# How terminal sterilization puts quality and safety first

With a proprietary process that combines aseptic processing with terminal sterilization—a proven pharmaceutical industry standard—we are able to achieve unprecedented sterility assurance and extended beyond-use date (BUD).

### COMBINING TWO STERILIZATION TECHNIQUES

**Aseptic processing:** A sterilization technique used by 503A compounding pharmacies to produce sterile drug products.

- Used to sterilize the patient-specific prescriptions dispensed by AIS Healthcare Targeted Drug Delivery
- Multiple 0.22-micron, sterilizing-grade filtration steps to ensure medication sterility, going beyond USP guidelines for preparing sterile solutions
- Goal is to remove any potential contaminants

**Aseptic processing provides a sterility assurance level of 1:1,000.**

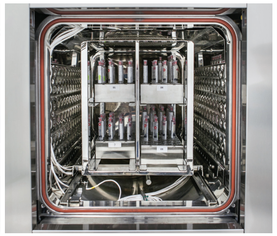
**Terminal sterilization:** A sterilization technique used by AIS Healthcare Targeted Drug Delivery to ensure the highest level of sterility assurance.

- Used in addition to aseptic processing to further sterilize patient-specific prescriptions dispensed by AIS Healthcare Targeted Drug Delivery
- A proven sterilization technique that is the pharmaceutical industry standard and the preferred method for the commercial preparation of injectable medications
- Our validated proprietary heat and steam terminal sterilization cycles are used to eradicate all theoretical bioburdens without compromising medication potency or purity
- Because the terminal sterilization process happens after the medication is in the syringe, there's no risk of further contamination from human handling post sterilization
- Goal is the destruction of all theoretical bioburdens

**Terminal sterilization provides a sterility assurance level of 1:1,000,000**

21-45
DAY BUD AT ROOM TEMPERATURE[1]

**By following aseptic processing with terminal sterilization, AIS Healthcare Targeted Drug Delivery achieves sterility assurance levels of 1:1,000,000 and BUD of 21-45 days (average of 34 days).[1]**



## Take a tour

Contact us to tour our industry-leading compounding pharmacies in Dallas, Texas (headquarters), or Ridgeland, MS, and see how our proprietary process can benefit you and your patients.

Can't visit in person?
**Take our virtual tour at tour.aishealthcarepharmacy.com.**

**aiscaregroup.com | 877.443.4006**

[1] All patient-specific formulary dispenses within maximum concentrations (based on AIS Healthcare in-house data for 120,000 aseptically processed and terminally sterilized patient-specific prescriptions in 2019).
[2] USP-NF. Accessed February 28, 2023. https://online.uspnf.com/uspnf/document/1_GUID-08D442A0-208E-4DCE-98BE-21C84C2D48AA_1_en-US?source=
[3] US Food and Drug Administration. Summary of Recent Findings Related to Glass Delamination. November 2018. Accessed February 28, 2023. http://www.fda.gov/drugs/pharmaceutical-quality-resources/summary-recent-findings-related-glass-delamination
[4] Iacocca RG, Toltl N, Allgeier M, et al. Factors affecting the chemical durability of glass used in the pharmaceutical industry. *AAPS PharmSciTech*. 2010;11(3):1340-1349. doi:10.1208/s12249-010-9506-9
[5] US Food and Drug Administration. FDA Form 483 Frequently Asked Questions. January 2020. Accessed February 28, 2023. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions#:~:text=A%3A%20An%20FDA%20Form%20483,FD%26C)%20Act%20and%20related%20Acts

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# How AIS Healthcare Targeted Drug Delivery achieves unprecedented sterility assurance and extended BUD

Advancing quality through terminal sterilization

AIS Healthcare
Targeted Drug Delivery

Advancing quality. Improving lives.

# Dedicated to a better terminal sterilization process

AIS Healthcare goes above and beyond standard terminal sterilization. Our industry-leading process and equipment reflect our dedication to do more to advance quality and patient safety in every prescription we deliver.

| The AIS Healthcare difference | | Why it matters | Did you know? |
|---|---|---|---|
| **Significant investment** | AIS Healthcare has made a multimillion-dollar, multi-year investment in our terminal sterilization equipment and processes. | USP <797> standards do not require terminal sterilization. We not only use terminal sterilization but have also made a significant investment in our equipment and processes, reflecting our long-term commitment to raising the bar for quality and sterility and doing what's right, not just what's expected. | Our investment often far exceeds what other pharmacies spend on their standard terminal sterilization equipment. |
| **Specially designed** | Our custom 1.5-ton autoclaves were designed in collaboration with industry experts and built by the world leader in the production of solutions for sterile processes and equipment in the pharmaceutical sector. | Our custom autoclaves allow our pharmacists control over critical parameter settings, including temperature, pressure, counter pressure and time, to eradicate all theoretical bioburdens in the syringes. | Standard autoclaves do not allow the same level of customization, limiting the ability to fine-tune the sterilization processes. |
| **Proprietary process** | We use a deeply researched and proprietary terminal sterilization process, developed in conjunction with industry experts, for patient-specific prescriptions. | This proprietary process applies the right temperature, pressure and time parameters to the syringes, effectively leveraging steam heat sterilization to achieve the highest levels of sterility assurance. | Achieving high levels of sterility assurance from terminal sterilization requires a process that has been thoroughly tested and confirmed by industry experts. |
| **Extensively studied** | We have conducted and continue to conduct rigorous and independent testing and validation studies, including extractable and leachable studies, of our terminal sterilization program. | These ongoing studies prove that our terminal sterilization process effectively eradicates contaminants that may have been introduced into our medications. | Asking about the requalification of the validation system for terminal sterilization process is a best practice. |
| **Lower heat** | Our terminal sterilization process uses steam heat cycles with temperatures that peak well below the conventional temperatures associated with autoclaving. | Lower temperatures and our proprietary terminal sterilization processes have been proven to effectively sterilize while reducing any potential damage to the medication during terminal sterilization. | Conventional high-temperature sterilization can reach 121 degrees Celsius. Providers should ask their pharmacies about the temperatures used during terminal sterilization. |
| **Enhanced convenience and safety** | Prescriptions are terminally sterilized in plastic syringes, which are then packaged and shipped directly to providers. | Delivering the medication in a syringe, which is the final container for each patient-specific prescription, instead of glass vials allows for fewer manipulations by the clinic and clinic staff, decreasing the possibility of introducing potential contaminants. This also eliminates the need for additional training on safely transferring the medication from a vial to a syringe. | Several studies have shown that leaching and delamination (when degradation of surface glass produces glass flakes) can occur with glass vials during terminal sterilization.[2] The FDA has issued an advisory stating terminal sterilization with glass vials is a risk for delamination.[3,4]<br>Also, puncturing the rubber stopper of a glass vial to transfer the medication to a syringe, in addition to requiring a needle change to fill the pump, can cause coring, in which sheared rubber particles can contaminate the medication. |
| **Pharmacists only** | All patient-specific prescriptions are only compounded by licensed pharmacists to ensure every prescription meets our industry-leading quality standards. | Licensed pharmacists have additional expertise and experience and are the most qualified to compound medications of the highest quality. | USP <797> guidelines just require a pharmacist to oversee compounding done by pharmacy technicians. AIS Healthcare makes the additional investment to have only pharmacists compound patient-specific medications. |
| **Inspected and accredited** | We are regularly inspected by the various state boards of pharmacy, the DEA and the FDA (with zero Form 483 observations on the last inspection in our Ridgeland, MS, facility). We are also dually accredited by URAC and the Accreditation Commission for Health Care (ACHC). | The absence of 483 observations and our dual accreditations show our commitment to quality and dedication to producing products under the highest possible standards. | An FDA Form 483 is essentially a report card that is issued following an inspection. Observations are made when, in the investigator's judgment, conditions or practices observed would indicate that any food, drug, device or cosmetic has been adulterated or is being prepared, packed or held under conditions that could cause it to become adulterated or potentially harmful to someone's health.[5] |


"I call AIS Healthcare my poster child of how to do it right."

**Eric Kastango**
*President of Clinical IQ and CriticalPoint*

urac ACCREDITED

ACHC

# Our compounding process

**Receipt and scheduling**
Customer service coordinates order intake and schedules orders for shipping.

**Entry**
AIS Healthcare Targeted Drug Delivery uses double-blind order entry and verification. All orders are entered and reviewed by two pharmacy technicians.

**Verification and reverification**
Two pharmacists then do a blind review of the order before the medication is compounded. This means that multiple licensed professionals have eyes on every order to reduce the chances of any human error.

**API procurement and stock solution preparation**
All USP-grade active pharmaceutical ingredients are sourced from FDA-registered manufacturers, and we obtain certificates of analysis from both manufacturers and distributors. All of our stock solutions are prepared by a licensed pharmacist and tested by an outside, independent lab for sterility, potency, particulate matter, pH, and endotoxins before use in compounding.

**Aseptic processing**
Prescriptions are compounded from sterile stock solutions in our state-of-the-art cleanroom. The pharmacist uses the compounding record to select the correct inventory items, and a pharmacy technician confirms the selection twice. The prescriptions are then put into previously sterilized syringes.

**Terminal sterilization prep**
After aseptic processing, a pharmacist visually inspects each syringe and then passes it to a pharmacy technician for labeling. A terminal sterilization label is put on each syringe and a bubble test is performed by a technician as a second visual inspection. Then, the syringes are loaded into the autoclave for the terminal sterilization cycle.

**Terminal sterilization**
In the autoclave, each syringe gets enough heat and steam to kill all theoretical bioburdens that may be present in that environment. Once terminal sterilization is complete, parametric release is achieved and the syringes are unloaded from the steam autoclave. Another check is then performed. No further stability or sterility testing is required.

**Staging**
An AIS Healthcare technician stages every labeled syringe, and a pharmacist inspects each syringe for any issues, matches it with the appropriate shipping packaging, and double-checks the volume.

**Packaging**
AIS Healthcare pharmacists package each prescription into an amber bag for light protection and then seal it in a shipping tube that can be surrounded by bubble wrap. Another check is then performed to ensure the packing label reflects the packing slip.

**Shipping**
The shipping tube is then placed in an International Safe Transit Association–certified box with tamper-evident tape and other proprietary safety precautions. We ship via first-class overnight air at no additional cost, which means patients across the country get their medication the next morning. We also monitor potential weather-related delays and proactively adjust when and how we ship medication, including shipping from our redundancy operations or using another shipping route, to make sure patients' prescriptions arrive on time.