing, and rinse solutions are used only once, but prove to be costly.
   - CIP processes require cleaning verification and validation.
5. **Expensive aseptic processing and packaging equipment**
   - Equipment for aseptic processing and packaging is typically more expensive than conventional technologies.
   - Processors must build a “clean room” to house the packaging operation.
   - Containers used for packaging must be hermetically sealed under a sterile environment.

Simplified diagram of an aseptic processing and packaging system



# Choosing the Best Packaging Technique

The biggest challenges for aseptic processing are the limitations and disadvantages encountered during actual application of this technology.

To minimize costs, cold aseptic filling has become a common technique with beverage manufacturers for products including UHT milk, fruit juices and sports/energy drinks. Its flexibility means that it is suitable for a wide range of products from fresh fruit dices and purees to marinades and dairy products. This diversity has also lead to the development of a wide range of fillers and packaging types.

Nevertheless, aseptic processing and filling has specific requirements as it combines several elements into a single, integrated production line. This ensures microbiological safety throughout the process from initial product treatment to sealing of the final product. Considerations include:

1. Thermal treatment
2. Cooling (where necessary)
3. Sterilization of the packaging
4. Filling and sealing under aseptic conditions

## Packaging type

Typically, based on the final product, you must first determine the type of aseptic packaging you want. Options include can systems, bottle systems, sachet and pouch systems, cup systems, carton systems, and bulk packaging systems. The packaging must not only protect the product, but it must maintain the quality of the products. Factors to consider when selecting the packaging material include seal strength and integrity, package shape, stiffness and durability, as well as barrier properties. Product containers should be sufficiently durable to withstand the mechanical, chemical, and thermal stresses encountered during normal distribution. For all these reasons, it is common to use aseptic packaging which incorporates multiple materials that are assembled either by lamination or co-extrusion processes to maximize integrity. Common packaging generally includes barriers to light, moisture, and oxygen. In addition, the sealant material used must be compatible with the product and the closure systems.

# Choosing the Best Packaging Technique

Next, determine what type of packaging line works the best for your product(s).

1. **Film and seal**
   Preformed containers are sterilized, filled in an aseptic environment, and then sealed.
2. **Form, film and seal**
   Sterilizing rolls of material which are then formed into the package in a sterile environment, followed by filling and sealing.
3. **Erect, film and seal**
   Knocked down blanks are then erected, sterilized, filled and sealed.
4. **Thermoform and seal**
   Roll stock is sterilized, thermoformed, filled, and sealed – all aseptically.
5. **Blow, mold, fill and seal**
   A wide range of possible materials that are sterilized, filled, and sealed.

## Choice of packaging must address the following considerations:

1. It should hold the product without leaking, thus maintaining the sterility of the product.
2. It should prevent physical damage to the product.
3. It should run effortlessly on the filling lines.
4. It should survive the packaging process.
5. It should be biologically safe, non-toxic and compatible with the foodstuff.
6. It should be resistant to environmental attack – rodents, insects, dirt, microorganisms, etc.
7. It should be tamper-proof – showing evidence when tampered with.
8. It should offer a barrier to oxygen and gas exchange (i.e., maintain the atmosphere it was packaged under).
9. It should be easy to open and handle.
10. It should communicate product and manufacturer information.
11. It should be cost efficient.

# Plant & Equipment Layout

The next consideration is the plant layout and all the equipment needed for manufacturing and packaging a product aseptically. The facility must be constructed as to minimize occluded surfaces, be well ventilated using HEPA (High Efficiency Particulate Air) filters and be easily cleaned, maintained, and decontaminated. The equipment used in this room is also a consideration. The proper equipment must be selected to ensure the components can be easily cleaned and maintained, while also remaining sturdy and non-shedding of particulates.

Even with the best equipment selection, another factor is developing the regular maintenance and qualifying/requalifying regime which will ensure minimal issues as long as equipment is installed and maintained correctly. Tied to this basic equipment are the additional tools used for maintenance, extraction or manufacture of the finished product. Since these all originate from an uncontrolled environment, there is risk of introducing contamination into the production area. Therefore, an established, verified decontamination method must be used to clean all tools before use and properly used to test the aseptic system following maintenance or repair. Methods must also be routinely re-evaluated for effectiveness and robustness, commonly known as re-validation.

An established, verified decontamination method must be used to clean all tools before use.

# Processing Options

## Thermal processor

The essential elements used for selecting a thermal processor are the heating characteristics of the food product and the inactivation kinetics of specific target microorganisms which could be present in the food product. The product is brought to sterilization temperature and held at that temperature for the time necessary to achieve commercial sterility. Depending on the process type, different flow rates may dictate the proper time and heat required to ensure aseptic processing is occurring.

For example, in continuous product flow systems, the time for which the product must be held at the sterilization temperature is achieved in the hold section or tube – therefore, the flow rate for the fastest particle or shortest particle retention time must be accurately determined. Many methods are available to determine the minimum residence time to ensure sterility. These include dye or salt injections or mathematical models. These models incorporate the flow rate, physical dimensions and design of the hold section and the flow properties of the product. When flow characteristics are unknown for the product, then actual measurements must be made to determine the proper calculations required to determine commercial sterility. Delivery of the energy to the food product must be controlled, monitored and recorded.

Image courtesy of Tetra Pak®

If steam injection or steam infusion is used, the addition of water increases the product volume by approximately 1% per 10°F above initial product temperature as it enters the sterilizer. There could also be volume increase due to thermal expansion of the food. This increase in product volume must be compensated for in the establishment of the process.

No matter what method is used for thermal processing, all must be equipped with accurate, calibrated, reliable temperature indicating devices and dated records of calibration testing must be kept. In addition, all devices must be inspected daily to ensure they are working properly. Sensors for these indicators need to be located in such a way as they do not alter product flow and in batch systems, multiple indicators must be used to ensure the entire batch is being heated equally.

# Processing Options

## Aseptic tank

The aseptic tank is used for intermediate storage of aseptically treated food products. It can be used in different ways depending on the plant design and the capacities of various units in the processing and packaging lines. For instance, it can be used to store surplus product during any stoppage, such as when the packaging machines stop. It can also be used for simultaneous packaging of two products. Volume considerations must also be taken into consideration. Typically, tanks are designed to hold a volume sufficient for a full shift of packaging. Nevertheless, the optimum tank size and arrangement must be decided for each individual process and must be compatible with the aseptic processing equipment and processes, and with the packaging machinery.

Image courtesy of Tetra Pak®

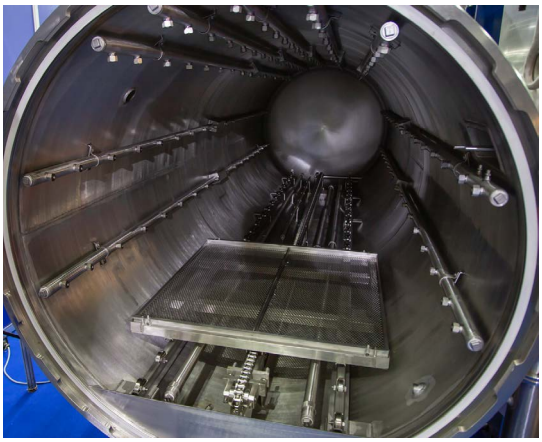
## Microprocessors

The use of microprocessors and microcomputers in aseptic packaging has grown significantly over the years. Microprocessors allow for the control of multiple process variables simultaneously. They have the ability to feed film into the packaging machine, convert the film into the required shape and dimensions, heat seal all seams, and shrink-wrap a specific number of packs into a single pack.

# Processing Options

## Sterilizer for packaging

No matter what packaging material is used, it must be pre-sterilized prior to filling. Since aseptic packaging systems are complex, care must be taken in choosing the best method for packaging material sterilization. Typical methods used include steam, hot air, hydrogen peroxide, UV light, or irradiation. The method chosen cannot damage the material and must also sterilize any surfaces or equipment that come in contact with the sterilized packaging.



## Aseptic filling lines

Following thermal processing, and packaging sterilization, food products are accumulated in an aseptic surge tank prior to packaging. Surge tanks are sterilized before start-up of product flow by steam or water and must be vented to remove all air pockets. Sterile air over-pressure must be maintained to ensure proper operation (flow of product to the fillers). Sterile gases such as nitrogen or carbon dioxide are used to provide overpressure and create a sterile barrier.

# Finished Products

## Storage and transport of finished product

Consideration must also be given to how finished product will be handled after aseptic filling and sealing. Conditions must preserve the integrity of the container and not impact the safety and quality of the product. Things to consider include handling during palletizing, shrink wrapping, temperature before stacking, humidity levels, additional labeling and dryness of surfaces. Storage conditions must be regulated to prevent deterioration or contamination of the product or the packaging, including maintaining a constant temperature and minimizing moisture which can affect packaging surfaces.

Storage conditions must be regulated to maintain a constant temperature.

# Above and Beyond Food Packaging

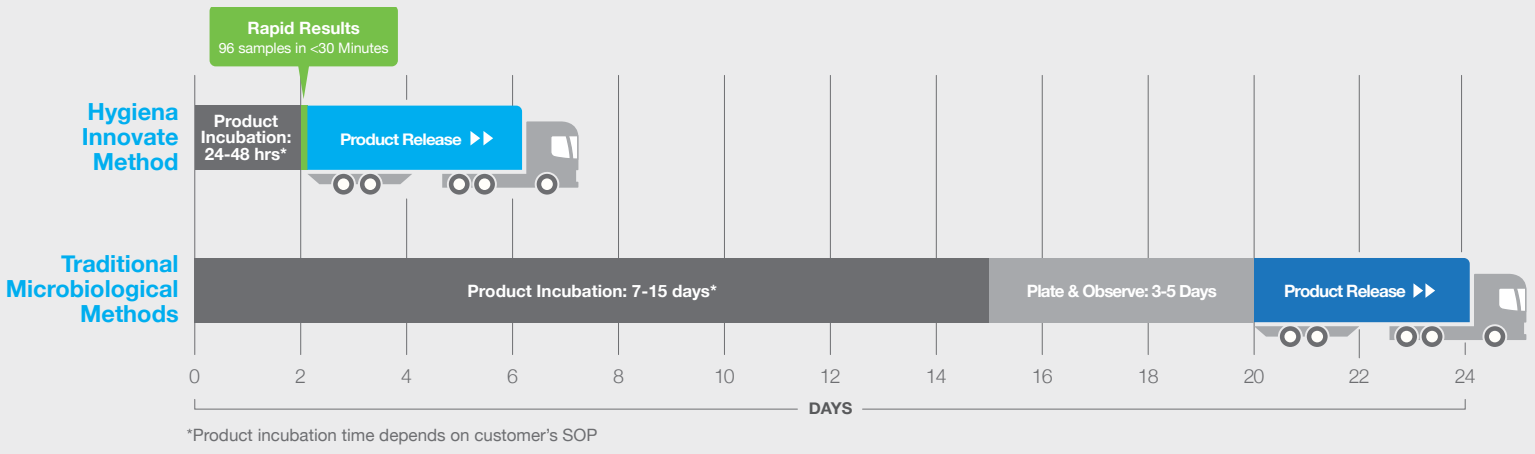
## Microbiological specifications

Closely tied to storage and transport are the microbiological specifications set for testing of the finished food products. The main objectives in aseptic processing here are to control the number of microorganisms in the food product and to prevent the recontamination of the food after processing. Therefore, strict microbiological specifications must be set and adhered to. Things to consider are sampling procedures, methodologies for testing, and limits for acceptance.

Two major sources of microbial contamination are:

1. Heat resistant spores present in the ingredients prior to processing and which survived.
2. Post-process contamination introduced through packaging or a failure in the integrity of the aseptic filling system.

These are typically controlled by the process design. Nevertheless, commercial sterility testing verifies that the process and controls are effective. Testing would involve incubating final food product samples in their final packaging at elevated temperatures (30°C, 55°C, the latter only if thermophilic organisms are a concern) for a range of 7-15 days. The samples are then examined for signs of microbial growth by plating onto non-selective agar media, incubating for 3-5 days and then examined for visible colonies. A stable product should normally contain less than 10 colonies on a agar plate.This process is quite tedious and can cause a bottleneck in product hold and release, taking almost 3 weeks to confirm a negative result.



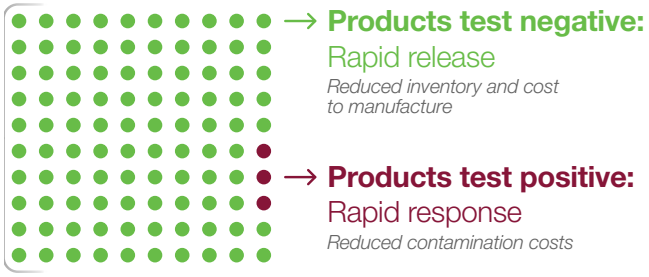
# Above and Beyond Food Packaging

## One alternative for testing: The Innovate System

An alternative to traditional plate testing is a rapid method utilizing ATP bioluminescence. Using this technology, Hygiena's Innovate System reduces testing and product hold time from 10-18 days to 48 hours or less, allowing faster release of product and reducing inventory costs. This technology is designed to detect light produced from microbial ATP while minimizing background levels of non-microbial ATP and is able to test a large number of samples at once. The Innovate System provides a microplate format to analyze up to 96 individual samples in less than 30 minutes.

The system has been validated on a wide variety of raw materials, in-process formulations, and finished goods. In addition to testing 96 different samples on a single microtiter plate every 30 minutes, subsequent assays can be prepared while the system is in use to keep high-volume operations running smoothly.

The Innovate System can be adapted to determine what is "pass" or "fail" criteria, making it even easier for a factory worker to monitor testing – green is pass and red is fail. Sample data from multiple instruments can be saved to a single database on the company's secure network, helping simplify regulatory compliance. Data can be securely viewed onsite or remotely, and reports can be generated for analysis.




Learn more about the Innovate System

# Above and Beyond Food Packaging

## The Innovate System

Use of the Innovate System helps food processors minimize costs for warehouse space or holding product while also feeling reassured that any contamination events will be identified early. In addition, the latest advancement, Innovate Autosampler III, can be paired with the Innovate platform to prepare up to 2,000 assays per hour for analysis in the Innovate System. This simplifies the workflow even more and frees up valuable technician time.

## Documented Proof of Performance

Customers have put the Innovate System to the test. A large dairy manufacturer partnered with us to test various types of dairy products from both animal and plant sources for low levels of contamination (manually introduced for the study). A wide range of organisms were tested depending on the type of milk product. Microorganisms used included *Salmonella, E. coli, Enterobacter, Pseudomonas, Bacillus, Staphylococcus, Saccharomyces, Aspergillus* and *Clostridium.*

In all cases, for all microorganisms tested (except for *Clostridium sporogenes* in ESL oat milk), the Innovate System was able to detect low spike levels (~10 CFU per pack) at a 24 hour time mark. RLU values in the spiked products exceeded the uncontaminated product RLU thresholds, set as three times the baseline values. Read the details of each study here:

**Oat Milk** | **Soy Milk** | **ESL Milk** | **UHT Milk**

Other customers have asked us about testing more highly acidic beverages, such as fruit juices, tomato juice and protein drinks for the presence of low levels of contamination. In these cases, all organisms tested were detected within 24-48 hours of incubation. Read the full report **here**.

# Above and Beyond Food Packaging

## Other Microbial Considerations

Additional problems that pose a risk of microbiological contamination include inefficient employee hygiene practices, ineffective training, the development of biofilms, ineffective use of cleaners and disinfectants, lack of sanitary equipment design, ineffective application of sanitation principles, reactive rather than routine maintenance, contamination of raw materials or the presence of niche environmental sites. These must be addressed by identifying the potential areas of concern and collecting environmental samples of the areas to test for possible microbial contamination. This includes monitoring rollers on conveyors, spacing between close-fitting metal or plastic parts, seams on rubber seals around piping or doors and any other possible niche. In addition, raw materials must be sourced from reputable suppliers, stored properly, and involve a kill-step during processing to eliminate any pathogens.

Visual monitoring of these risks can help minimize the presence of these potential sources of contamination. However, it is not enough. Each processing facility must have an environmental and food-contact surface testing program in place. It must be designed to detect trends that indicate a potential loss of sanitation control has occurred so timely corrective actions can be taken. The program must include sample sites for testing, sampling frequency, and a quick way to analyze results as soon as they become available.

Collect samples to test for possible microbial contamination.

# Above and Beyond Food Packaging

## Environmental monitoring solutions

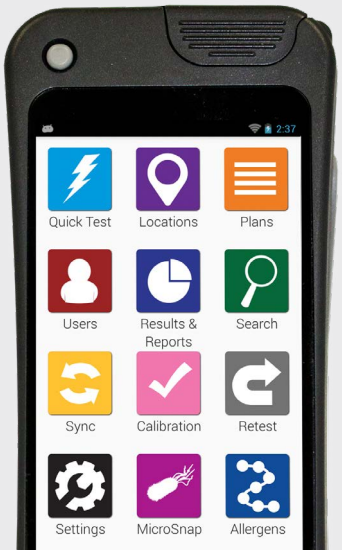
A rapid way to test the environment is to perform simple surface environmental monitoring of equipment, work areas, floors, and walls. The fastest and simplest way to do this is through swabbing of high-risk surfaces with swabbing devices that can be quickly read in an environmental monitoring device. Hygiena's EnSURE™ Touch monitoring system works perfect for this application.

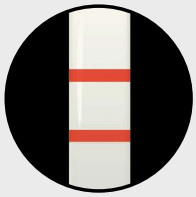
EnSURE Touch works much like a smartphone. Select the proper swabbing device, collect a sample using the prewetted swab, activate the device and get a reading in 15 seconds.

Swabbing devices such as UltraSnap™ can detect very low levels of ATP (below 1 fmole) – the level of ATP is correlated to the level of bioorganic load, a direct measurement of potential contamination. Hygiena also offers SuperSnap™ devices for the detection of extremely low levels of ATP (down to 0.1 fmole) allowing it to be used as an allergen cross-contamination prevention tool. If specific allergens are of concern, rapid testing can be performed with our AlerTox® sticks which provide rapid results in 10 minutes with no cross-reactivity for a number of allergens from egg to casein to peanut.

Many aseptic processing facilities also have concerns about *Listeria* contamination in their food products. *Listeria* tends to be more prevalent under cooler conditions but still can become a problem in an aseptic processing facility. Rapidly identifying this organism can prevent product discards, production delays, and reassure product is safe. BAX® System *Listeria* PCR Assays allow for the detection of various *Listeria* species, including *L. mono*. All tests are AOAC-RI*PTM* approved and provide results within hours after enrichment.

No matter what aseptic processing system you employ, keep in mind that constant monitoring of processes will ensure a final food product that is safe for consumer consumption. Being proactive is essential to streamlined processes and maximizes product output and profit.



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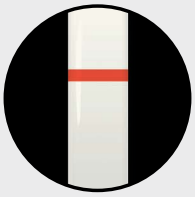

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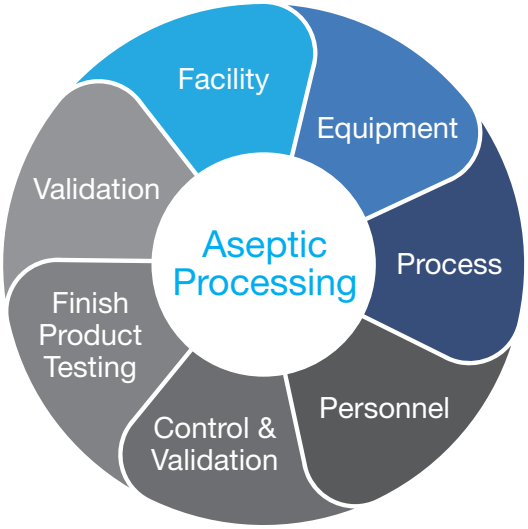
# Conclusion

## Aseptic manufacturing requires multiple considerations

To decide the best option for your finished product, you must first consider the advantages and disadvantages of the processing method– is it the proper method for your finished product? Next, you must understand packaging options based on how the product will be used by consumers. Alternative processing options are available as well and pose their own challenges. Last, you must consider how you will ensure the final product passes all microbial testing options and how to ensure your manufacturing environment is clean. This will ensure your product is safe for consumers once it leaves your facility.

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