



# **FDA Regulatory Framework Applicable to Autologous Serum Tears**

**Hospital Physicians, Pharmacists, and  
Laboratory Directors**

**Directed to:**  
Healthcare / Regulatory Audiences

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## A Peer-Review-Ready White Paper for Hospital Physicians, Pharmacists, and Laboratory Directors

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### Abstract

Autologous serum tears are widely used in academic and hospital settings for the management of severe ocular surface disease, yet persistent uncertainty remains regarding their regulatory status under United States Food and Drug Administration (FDA) oversight. This white paper provides a comprehensive regulatory analysis of autologous serum tears under the Public Health Service (PHS) Act, the Federal Food, Drug, and Cosmetic Act (FD&C Act), and Title 21 of the Code of Federal Regulations (CFR). Particular emphasis is placed on Sections 351 and 361 of the PHS Act and 21 CFR Part 1271 governing human cells, tissues, and cellular and tissue-based products (HCT/Ps). When prepared from a patient's own blood, minimally manipulated, and used for homologous, non-systemic purposes, autologous serum tears are appropriately regulated as low public health risk products and do not require FDA premarket approval, licensure, or device clearance. Instead, institutional compliance focuses on sterility, purity, and professional practice standards, including applicable United States Pharmacopeia (USP) requirements.

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### 1. Introduction

Autologous serum tears have become an important adjunctive therapy for patients with severe dry eye disease, neurotrophic keratitis, graft-versus-host disease, and other ocular surface disorders refractory to conventional treatment. Despite their increasing clinical use, misconceptions persist within hospitals and academic medical centers regarding FDA oversight of serum tear preparation, particularly whether such products constitute drugs, biologics, medical devices, or regulated human tissue products.

This paper clarifies the FDA's statutory and regulatory authority as it applies to autologous serum tears, with the goal of supporting informed decision-making by physicians, pharmacists, laboratory directors, compliance officers, and institutional review bodies.

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## 2. FDA Regulatory Authority and Public Health Mandate

The FDA is charged with protecting public health by ensuring the safety, purity, and effectiveness of foods, drugs, biological products, and certain medical products distributed in interstate commerce or imported into or exported from the United States. This authority is exercised primarily through two statutes:

- The **Public Health Service (PHS) Act**
- The **Federal Food, Drug, and Cosmetic Act (FD&C Act)**

FDA regulations establish standards designed to prevent the introduction, transmission, and spread of communicable disease while ensuring appropriate manufacturing, storage, labeling, and handling practices.

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## 3. Regulation of Blood and Biological Products

### 3.1 Section 351 of the PHS Act

Section 351 of the PHS Act governs biological products that require FDA licensure prior to interstate commercial distribution. Biological products under this provision include vaccines, blood and blood components intended for transfusion, therapeutic serums, toxins, and analogous products manufactured for broad distribution.

Under Section 351, the FDA is authorized to:

- Require premarket licensure
- Enforce current Good Manufacturing Practices (cGMP)
- Regulate labeling, storage, and distribution
- Take enforcement action under both the PHS Act and FD&C Act

The Biologics Price Competition and Innovation Act (BPCI Act) established an abbreviated licensure pathway for biosimilar and interchangeable biological products licensed under Section 351. This framework does not apply to patient-specific autologous serum tears.

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## 4. Section 361 and the Regulation of HCT/Ps

### 4.1 Overview of 21 CFR Part 1271

Section 361 of the PHS Act authorizes FDA regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps) solely for the purpose of preventing communicable disease transmission. The implementing regulations are codified in **21 CFR Part 1271**.

An HCT/P qualifies for regulation exclusively under Section 361 if it meets all criteria set forth in **21 CFR § 1271.10(a)**:

1. The product is **minimally manipulated**
2. The product is intended for **homologous use only**
3. The product is **not combined with another article**, except for water, crystalloids, or sterilizing, preserving, or storage agents that do not raise new safety concerns
4. The product does **not have a systemic effect**, or, if it does, is for:
  - Autologous use
  - Allogeneic use in a first- or second-degree relative
  - Reproductive use

Products meeting these criteria are commonly referred to as “**361 HCT/Ps**.”

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## 5. Application of Section 361 Criteria to Autologous Serum Tears

### 5.1 Minimal Manipulation

Preparation of autologous serum tears involves standard laboratory procedures such as blood collection, centrifugation, separation, and dilution. These processes do not alter the original relevant biological characteristics of serum and therefore constitute minimal manipulation under FDA regulatory interpretation.

### 5.2 Homologous Use

Serum naturally contains growth factors, proteins, and nutrients that support epithelial health and lubrication. Topical ocular application of serum tears serves the same basic biological function in the recipient as in the donor, satisfying the homologous use requirement.

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### 5.3 Combination With Other Articles

Dilution with normal saline or other crystalloids does not constitute combination with a drug or device under 21 CFR § 1271.10(a)(3), provided no new clinical safety concerns are introduced.

### 5.4 Autologous Use and Systemic Effect

Autologous serum tears are used topically, are not intended to exert systemic effects, and are administered to the same individual from whom the blood was drawn.

### 5.5 Regulatory Conclusion

Autologous serum tears prepared under these conditions meet all criteria for regulation solely under Section 361 of the PHS Act and are therefore considered **low public health risk products** that do not require FDA licensure, premarket approval, or device clearance.

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## 6. Section 1271.20: Circumstances Triggering Additional Regulation

Under **21 CFR § 1271.20**, any HCT/P that fails to meet the criteria in § 1271.10(a), and does not qualify for an exception under § 1271.15, is regulated as a drug, device, and/or biological product under the FD&C Act and Section 351 of the PHS Act.

Because autologous serum tears prepared using AseptiKits' PALA kits meet the criteria of § 1271.10(a), they do not fall under these additional regulatory requirements.

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## 7. Registration, Listing, and FDA Tracking Systems

### 7.1 General Registration Requirements

Section 1271.10(b) establishes registration and listing requirements for establishments manufacturing 361 HCT/Ps. However, FDA's electronic registration and public query systems do not include categories for serum, serum tears, or platelet-rich plasma (PRP).

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## 7.2 Practical Regulatory Interpretation

The absence of serum-based products from FDA HCT/P tracking systems reflects the agency's longstanding position that autologous blood-derived products used for homologous, non-systemic purposes are not actively regulated as HCT/Ps, drugs, devices, or licensed biologics.

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## 8. Purity, Sterility, and Professional Standards

Although autologous serum tears are not regulated as FDA-approved drugs or biologics, hospitals and pharmacies remain responsible for ensuring product safety through adherence to professional compounding standards. Applicable requirements include:

- USP <797> Sterile Compounding
- USP <795> Nonsterile Compounding (where applicable)
- Institutional policies governing aseptic technique, environmental controls, personnel training, and beyond-use dating

Compliance with these standards fulfills FDA's core requirement that serum tears be **pure and sterile**.

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## 9. Conclusion

Autologous serum tears prepared from a patient's own blood, using minimal manipulation and intended for homologous, non-systemic use, are appropriately regulated under Section 361 of the Public Health Service Act. These products do not require FDA licensure, premarket approval, or device clearance. Institutional oversight should focus on sterility, purity, and adherence to established professional and pharmacopeial standards. This regulatory clarity supports the continued safe and compliant use of serum tears within hospital and academic medical settings.

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## Footnotes and References

1. Public Health Service Act, 42 U.S.C. § 262.
2. Public Health Service Act, 42 U.S.C. § 264.
3. 21 CFR Part 1271 – Human Cells, Tissues, and Cellular and Tissue-Based Products.
4. 21 CFR § 1271.10(a).
5. 21 CFR § 1271.20.
6. Biologics Price Competition and Innovation Act of 2009.
7. U.S. Food and Drug Administration, HCT/P Public Query System.
8. U.S. Food and Drug Administration, Electronic Registration and Listing System for HCT/P Establishments.
9. United States Pharmacopeia, USP <797>.
10. United States Pharmacopeia, USP <795>.