Securing the Sky: A Chain of Custody Framework for Medical Drone Delivery in the United States

INDUSTRY WHITEPAPER

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For healthcare institutions, regulators, and drone industry stakeholders

AeroX | *Accelerating the commercialization of next-generation flight*

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Executive Summary

Medical drone delivery is transforming healthcare logistics across the United States. From prescription medications and lab samples to blood products and vaccines, autonomous aerial vehicles are delivering critical medical cargo faster and to more locations than ever before. The market has grown to $294 million in 2024 and is projected to reach $2.5 billion by 2034, driven by a 24.1% compound annual growth rate.

Yet as the technology matures, a critical gap has emerged: no unified chain-of-custody standard exists for medical drone delivery in the United States.

Chain of custody, the documented, verifiable record of every entity that has handled a medical package from origin to destination, is foundational to patient safety, regulatory compliance, and legal accountability. In traditional pharmaceutical distribution, chain of custody is well established. In autonomous aerial delivery, it is not. The regulatory framework is fragmented across at least seven federal and state agencies, including the FAA, FDA, DEA, state pharmacy boards, and HIPAA, and no single agency owns end-to-end oversight of the medical drone delivery process.

This whitepaper examines the current state of chain of custody in medical drone delivery, maps the regulatory landscape and its gaps, draws lessons from ground-based autonomous delivery systems, and proposes the AeroX Chain of Custody Framework, a six-stage, technology-enabled approach to securing medical cargo from pharmacy to patient. The framework integrates IoT sensor telemetry, tamper-evident digital ledger technology, biometric authentication, and healthcare system interoperability into a cohesive standard that the industry can adopt.

The stakes are clear. Without a unified chain-of-custody standard, the industry risks regulatory action, patient harm, and erosion of the institutional trust required for widespread adoption. AeroX believes the time for industry-driven standardization is now.

Framed correctly, medical drone delivery is not solely an aviation innovation. It is a medication-use process, and it must meet or exceed the pharmacy standards that already govern dispensing, counseling, storage, privacy, delivery confirmation, exception handling, and accountability. Aviation approval determines whether the aircraft may fly; it does not determine whether the medication may be trusted on arrival.

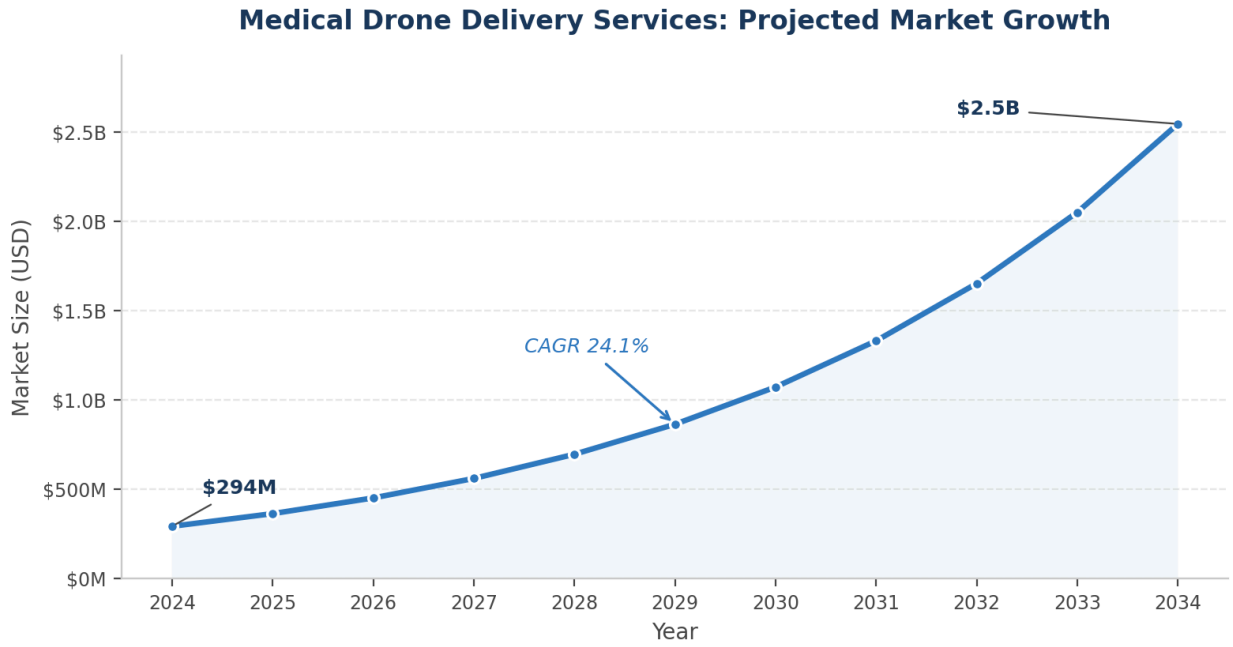
1. Introduction: The Rise of Medical Drone Delivery

The Gap

The concept of delivering medical supplies by drone is no longer theoretical. The technological capability for medical drone delivery has been demonstrated. Since Zipline launched the world's first national medical drone delivery service in Rwanda in 2016, the industry has matured from proof-of-concept to scaled commercial operations across multiple continents. What has not been established is a unified, industry-wide standard for securing the integrity of medical cargo throughout the delivery process. Each operator has developed proprietary chain-of-custody approaches that are not interoperable, not publicly documented in detail, and not validated against a common standard. This whitepaper addresses that gap.

Market Context

The global medical drone delivery services market reached $294 million in 2024 and is projected to grow at a 24.1% compound annual growth rate to reach $2.5 billion by 2034 (Global Market Insights, 2025).



Source: Global Market Insights (2025). Medical Drone Delivery Services Market Size Report, 2025–2034.

Figure 1. Medical Drone Delivery Services: Projected Market Growth, 2024-2034. Source: Global Market Insights (2025).

This growth is driven by three converging forces: regulatory progress, technological maturation, and healthcare system demand for faster, more reliable logistics. The projected market expansion reflects increasing adoption across core healthcare delivery use cases.

Use Cases

As the market expands, medical drone delivery is being deployed across a range of clinical and operational use cases that place new demands on logistics, safety, and custody control.

- **Pharmaceuticals and prescriptions**: Routine and specialty medications, including temperature-sensitive biologics
- **Laboratory samples**: Blood, tissue, and diagnostic specimens transported between hospital facilities
- **Blood products**: Whole blood, plasma, and platelets delivered to trauma centers and rural facilities
- **Vaccines**: Cold-chain-maintained deliveries demonstrated at 3-4°C with no viability impact (Aggarwal et al., 2025), include COVID-19 vaccine drone delivery by UPS Flight Forward at Atrium Wake Forest Baptist hospital in Winston-Salem in 2021
- **Organs for transplant**: The world's first drone organ delivery, a kidney transported 4.3 km in Baltimore in 2019, was successfully transplanted
- **Medical supplies and equipment**: Surgical supplies, PPE, and hospital-at-home materials

Current Operations in the United States

As of early 2026, seven drone operators hold FAA Part 135 air carrier certificates specifically for UAS commercial delivery, with additional manned carriers adding drone operations to their existing certificates.

Table 1 below summarizes current U.S. drone delivery operators authorized under FAA Part 135, highlighting the scale, maturity, and healthcare capabilities of active programs. It shows that while medical delivery is expanding rapidly, operators vary widely in deployment scale and in the sophistication of their healthcare and chain-of-custody practices.

Operator	Cert Year	Scale (Overall)	Healthcare Capability	Differentiator
Zipline	2022	2M+ deliveries	Major hospital partners (Advocate, Mayo, Cleveland Clinic, etc.)	Fastest growth (+15% weekly)
Wing	2019	450K+ deliveries	NHS integration, RFID, LIS	Most advanced chain-of-custody system

Causey (CAU)	2023	200K+ deliveries	Meds, blood, lab transport (SUNY Upstate)	Established medical operator
UPS Flight Forward	2019	Enterprise networks	Hospital systems + Matternet (Advocate Health)	3 min delivery (vs 30 min ground)
Amazon Prime Air	2020	Early US scale	Pharmacy integration	Logistics infrastructure advantage
DroneUp	2024	Early stage	Rural health pilots	Focus on underserved communities
DEXA	2025	Scaling	Small package delivery	New entrant scaling nationally
Ameriflight	2023	National cargo base	UAS + manned integration	Hybrid cargo + drone model

Table 1. Healthcare Drone Delivery Operators by Scale

Further detail on each Part 135 drone delivery operator:

- **Wing** (Alphabet) received the first FAA Part 135 air carrier certificate for drone delivery in April 2019 and has since completed over 450,000 commercial deliveries globally. Through its Apian partnership with the UK National Health Service, Wing operates one of the most sophisticated medical chain-of-custody systems in the world, featuring RFID tagging, tamper-evident seals, and Laboratory Information System (LIS) integration.
- **UPS Flight Forward**, a wholly owned subsidiary of UPS, received the first Part 135 Standard certification (unrestricted fleet size and scope) in October 2019. Partnering with Matternet, which holds the first and only FAA Type Certificate for a drone delivery system, UPS Flight Forward pioneered medical drone delivery at WakeMed Health, Wake Forest Baptist Health, UC San Diego Health, and CVS Pharmacy, reducing hospital transport times from 30 minutes by ground courier to 3 minutes by drone.
- **Amazon Prime Air** received its Part 135 certificate in August 2020 and has since obtained certification for its MK30 drone. Amazon has integrated Amazon Pharmacy prescription fulfillment into its drone delivery pipeline, leveraging its existing logistics infrastructure to position drone delivery as a last-mile healthcare option.
- **Zipline** received its Part 135 certificate in June 2022 as the first fixed-wing UAS operator to achieve the milestone and has completed over 2 million commercial deliveries globally. Zipline is deploying its Platform 2 system with Mayo Clinic, Memorial Hermann, OhioHealth, Cleveland

Clinic, Michigan Medicine, and Advocate Health, among others, with US deliveries growing approximately 15% week-over-week for seven consecutive months.

- **Causey Aviation Unmanned (CAU)**, a subsidiary of Causey Aviation Service (founded 1967), received its Part 135 certificate in January 2023 and has completed over 200,000 commercial deliveries. CAU operates the "Air Upstate" program at SUNY Upstate Medical University in Syracuse, NY, delivering prescription medications, blood products, and lab samples between medical facilities through its Meds to Beds program and home prescription delivery service.
- **DroneUp** received its Part 135 certificate in November 2024 and has conducted medical delivery demonstrations with Riverside Health System in Virginia, focusing on hypertension medication delivery to underserved rural communities. DroneUp is positioning its delivery infrastructure for expanded healthcare logistics applications.
- **DEXA** (formerly Drone Express) received its Part 135 certificate in April 2025 along with S-1 List approval for its proprietary DE-2020 drone. Based in Dayton, OH, DEXA conducts on-demand small package delivery and is scaling its autonomous delivery operations nationally.

Additionally, **Ameriflight**, the nation's largest Part 135 cargo airline, added the Matternet M2 to its existing certificate in 2023, becoming the first manned Part 135 cargo carrier to incorporate UAS operations and focusing on healthcare and e-commerce deliveries in urban and suburban environments.

While current operators demonstrate that medical drone delivery is operationally viable at scale, they also expose a critical dependency: reliable chain-of-custody controls across every transfer of medical cargo.

2. Why Chain of Custody Is Critical for Medical Cargo

Chain of custody in medical delivery is not an administrative formality. It is a patient safety mechanism, a regulatory requirement, and a legal shield. When a pharmaceutical product leaves a pharmacy and arrives at a patient's door via an autonomous aircraft, every transfer, every environmental condition, and every identity verification must be documented and verifiable.

Figure 2 shows how assurance can decline after medication leaves pharmacy control when existing chain-of-custody practices are not adapted for drone transport. When custody, monitoring, and verification are explicitly designed for autonomous delivery, assurance remains consistently higher, framing the patient safety, regulatory, and trust risks discussed below.

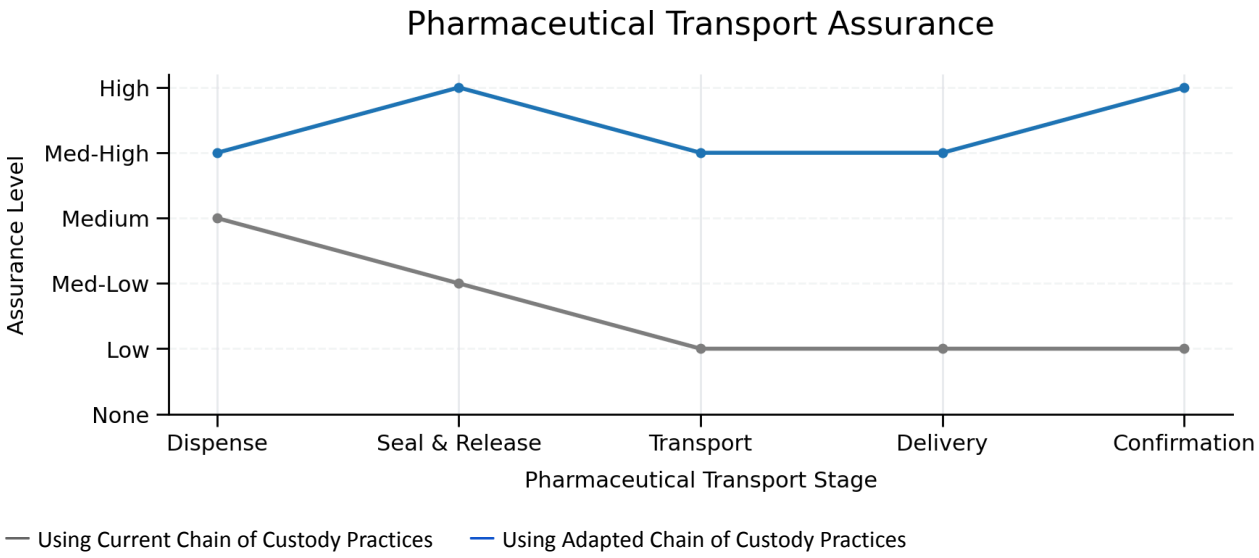


Figure 2. Illustrative example of assurance levels across pharmaceutical transport stages with and without formal chain of custody.

2.1 Patient Safety Risks

Temperature excursions. Many medications, biologics, and vaccines require strict temperature control. Unopened insulin vials must be stored between 2°C and 8°C. Most refrigerated vaccines must be held within the 2-8°C range per CDC, WHO, and USP <659> standards, with study-observed drone performance in the 3-4°C band (Aggarwal et al., 2025). Monoclonal antibodies are sensitive to vibration-induced aggregation. Critically, compliance for stability-sensitive products is not evaluated by instantaneous temperature alone but by **Mean Kinetic Temperature (MKT)** calculated over the full transit window; the chain-of-custody system must be able to compute MKT and compare it to each product's stability budget. Without continuous environmental monitoring and documented chain of custody, a temperature excursion during transit could render a medication ineffective or harmful, with no record to trigger a recall or alert.

Contamination and tampering. Autonomous delivery removes the human oversight present in traditional courier delivery. A package traveling by drone from a pharmacy to a patient's home is

unattended for the duration of flight and, in many cases, during the final handoff at the delivery location. Without tamper-evident packaging and documented integrity verification, there is no assurance that the delivered product is the same product that left the pharmacy.

Misdelivery. GPS-based delivery to a location is not the same as verified delivery to a patient. Most current drone operators deliver to a geographic coordinate. If the wrong person retrieves a prescription, particularly a controlled substance or a patient-specific biologic, the consequences range from medication errors to diversion

2.2 Regulatory and Legal Liability

The liability question. When a drone-delivered medication is compromised, who bears responsibility? The dispensing pharmacy? The drone operator? The technology platform provider? The healthcare institution that contracted for drone delivery? Current regulations do not clearly allocate liability in the autonomous delivery context. Chain-of-custody documentation provides the evidentiary foundation for determining where a failure occurred and who is responsible.

Multi-agency compliance. A single drone delivery of a prescription medication must simultaneously satisfy FAA operational rules, FDA drug safety requirements, state pharmacy board dispensing regulations, HIPAA patient data protections, and potentially DEA controlled substance requirements. Without a chain-of-custody system that addresses all of these simultaneously, operators face compliance risk across multiple regulatory domains.

Malpractice and product liability. Healthcare institutions that adopt drone delivery assume the risk that delivery failures could result in patient harm claims. A documented chain of custody that demonstrates compliance with applicable standards is the primary defense against such claims.

2.3 Trust and Adoption Barriers

Institutional confidence. Healthcare systems evaluating drone delivery need assurance that the technology meets or exceeds the safety and compliance standards of existing delivery methods. Hospital pharmacy directors, compliance officers, and chief medical officers require documented chain-of-custody protocols before approving drone delivery for their institutions.

Regulatory confidence. As the FAA, FDA, and state pharmacy boards develop guidance for drone delivery, they will look to industry practices as a baseline. An industry that can demonstrate robust, standardized chain-of-custody practices is more likely to receive favorable regulatory treatment than one operating with fragmented, proprietary approaches.

Patient trust. Patients must be willing to receive medications delivered by an autonomous aircraft. Surveys consistently show that confidence in the security and integrity of the delivery process is a primary factor in patient acceptance.

3. The Regulatory Landscape: A Fragmented Framework

Medical drone delivery in the United States operates at the intersection of at least seven regulatory authorities. No single agency has comprehensive jurisdiction over the end-to-end process, creating both gaps and overlaps that complicate compliance.

3.1 FAA: Airspace and Aircraft Certification

The Federal Aviation Administration governs the aircraft, the airspace, and the operational rules for drone delivery.

Part 107 (Small UAS Rule) permits transportation of property for compensation within state boundaries for aircraft under 55 pounds but requires visual line of sight, limits altitude to 400 feet, and prohibits carriage of hazardous materials. Part 107 does not address chain of custody, product integrity, or temperature monitoring.

Part 135 (Air Carrier Certification) is currently the only pathway for BVLOS commercial delivery and interstate operations. Seven drone operators hold Part 135 certificates specifically for UAS delivery as of early 2026, with additional manned carriers adding drone operations to their existing certificates. Each Part 135 certificate holder is issued Operations Specifications (OpSpecs) designating either a "Will Carry" or "Will Not Carry" hazardous materials policy. "Will Carry" operators are authorized to transport dangerous goods under an FAA-approved HAZMAT program compliant with 49 CFR Parts 100-185 and ICAO Technical Instructions, while "Will Not Carry" operators are prohibited from transporting hazmat and need only maintain a recognition program. This distinction is consequential for medical drone delivery: many medical payloads, including Category A and B infectious substances (UN2814, UN2900, UN3373), dry ice for cold-chain biologics, lithium batteries in medical devices, and radiopharmaceuticals, are classified as hazardous materials. Most current drone Part 135 operators hold "Will Not Carry" OpSpecs, effectively excluding a significant portion of medical cargo from drone delivery. Section 933 of the FAA Reauthorization Act of 2024 directed the FAA and PHMSA to develop a risk-based approach for authorizing UAS to carry hazmat under Part 135, with joint guidance issued in November 2025. Even with this progress, Part 135 certification does not include medical cargo handling standards specific to UAS.

Proposed Part 108 (BVLOS Operations), published in August 2025, represents the most significant regulatory development for medical drone delivery to date. It would create a standardized pathway for routine BVLOS operations without individual waivers, accommodating aircraft up to 1,320 pounds, and establishes a two-tier authorization structure based on risk. **Permitted operations** (the lower-risk tier) prohibit hazardous materials onboard as defined by 49 CFR 171.8, except under the narrow exception of 49 CFR 176.9(b), effectively excluding most medical cargo classified as hazmat. **Certificated operations** (the higher-risk tier) allow hazardous materials transport, with §108.570 establishing a dedicated Hazmat category and requiring initial and recurrent hazmat recognition training every 24 months, along with safety management systems (SMS), risk assessments, and packaging requirements. While Part 108 expands the pathway for hazmat-bearing medical drone delivery, it relies on the existing 49 CFR Parts 100-185 hazmat framework, which was designed for manned aircraft, and does not establish UAS-specific standards for medical cargo handling, cold-chain integrity, or chain-of-custody documentation. A final rule is expected in 2026.

What the FAA does not regulate: The FAA has no authority over the contents of packages, the conditions under which medical products are stored or handled, or the verification of recipient identity. These fall to other agencies. For example, hazardous materials transportation, including the medical-cargo categories most relevant to drone delivery (Category A and B infectious substances, dry ice, lithium batteries in medical devices, and radiopharmaceuticals), is regulated by the Department of Transportation through the Pipeline and Hazardous Materials Safety Administration (PHMSA), which authors 49 CFR Parts 100-185. The FAA enforces these PHMSA-authored standards within air carrier operations under Part 135 and the proposed Part 108, but does not write the underlying hazmat classification, packaging, marking, or labeling rules. Similarly, the safety, identity, and quality of the drug product itself fall to the FDA, controlled substance security falls to the DEA, dispensing authority falls to state pharmacy boards, and patient data protection falls to HHS under HIPAA. The result is a regulatory mosaic in which no single agency owns the end-to-end medical drone delivery process. The final rule is targeted for the end of 2026, with operator implementation expected to follow through 2027.

3.2 FDA: Drug Safety and Quality

The FDA governs the safety, quality, and integrity of pharmaceutical products throughout the supply chain.

Good Distribution Practice (GDP) requires that conditions during transportation do not adversely affect the quality and stability of medical cargo. This applies to drone delivery, but the FDA has not issued guidance on how GDP requirements apply to autonomous aerial transport.

The Drug Supply Chain Security Act (DSCSA), enacted in 2013 with final serialized traceability requirements taking effect in November 2023, followed by a one-year stabilization period and staggered FDA enforcement exemptions extending through November 2026 for small dispensers, mandates electronic, interoperable tracking of prescription drugs at the package level across the US supply chain. The DSCSA requires transaction information, transaction history, and transaction statements to accompany each sale or transfer. No published guidance addresses how DSCSA serialization requirements integrate with drone delivery operations, and the classification of drone operators within the DSCSA framework (distributor, third-party logistics provider, or common carrier) remains unresolved. The most probable classification for a drone operator transporting prescription product between pharmacies, wholesalers, or dispensing sites is Third-Party Logistics Provider (3PL), which triggers state 3PL licensure and facility-registration requirements in most jurisdictions and requires explicit inclusion in the DSCSA electronic transaction chain. By contrast, last-mile delivery of a dispensed, patient-specific prescription from the dispensing pharmacy to the patient more closely resembles a courier or common-carrier function and would generally fall outside the DSCSA 3PL framework, which governs the supply chain up to the point of dispensing.

USP <1079> (Good Storage and Shipping Practices) is a general chapter in the United States Pharmacopeia that establishes the foundational standards for storing, handling, and transporting pharmaceutical products throughout the supply chain. It defines temperature and humidity controls for refrigerated (2-8°C), frozen, and Controlled Room Temperature (CRT, 20-25°C) products; methodologies for Mean Kinetic Temperature (MKT) calculation to evaluate thermal exposure during transit; qualification criteria for shipping containers and monitoring devices; carrier qualification and chain-of-custody documentation requirements; and corrective action procedures for environmental

excursions. Although classified as a general information chapter (and therefore advisory rather than mandatory on its own), USP <1079> is widely referenced in FDA inspections, state pharmacy board standards, and industry contracts, and its companion chapters <1079.1> through <1079.4> extend its scope to investigational products, MKT methodology, and continuous monitoring systems. However, its methodology assumes transit times of hours to days and was developed for ground, ocean, and manned air freight. Qualification of shipping systems for 10-30 minute drone deliveries, with their distinct thermal transitions, rotor-induced vibration, and unattended last-meter handoffs, lacks a standardized approach.

USP <797> (Sterile Compounding) and USP <800> (Hazardous Drugs) govern the handling, containment, and transport of sterile compounded preparations and hazardous drugs, including many chemotherapy agents, hormones, and biologics on the NIOSH hazardous drug list. Drone delivery of these product categories requires USP <797>-compliant sterile packaging, USP <800> double-containment with segregation from non-hazardous cargo, and documented spill-response capability at the delivery endpoint. No operator has publicly established a USP <800>-compliant drone delivery pathway.

Risk Evaluation and Mitigation Strategies (REMS). A growing list of high-risk drugs (including clozapine, isotretinoin, mifepristone, and several biologics) are dispensed under FDA REMS programs that impose prescriber, pharmacy, and patient enrollment and distribution restrictions. Some REMS programs require in-person patient interaction, laboratory confirmation prior to dispensing, or dispensing conditions that are difficult or impossible to satisfy through autonomous delivery. Drone delivery models must either exclude REMS-restricted products or engineer program-specific compliance pathways, with the applicable REMS Element To Assure Safe Use (ETASU) captured in the chain-of-custody record.

The gap: The FDA has not issued any guidance documents, proposed rules, or policy statements specifically addressing drone delivery of pharmaceuticals, biologics, or medical devices.

3.3 DEA: Controlled Substances

The Drug Enforcement Administration regulates the handling, transportation, and security of controlled substances under Schedules I-V , classified by their potential for abuse and accepted medical use. **Schedule I** substances have no currently accepted medical use and a high potential for abuse (e.g., heroin, LSD, MDMA, cannabis at the federal level). **Schedule II** substances have accepted medical uses but a high potential for abuse and severe dependence (e.g., oxycodone, hydrocodone, morphine, fentanyl, methadone, amphetamine and methylphenidate-based ADHD medications such as Adderall and Ritalin). **Schedule III** substances have moderate to low potential for physical dependence (e.g., buprenorphine, ketamine, products containing codeine, anabolic steroids). **Schedule IV** substances have lower abuse potential (e.g., alprazolam (Xanax), diazepam (Valium), lorazepam (Ativan), tramadol, zolpidem (Ambien)). **Schedule V** substances have the lowest abuse potential and contain limited quantities of certain narcotics (e.g., cough preparations with codeine, pregabalin (Lyrica)). Schedules II-V represent the medications most relevant to drone delivery, as they are routinely prescribed and dispensed to outpatients.

DEA security requirements (21 CFR 1301.71-1301.76) mandate physical security controls including substantial construction, alarm systems, and access limitations. These standards were designed for buildings and storage facilities, not airborne payload compartments. There is no objective measure for whether a drone's payload security meets DEA requirements.

The gap: The DEA has not issued any formal guidance on drone delivery of controlled substances. All current drone operators exclude controlled substances from their delivery programs. This leaves a significant category of medications, including opioid prescriptions, ADHD medications, and anxiety treatments, entirely unaddressed. That said, the DEA has indicated willingness to consider pilot programs operating within existing registrant authority, leaving a possible near-term path short of new rulemaking.

3.4 State Pharmacy Boards

State pharmacy boards regulate the dispensing and delivery of prescription medications within their jurisdictions. Requirements vary significantly by state, creating a patchwork of compliance obligations for operators serving multiple markets.

Texas has taken the lead with proposed Section 291.12, filed with the Office of the Secretary of State on June 16, 2025, and published in the Texas Register on June 27, 2025. It would be the first state rule specifically addressing autonomous prescription delivery, including chain-of-custody safeguards, tracking system requirements, and patient consent provisions. The rule explicitly excludes controlled substances and sterile compounded preparations from drone-eligible delivery, and requires that unmanned aircraft systems maintain federal registration and comply with all applicable state and federal laws. Following the initial comment period, the Texas State Board of Pharmacy reopened the rule for further consideration after debate over cold-chain temperature controls, approved delivery locations, and provider responsibility, illustrating the practical complexity of translating chain-of-custody principles into enforceable state pharmacy regulation.

OBRA ’90 patient counseling. The Omnibus Budget Reconciliation Act of 1990 and most state pharmacy laws require pharmacies to offer counseling on new prescriptions. Doorstep drone delivery without pharmacist interaction does not satisfy this requirement on its own. Compliant models pair drone delivery with telephonic or telehealth pharmacist counseling completed before flight dispatch (or offered at delivery via a video/audio channel), with the counseling event (offered, accepted, declined, or completed) documented in the chain-of-custody record. State rules illustrate the same principle: Indiana, for example, permits a written notice bearing the pharmacy's phone number and a bona fide offer to counsel for mail, parcel, or hand delivery, but expects counseling in person or by telephone when practicable and does not permit blanket future waivers. The delivery record should therefore capture the counseling offer and how the patient can reach a pharmacist before using the medication.

Key unresolved questions include:

- Who is the “dispensing entity” when a drone delivers a prescription? The pharmacy, the drone operator, or both?
- How do interstate drone deliveries comply with both the originating and destination state’s requirements?
- Can state pharmacy boards regulate the drone delivery process itself, or only the pharmacy dispensing process?

3.5 HIPAA: Patient Data Protection

Medical drone delivery creates HIPAA compliance challenges on two fronts: physical protected health information (PHI) on prescription labels and package markings, and electronic PHI transmitted as part of delivery telemetry, tracking data, and healthcare system integration.

Drone telemetry data that includes delivery location becomes PHI when linkable to patient identity or medical information. Real-time tracking features must be HIPAA-compliant. Drone operators handling PHI are business associates requiring Business Associate Agreements (BAAs) with covered entities.

AES-256 encryption for data at rest and TLS 1.3 in transit represent a strong, widely used industry baseline (Gilmour & Hoff, 2025). It should be noted, however, that the HIPAA Security Rule treats encryption as an addressable implementation specification (45 CFR 164.312) rather than mandating any specific algorithm; these ciphers are a recommended baseline, not a black-letter HIPAA requirement. What is less clear is where the boundary falls between operational telemetry (non-PHI) and delivery-specific data (potentially PHI). A January 2025 HIPAA Security Rule NPRM proposes to remove the addressable designation and make encryption of ePHI at rest and in transit mandatory (with limited exceptions); as of mid-2026 that rule is not yet final, so the addressable standard still governs.

3.6 Lessons from Ground-Based Autonomous Delivery

Ground-based autonomous delivery robots have operated in US healthcare settings for over a decade, providing practical lessons for drone chain of custody.

What has worked:

- **Locked compartments with authenticated access** are a universal standard. Starship Technologies uses app-based locks with multi-camera monitoring and alarm systems. Serve Robotics uses QR-code locks with live contact center escalation on tampering.
- **Aethon's MedEx system** represents the most mature automated chain-of-custody solution in healthcare. Deployed in 150+ US hospitals, MedEx uses passive RFID, barcodes, biometric fingerprint authentication, and secure locked carts to generate electronic chain-of-custody receipts with person, location, and timestamp for every access event. Geisinger's MedEx deployment completed 49,435 deliveries with 40-50% cost savings (RFID Journal, 2010).
- **Arrive AI's asynchronous handoff model** uses patented Arrive Points as secure, climate-assisted intermediary hubs that solve the "nobody home" problem. In partnership with Ottonomy at Hancock Regional Hospital, Arrive AI operates the world's first fully asynchronous robotic medical delivery inside a hospital.
- **Temperature-controlled compartments** have proven cold-chain compliance is achievable. Nuro's R3 robot maintains temperatures from -6°C to 47°C (22°F to 116°F).

What has failed:

- **Cybersecurity vulnerabilities.** In 2022, five zero-day vulnerabilities (CVSS 9.8) were discovered in Aethon TUG hospital robots, allowing remote hijacking of cameras, robot control, and medication delivery disruption. The vulnerabilities were patched in firmware v24.

- **Physical theft and vandalism.** Delivery robots in urban environments have been kicked open, had packages stolen, and been destroyed.
- **No controlled substance pathway.** No ground robot operator has established a viable pathway for DEA-scheduled substance delivery.

Key takeaway: The regulatory gap is universal across both drone and ground robot modalities. No state PDD (Personal Delivery Device) law includes medical-specific chain-of-custody requirements. The drone industry should build on ground robot lessons rather than starting from scratch.

3.7 Specimen and Biologics-Specific Regulations

Medical drone delivery is often framed as a single cargo category, but three high-value categories (blood products, organs for transplant, and clinical laboratory specimens) operate under their own regulatory regimes that any chain-of-custody framework must explicitly address.

Blood products. Transport of whole blood, red cells, platelets, and plasma is governed by FDA 21 CFR 606 and 640 and by the **AABB Standards for Blood Banks and Transfusion Services**. These standards prescribe temperature ranges (1-6°C for red cells, 20-24°C with continuous agitation for platelets, frozen for plasma), component-specific handling, and detailed documentation. Chain of custody for drone blood delivery must capture continuous temperature (and, for platelets, agitation status), and must integrate with the receiving blood bank's Laboratory Information System and transfusion-service records.

Organs for transplant. Organ transport is governed by **UNOS/OPTN policies** and the Organ Procurement and Transplantation Network Final Rule (42 CFR Part 121). The 2019 Baltimore drone kidney transport operated under a one-time research arrangement, not as routine UNOS-compliant transport. Any scaled drone organ delivery framework must satisfy OPTN chain-of-custody, cold-ischemia-time tracking, organ identity verification, and donor-recipient matching documentation requirements, all of which are more stringent than standard pharmaceutical chain of custody.

Clinical laboratory specimens. Specimen transport is governed by **CLIA (42 CFR 493)** and **CAP accreditation standards** for specimen integrity and documentation, and by **IATA Packing Instruction 650 (UN3373, Biological Substance Category B)** for in-flight packaging. Drone transport of clinical specimens must satisfy specimen labeling, transport-condition documentation, and time-from-collection requirements. Results can be invalidated (and patient care delayed or misdirected) if chain-of-custody documentation is incomplete.

Framework implication: A one-size-fits-all chain of custody is insufficient. The framework defined in Section 4 must route cargo by category at origin and apply category-specific controls throughout.

3.8 The Gap

No single agency owns end-to-end chain of custody for medical drone delivery. The FAA regulates the aircraft and airspace. The FDA regulates the drug product. The DEA regulates controlled substances. State pharmacy boards regulate dispensing. HIPAA regulates patient data. The FCC regulates communication links. Each agency owns a slice, but the seams between them, where a pharmacy hands a package to a drone, where a drone delivers to a patient, where telemetry data crosses from operational to clinical, are unregulated.

Table 2 maps each regulatory authority against the stages of pharmaceutical transport by drone, making visible how oversight is distributed by domain rather than end-to-end and where custody handoffs fall outside any single regulator's responsibility.

Transport Stage → Regulatory Body ↓	Dispense	Seal & Release	Drone Transport	Drone Delivery	Confirmation
FAA	❌ Not regulated	❌ Payload not assessed	✅ Flight safety & airspace	⚠️ Landing behavior only	❌ Not regulated
FDA	✅ Drug safety & quality	⚠️ Packaging integrity risk	⚠️ Temperature & handling	❌ No delivery authority	❌ No verification role
DEA	✅ Controlled substance rules*	⚠️ Security unclear	❌ No approved pathway	❌ Diversion risk	❌ No receipt validation
State Pharmacy Boards	✅ Dispensing authority	⚠️ Custody responsibility unclear	❌ No transit oversight	✅ Delivery location rules	⚠️ Patient receipt
HIPAA	⚠️ PHI on labels	❌ No custody role	⚠️ Telemetry may be PHI	✅ PHI exposure	✅ Identity-linked PHI
FCC	❌ Not applicable	❌ Not applicable	✅ Comms & telemetry	❌ Not applicable	❌ Not applicable
Chain of Custody (Gap)	✅ Initial custody known	❌ Custody handoff unowned	❌ Unattended custody	❌ Handoff not verified	❌ Proof not defensible

* DEA authority applies only if controlled substances are permitted; no current U.S. medical drone delivery programs include them.

Table 2. Regulatory Concerns Across Pharmaceutical Transport Stages (Drone Delivery)

This gap is not theoretical. It is the defining challenge for scaling medical drone delivery in the United States, and it is exactly the gap that an industry-driven chain-of-custody framework must fill.

4. AeroX Chain of Custody Framework for Medical Drone Delivery

The AeroX Chain of Custody Framework defines six sequential stages that together constitute an unbroken, verifiable record from the moment a medical package is prepared for delivery to its final receipt and beyond. Each stage specifies the controls, technologies, and documentation required to maintain chain of custody.

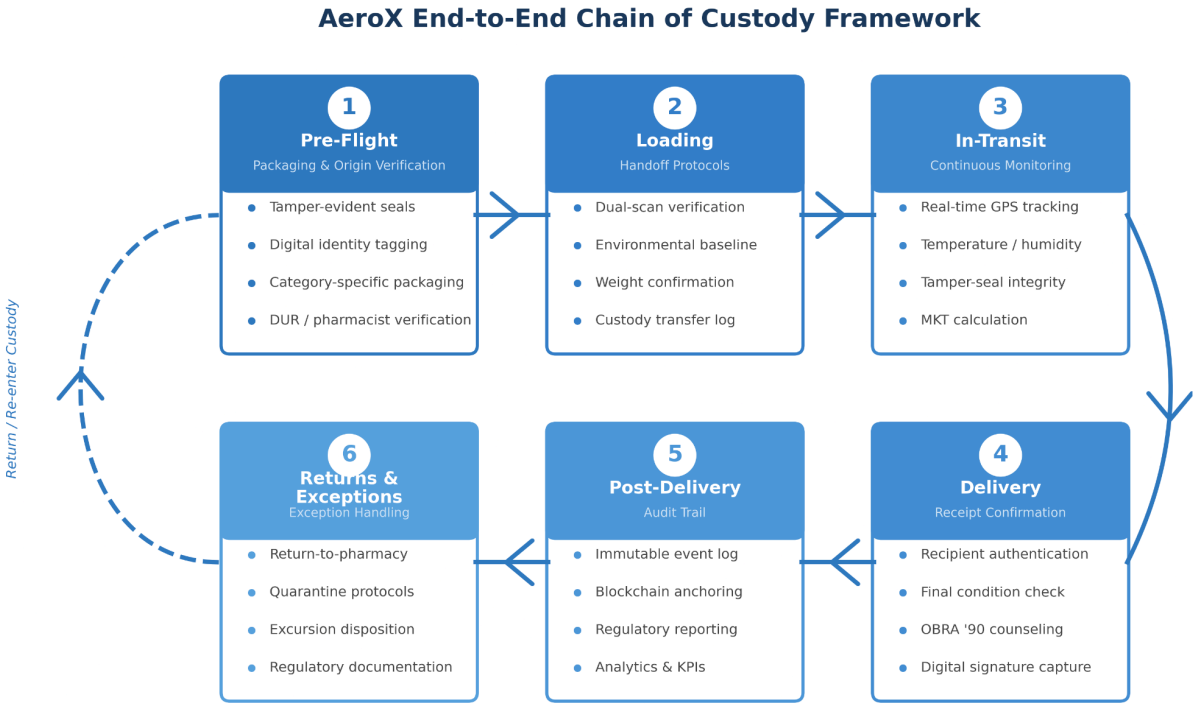


Figure 3. AeroX End-to-End Chain of Custody Framework. Six sequential stages maintain an unbroken, verifiable record from packaging through delivery, with a return path for exceptions.

Controls scale to product risk. Not every delivery invokes every control. The framework applies a tiered model in which the intensity of custody controls, authentication method, tracing granularity, and documentation, scales with the clinical and regulatory risk of the cargo. A routine antibiotic may require barcode-scan verification and standard telemetry, while a controlled substance or temperature-sensitive biologic invokes biometric authentication, full DSCSA/REMS capture, and continuous excursion monitoring. Where useful, each stage is benchmarked against established mail-order and specialty-pharmacy practice, which already performs remote dispensing, delivery confirmation, and cold-chain accountability at scale.

Applicability across use cases and business models. Although the framework is illustrated primarily with pharmaceutical and patient-facing (B2C) examples, the same six stages apply to laboratory specimens, blood products, and facility-to-facility (B2B) transfers. What changes across use cases is the specific control invoked at each stage, the packaging standard, the authentication method, the retention rule, not the structure of the chain itself.

The six stages apply to every delivery, but the pharmacy risk profile shifts with the delivery model. The table below summarizes the forward delivery models; failed, refused, and returned deliveries are governed by Stage 6 (Section 4.6).

Delivery model	Custody endpoint / recipient	Key pharmacy risk	Primary controls
Direct-to-patient (home)	Patient or authorized agent	Counseling obligation; recipient identity; storage conditions after handoff	Risk-based authentication; documented counseling offer; stability handoff to patient
Facility / institutional	Badged staff at hospital or clinic	Receipt into the correct department; after-hours handling	Credential-based authentication; facility receipt log; integration with pharmacy system
Interfacility (B2B)	Authorized personnel at receiving site	DSCSA/3PL status; specimen and product integrity in transit	Sealed container; itemized manifest; 3PL licensure where applicable; category-specific packaging
Secure hub / locker	Authenticated locker; asynchronous patient pickup	Unattended dwell time; stability window; who holds custody while product waits	Sealed container with itemized list; verified access or secured area; continuous environmental monitoring; maximum dwell time

Table 3. Forward Delivery Models and Pharmacy Risk Profiles

A secure hub or locker is best understood as a regulated extension of the pharmacy delivery workflow rather than an unattended drop point. Indiana's remote dispensing facility statute is instructive: drugs transported to a remote site must be in sealed containers with an itemized list, accepted and verified by authorized personnel or placed in a secured delivery area, and stored so as to protect the drug's identity, safety, security, and integrity.

4.1 Stage 1: Pre-Flight — Packaging and Origin Verification

Chain of custody begins before the drone leaves the ground. The origin verification stage establishes the baseline identity, condition, and authorization of the medical package.

Tamper-evident packaging. Every medical package must be sealed in tamper-evident packaging with both visual indicators (breakable seals, color-changing labels) and electronic indicators (RFID seal-status

tags) that can be verified at subsequent stages. Packaging must meet or exceed the standards demonstrated in Wing's Apian/NHS partnership, which represents the current best practice.

Category-specific packaging and routing. Packaging requirements vary by cargo category and must be determined at origin, not in flight: USP <797>-compliant sterile packaging for compounded sterile preparations; USP <800> double-containment with segregation from non-hazardous cargo for NIOSH-listed hazardous drugs; IATA Packing Instruction 650 (UN3373) for Category B biological specimens; AABB-compliant temperature-controlled containers with agitation (where applicable) for blood products; OPTN-compliant containers with cold-ischemia-time tracking for organs. The chain-of-custody record captures the applied packaging standard and any category-specific handling constraints. These category-specific requirements are enforced through a payload-specific pre-flight checklist keyed to the cargo type, so that the verification steps performed always match what is actually being flown.

Digital identity tagging. Each package receives a unique digital identity via QR code, RFID tag, or NFC marker linked to a digital record containing the package contents, sender identity, intended recipient, environmental requirements, category-specific regulatory markers (REMS program code, DEA schedule, DSCSA transaction information, CLIA specimen ID), and expiration or time-to-administration. This identity follows the package through every subsequent stage.

Dispensing workflow integration and sender authentication. For prescription medications, chain of custody begins *after* the pharmacy's standard dispensing workflow is complete: prospective drug utilization review (DUR), pharmacist verification (PV) of the order, final product check against the prescription, and (for new prescriptions) offer of patient counseling per OBRA '90 and applicable state law. The individual (or automated system) releasing the verified product into the drone delivery pathway must authenticate through credentials or biometrics. The chain-of-custody record incorporates the verifying pharmacist's NPI/state license identifier, PV timestamp, counseling-offer disposition, and (where applicable) REMS ETASU completion.

Patient delivery authorization. For patient-facing deliveries (home delivery, hospital-at-home), the chain of custody must include the patient's documented consent to drone delivery as a modality, captured at the time of prescription or on a standing basis. This mirrors the Texas 291.12 proposed requirement and establishes that autonomous delivery is a patient-authorized modality, not a default.

Environmental baseline recording. Temperature, humidity, and other relevant environmental conditions are recorded at the point of origin using calibrated IoT sensors. For temperature, the pharmaceutical cold-chain standard is NIST-traceable calibration to tolerances below ±0.5°C, achievable with PT1000 resistance temperature detectors. This baseline becomes the reference point against which in-transit conditions and Mean Kinetic Temperature are computed.

4.2 Stage 2: Loading — Handoff Protocols

The transfer of a package from a facility to a drone is a critical custody transition that must be documented with the same rigor as any other transfer in the pharmaceutical supply chain. The framework introduces no additional courier or intermediary into this handoff; custody passes directly from the dispensing facility to the drone, preserving the close facility-to-aircraft connection rather than adding a transporter to the chain.

Verified loading with digital confirmation. The loading process generates a digital record linking the specific package (via its digital identity tag) to the specific drone (via its aircraft identifier). This record includes the identity of the person or automated system performing the loading, the timestamp, and the location.

Authenticated access to payload compartment. The drone's payload compartment requires biometric or credential-based authentication to open. This prevents unauthorized access and creates an access log comparable to Aethon MedEx's electronic chain-of-custody receipts.

Automated integrity verification. Upon loading, automated sensors verify the package weight against the expected weight and confirm that tamper-evident seals are intact. Any discrepancy triggers a hold for manual inspection.

4.3 Stage 3: In-Transit — Continuous Monitoring

The in-transit stage represents the period of autonomous operation where no human is present with the cargo. This is where technology must substitute for human oversight.

Real-time IoT telemetry. A sensor suite continuously monitors and streams data for:

- Temperature (critical for pharmaceuticals, biologics, vaccines)
- Humidity (relevant for moisture-sensitive products)
- Vibration and shock (relevant for biopharmaceuticals sensitive to aggregation)[1]
- Barometric pressure (relevant for altitude-sensitive products)
- Light exposure (relevant for photosensitive medications)
- GPS position (continuous location tracking)

Research demonstrates this monitoring is feasible and reliable. Gilmour and Hoff (2025) describe IoT containers that maintained organ temperatures at approximately 2.5°C across transport missions, with vibration forces less than 0.5 G. Aggarwal et al. (2025) demonstrated vaccine cold-chain maintenance at 3-4°C across drone flights up to 17 km.

Tamper-evident logging. All sensor data is cryptographically hashed and recorded to a tamper-evident, append-only record (Section 5.2 describes the implementation options, of which distributed ledger technology is one). This ensures that records cannot be altered after the fact without detection, providing the evidentiary integrity required for regulatory audits and legal proceedings. Where distributed ledger technology is used, research supports hybrid on-chain/off-chain architectures where critical chain-of-custody transfers are stored on-chain while high-volume telemetry data is stored off-chain with cryptographic anchors (Betti Sorbelli, 2024).

[1] Clarification: aggregation here means protein aggregation, the molecular clumping that can degrade biologics such as vaccines, insulin, and monoclonal antibodies when subjected to excessive vibration or shock.

Automated excursion alerts and disposition authority. When any monitored parameter exceeds predefined thresholds, the system automatically generates alerts to the operations center, the sending facility, and the receiving facility. As previously noted, for stability-sensitive pharmaceutical products, compliance is evaluated not solely by instantaneous temperature but by Mean Kinetic Temperature (MKT) calculated over the transit window against the product-specific stability budget; the chain-of-custody system must compute MKT in real time and flag legs that consume disproportionate stability margin even when instantaneous readings remain in range.

Disposition authority for excursion events must be explicitly assigned. The dispensing pharmacist of record (or a designated pharmacy-side QA authority) retains disposition authority for pharmaceutical products: whether a compromised shipment may proceed to the patient, must divert to an alternate recipient or climate-controlled intermediate hub, must return for quarantine, or must be destroyed. For blood products, the responsible transfusion-service medical director retains equivalent authority; for organs, the OPO and receiving transplant center. Drone operators do not have independent authority to release potentially compromised medical product to a patient. The decision, the telemetry supporting it, and the authorizing individual's identity are recorded to the chain-of-custody ledger.

Geofencing and route deviation detection. The drone's flight path is continuously compared against the authorized route. Any deviation triggers investigation. Combined with Remote ID (14 CFR Part 89), this provides regulators and airspace managers with real-time visibility into the delivery operation.

4.4 Stage 4: Delivery — Receipt Confirmation

The delivery stage transfers custody from the drone to the recipient. For medical cargo, this transfer must be more rigorous than a package left on a doorstep.

Recipient identity verification. The recipient must verify their identity before the payload compartment opens. Verification methods include:

- Biometric authentication (fingerprint, facial recognition)
- Credential-based authentication (healthcare facility badge, as demonstrated by Matternet Station)
- Code-based authentication (one-time PIN, QR code via patient app)

The appropriate verification level should scale with cargo sensitivity. Routine OTC medications may require code-based verification. Controlled substances, when eventually permitted, should require biometric verification.

Timestamp and location confirmation. The delivery event is recorded with a precise GPS-confirmed location and timestamp, creating an unambiguous record of when and where custody transferred.

Photo/video documentation. Onboard cameras capture the delivery event, providing visual evidence for the audit trail. This documentation addresses the "last-meter problem" identified across current operators, the unmonitored moment between package release and patient pickup.

Digital signature or acknowledgment. The recipient provides a digital acknowledgment of receipt, completing the active custody chain.

Closing the loop with existing patient workflows. Delivery confirmation can feed the same population-health and medication-adherence workflows health systems already run, for example an automated call or text to the patient confirming receipt and prompting adherence, mirroring how mail-order and specialty pharmacies confirm delivery today.

Home-health handoff. For higher-acuity patients who already receive scheduled home-health visits, the attending nurse or aide can serve as the authenticated recipient, closing the custody loop in person. When turnaround time permits, an order can be placed and delivered while the home-health worker is on-site.

Counseling and stability handoff. For new prescriptions, the pharmacist counseling event must be recorded, including whether counseling was offered and completed pre-flight, offered at the time of delivery via a live channel, or declined by the patient. For temperature-sensitive products delivered to a patient's home, the delivery record must capture that the patient has been informed of the required storage conditions and the maximum time to refrigeration. Custody of the product's *stability* (as distinct from its physical location) transfers to the patient only after this handoff is documented; prior to this point, stability responsibility remains with the dispensing pharmacy. For REMS-restricted products, any ETASU requirements due at delivery (for example, patient acknowledgment of medication guide receipt) are captured here. The record also captures how the patient can reach a pharmacist with questions before using the medication.

4.5 Stage 5: Post-Delivery — Audit Trail

The chain of custody does not end at delivery. The post-delivery stage ensures that the complete record is preserved, integrated, and accessible for as long as regulatory and legal requirements demand.

Tamper-evident origin-to-receipt record. The complete chain of custody, from origin verification through delivery confirmation, is consolidated into a single, tamper-evident record anchored to the integrity layer described in Section 5.2. This record includes every sensor reading, every authentication event, every custody transfer, and every alert or exception

Healthcare system integration. Chain-of-custody data integrates with the receiving institution's systems via HL7 FHIR APIs:

- Electronic Health Records (EHR): delivery confirmation linked to patient record
- Pharmacy management systems: dispensing record updated with delivery data
- Laboratory Information Systems (LIS): sample transport conditions linked to test results

This integration is not optional. Without it, the chain of custody exists in isolation from the clinical record, creating gaps in the patient's care documentation.

Regulatory-aligned retention. Records are retained according to the most stringent applicable requirement across all regulatory bodies. FDA drug distribution records (21 CFR 211.196) require retention for at least one year after expiration. DEA controlled substance records require two-year retention. State pharmacy boards may require longer periods.

Audit-ready reporting. The system generates on-demand reports formatted for specific regulatory audiences: FDA inspection reports, DEA audit packages, state pharmacy board compliance documentation, and HIPAA breach investigation records.

4.6 Stage 6: Returns and Exception Handling

Not every delivery succeeds. A complete chain-of-custody framework must specify the workflow for failed, refused, aborted, and damaged deliveries, because a medical product that has left the dispensing pharmacy cannot simply be re-entered into dispensable inventory without documented review. Omitting this stage is one of the most common deficiencies in current operator practice.

Failure modes addressed:

- Recipient unavailable or fails identity verification at handoff
- Patient refuses delivery
- Drone aborts mid-flight (weather, mechanical, airspace conflict, sensor excursion) and returns with payload
- Package is damaged in flight, on landing, or on return
- Delivery is completed but to the wrong recipient and requires retrieval
- Shipment is held at an intermediate hub (e.g., Arrive AI Arrive Point) beyond the product's stability window

Continuous return-leg custody. A returned or diverted package remains under continuous chain of custody through the return flight, receipt at the originating facility, and quarantine pending disposition. The same telemetry streams, tamper-evidence checks, and authenticated-access controls that applied to the outbound flight apply to the return leg and to any intermediate handoff.

Disposition pathways. Returned pharmaceutical product is not returned to dispensable stock except in the narrow circumstances permitted by state pharmacy law, manufacturer stability data, and the dispensing pharmacist's documented review. Default pathways are:

1. **Quarantine and destroy:** product whose stability budget is exhausted, whose tamper evidence is compromised, or whose chain of custody is broken
2. **Quarantine and manufacturer return:** where a manufacturer return program exists and the product qualifies
3. **Re-dispense under pharmacist review:** only for product with intact tamper evidence, unbroken chain of custody, and MKT within stability budget, with pharmacist approval recorded to the ledger
4. **Re-route:** delivery retried or redirected to an alternate authorized recipient within the product's remaining stability window

Asynchronous handoff as a structural mitigation. Shared-infrastructure models such as Arrive AI's Arrive Points (climate-assisted, authenticated intermediate hubs) reduce the frequency of failed deliveries by decoupling flight timing from recipient availability, while preserving chain of custody through authenticated locker access, continuous environmental monitoring, and explicit custody transfer events at the hub.

Adverse event linkage. If a patient experiences an adverse drug reaction following drone delivery, the complete chain-of-custody record (including MKT history, tamper-evidence state, and delivery-point conditions) must be retrievable and integrable with MedWatch/FAERS reporting, manufacturer complaint investigations, and any state board of pharmacy or UNOS/OPTN inquiry. The chain of custody is the evidentiary record through which drone delivery is either exonerated or identified as a contributing cause.

5. Technology Enablers

The AeroX Chain of Custody Framework depends on a technology stack that spans from physical sensors to cloud-based integration platforms. Each layer serves a specific function in maintaining and documenting chain of custody. Critically, the framework specifies required outcomes rather than required products. The subsections that follow describe technologies capable of meeting each outcome, but any implementation that demonstrably satisfies the minimum auditable standards below is acceptable. This distinction matters to regulators and pharmacy permit holders, whose obligation is to demonstrate that a standard was met, not to adopt any particular vendor's stack.

Minimum auditable standards. The following outcomes constitute the minimum auditable standard for a medical drone delivery chain of custody. Each must be demonstrable on audit regardless of the technology chosen to achieve it.

Required outcome	What must be demonstrable on audit	Addressed in
Tamper-evident packaging	Seal integrity verifiable at each custody transfer; any breach detected, logged, and actionable	4.1, 4.2
Validated temperature control	Shipping system qualified against the product's stability budget, including seasonal extremes	4.1, 4.3
Calibrated logging	NIST-traceable calibration; readings time-stamped and attributable to a device and an actor	4.1, 4.3, 5.1
Pharmacist-controlled excursion disposition	A named pharmacy authority decides release, divert, quarantine, or destroy; decision and rationale recorded	4.3
Risk-based recipient authentication	Authentication strength matched to the product's risk tier	4.4
Failed-delivery rules	Predefined handling for unavailable, refused, aborted, damaged, or misdelivered shipments	4.6
Quarantine, destruction, re-dispense criteria	Documented disposition pathways; no undocumented return to dispensable stock	4.6
Patient complaint and adverse event capture	Complaints and adverse events linkable to the complete custody record	4.6
Record retention and audit retrieval	Retention to the most stringent applicable requirement; audit-ready retrieval on demand	4.5

Table 4. Minimum Auditable Standards for Medical Drone Chain of Custody

Benchmark. Texas's proposed Section 291.12 is a useful yardstick for these standards: it addresses tamper-evident packaging, maintenance of appropriate temperature, patient notification, reporting of

delivery irregularities, the pharmacist's authority to refuse a delivery that may compromise the drug, replacement of compromised product, and two-year retention of delivery records.

5.1 IoT Sensor Suite

The physical layer of chain of custody relies on miniaturized, medical-grade sensors embedded in or attached to the drone payload compartment and individual packages:

- **Temperature:** PT1000 resistance temperature detectors with NIST-traceable calibration to tolerances below ±0.5°C (the pharmaceutical cold-chain standard per USP <1079> and USP <659>), supporting tighter tolerances where individual product stability budgets require
- **Humidity:** Capacitive humidity sensors for moisture-sensitive medications
- **Vibration:** MEMS accelerometers measuring multi-axis vibration (critical for biopharmaceuticals; drone vibration frequencies measured at 0.1-3.4 Hz per Hii et al., 2019)
- **Pressure:** Barometric sensors for altitude-related pressure changes
- **Light exposure:** Photodiode sensors for photosensitive medications
- **Tamper detection:** Electronic seal-status sensors and compartment access detectors
- **Payload and airworthiness impact:** sensor mass counts against the aircraft's usable payload and is specified in the tens-of-grams range so instrumentation does not materially reduce deliverable cargo.[2]

5.2 Data Integrity: Tamper-Evident Audit Records

The required outcome is a chain-of-custody record that is tamper-evident, attributable, and independently verifiable: any alteration after the fact must be detectable, every entry must trace to an authenticated actor, and an auditor must be able to confirm integrity without relying on the good faith of the party holding the data. Several technologies satisfy this standard. Blockchain is one of them, and it is described here in the most detail because it is the most discussed, but it is an option rather than a requirement of this framework.

Why tamper-evidence matters. Traditional databases can be modified by administrators. In a multi-stakeholder delivery chain involving pharmacies, drone operators, healthcare institutions, and regulators, no single party should hold the unilateral ability to alter records. Distributed consensus is one answer. Others include append-only (WORM) storage, cryptographically chained hash logs, digitally signed records with independent trusted timestamping, and third-party escrow of audit logs. The right choice follows the trust model: distributed ledger technology earns its added complexity where multiple independent parties must share one record without a trusted intermediary, whereas a single health system working with one contracted carrier may meet the identical standard using simpler, well-understood controls. Implementers should choose the least complex architecture that demonstrably delivers tamper-evidence, attribution, and independent verification, and should be prepared to evidence that choice to an auditor.

[2] Where a sensor or active (powered) container includes lithium batteries, it is treated as an FAA/DOT-regulated hazardous material and must satisfy the operator's dangerous-goods authorization and packaging requirements.

Architecture. Where a distributed ledger is the chosen implementation, the framework recommends a hybrid on-chain/off-chain architecture:

- **On-chain:** Custody transfer events (loading, delivery), identity verification records, compliance snapshots, exception alerts
- **Off-chain:** High-frequency sensor telemetry (temperature readings every 5 seconds, GPS positions), with cryptographic hashes anchored to the blockchain at regular intervals

Smart contracts. Where the chosen ledger supports programmable logic, automated compliance verification via smart contracts can confirm in real time that temperature remained within range, that the delivery occurred within the authorized time window, and that the recipient was verified. Noncompliance triggers automated exception handling.

Multi-stakeholder transparency. However the integrity layer is implemented, the shipper, carrier, receiver, and regulator should each access the same tamper-evident record through role-based permissions, eliminating disputes about what happened during transit.

5.3 Data Security and HIPAA Compliance

Every element of the chain-of-custody system that touches patient-identifiable information must comply with HIPAA Security Rule requirements[3]:

- **AES-256 encryption** for all data at rest, including stored sensor telemetry, delivery records, and patient information
- **TLS 1.3** for all data in transit, including real-time telemetry streaming, system integrations, and user-facing applications
- **Role-based access controls (RBAC)** ensuring that each stakeholder accesses only the data necessary for their function
- **De-identification protocols** for aggregate data sharing, research, and operational analytics
- **Business Associate Agreements (BAAs)** between all entities in the data chain

5.4 AI and Machine Learning

Intelligence capabilities enhance chain of custody from reactive documentation to proactive risk management:

- **Predictive environmental monitoring:** ML models trained on historical flight data predict potential cold-chain failures before they occur, enabling preemptive route changes or packaging adjustments
- **Anomaly detection:** Real-time detection of route deviations, unexpected stops, unusual vibration patterns, or other indicators of tampering or system failure

[3] HIPAA treats encryption as an addressable specification under 45 CFR 164.312; the algorithms listed below are AeroX's recommended baseline rather than HIPAA-mandated ciphers.

- **Automated compliance checking:** Continuous comparison of in-flight conditions against applicable regulatory requirements, with automatic flagging of potential noncompliance

5.5 Integration Architecture

Chain of custody data is only valuable if it connects to the systems that manage patient care and regulatory compliance. In practice these connections are intended to converge in a single chain-of-custody platform, giving every stakeholder, pharmacy, drone operator, receiving facility, and regulator, one integrated view of the package's full lifecycle rather than siloed records held by each vendor.

- **HL7 FHIR APIs** for interoperability with EHR, pharmacy management, and laboratory information systems
- **DSCSA-compatible transaction records** for integration with the national drug supply chain tracking infrastructure
- **Real-time operations dashboards** for drone fleet management and chain-of-custody monitoring
- **Regulatory reporting interfaces** generating formatted documentation for FDA, DEA, state pharmacy board, and HIPAA audits

6. Recommendations for the Industry

6.1 For Healthcare Institutions

- **Require chain-of-custody documentation** from any drone delivery partner as a condition of contract. Documentation should cover all six stages of the framework.
- **Integrate drone delivery data** into existing pharmacy and logistics workflows. Chain-of-custody records should flow into the same systems used for traditional delivery documentation.
- **Establish internal protocols** for receiving drone-delivered medical packages, including staff training on verification procedures and exception handling.
- **Execute Business Associate Agreements** with drone delivery operators that specifically address HIPAA compliance for delivery telemetry and tracking data.
- **Sequence controlled substances after an initial non-controlled phase.** Early drone delivery programs are best launched with non-controlled medications, with controlled substances phased in as DEA and state board of pharmacy guidance matures.[4]

6.2 For Regulators

- **Develop unified, multi-agency guidance** for medical drone delivery chain of custody. An interagency working group involving the FAA, FDA, DEA, and HHS should coordinate to eliminate regulatory gaps and overlaps.
- **Establish minimum chain-of-custody standards** as a condition of Part 135 medical delivery operations and under the forthcoming Part 108 framework.
- **Create a certification or compliance framework** for drone delivery chain-of-custody systems, analogous to FDA's certification of electronic health record systems.
- **Issue controlled substance guidance.** The DEA should publish formal guidance on the conditions under which controlled substances may be delivered by autonomous aerial or ground-based systems.
- **Recognize industry frameworks.** Regulators should engage with industry-developed standards, including this framework, as inputs to future rulemaking.

6.3 For the Drone Industry

- **Adopt standardized chain-of-custody data formats** and protocols. Proprietary approaches that cannot interoperate with other operators and healthcare systems are insufficient for an industry seeking mainstream healthcare adoption.

[4] This sequencing reflects input from pharmacy practice subject-matter experts consulted during the development of this framework, and it is consistent with current practice: every Part 135 drone operator presently excludes controlled substances, and Texas's proposed Section 291.12 would do the same. When controlled substances are later introduced, the model should address pharmacist corresponding responsibility (21 CFR 1306.04), payload security evaluated against DEA physical-security expectations (21 CFR 1301.71-1301.76), positive recipient identification, prescription drug monitoring program reporting (for example, Indiana's INSPECT), and DEA theft or loss reporting (DEA Form 106).

- **Collaborate through industry working groups.** Organizations like the UPDWG (Unmanned Aircraft for Payload Delivery Working Group), AUVSI, and ASTM provide existing forums for developing consensus standards.
- **Invest in interoperable technology platforms.** Chain-of-custody systems should be designed for multi-operator environments where healthcare institutions may work with different drone providers.
- **Publish chain-of-custody practices.** Transparency builds trust. Operators should publicly document their chain-of-custody approaches in sufficient detail for healthcare institutions and regulators to evaluate.
- **Prepare for multi-modal convergence.** As drone delivery, ground robot delivery, and traditional courier delivery converge, chain-of-custody systems must work across modalities. Infrastructure like Arrive AI's Arrive Points and DroneUp's DBX stations point toward shared chain-of-custody nodes that serve multiple delivery methods. A single chain-of-custody record should track a package across modalities under one custody identity, for example a leg flown by drone and a leg carried by a ground courier, so hybrid operations remain auditable end to end.

7. Conclusion

Medical drone delivery is no longer a question of if, but of how. The technology works. The market is growing. The regulatory pathway, particularly with the proposed Part 108 BVLOS rule, is becoming clearer. What remains missing is the connective tissue of trust: a standardized, technology-enabled chain-of-custody framework that gives healthcare institutions, regulators, and patients confidence that medical cargo delivered by drone is as safe as cargo delivered by any other means. That confidence depends on treating drone delivery as a medication-use process rather than an aviation one: each stage must meet or exceed the pharmacy standards that already govern dispensing, counseling, storage, privacy, delivery confirmation, exceptions, and accountability.

The AeroX Chain of Custody Framework, spanning pre-flight packaging and verification, loading handoff protocols, in-transit continuous monitoring with MKT-based disposition authority, delivery receipt confirmation with counseling and stability handoff, post-delivery audit trails, and, critically, returns and exception handling, provides a comprehensive foundation for this trust. It leverages proven technologies, draws on lessons from both drone and ground-based autonomous delivery, and addresses the requirements of every relevant regulatory body, including the specimen-, blood-, and organ-specific regimes that a one-size-fits-all framework would otherwise leave exposed.

No single company can solve this alone. AeroX calls on healthcare institutions to demand chain-of-custody standards from their delivery partners. We call on regulators to convene multi-agency guidance development. And we call on the drone industry to move from proprietary, siloed approaches to interoperable, transparent, and auditable chain-of-custody practices.

The sky is open. It is time to secure it.

Glossary

Definitions for acronyms and specialized terms used throughout this whitepaper.

3PL (Third-Party Logistics Provider). A DSCSA-defined entity that provides logistics services for prescription drugs without taking ownership of the product. Requires state licensure in most jurisdictions.

AABB. Standards-setting organization (formerly the American Association of Blood Banks) whose *Standards for Blood Banks and Transfusion Services* govern collection, storage, and transport of blood products in the United States.

BAA (Business Associate Agreement). A HIPAA-required contract between a covered entity (e.g., a hospital or pharmacy) and a business associate (e.g., a drone operator handling PHI) specifying permitted uses, safeguards, and breach responsibilities for protected health information.

BVLOS (Beyond Visual Line of Sight). Drone operation in which the remote pilot cannot directly observe the aircraft without visual aids.

CFR (Code of Federal Regulations). The codification of general and permanent US federal regulations, organized by title and part.

CLIA (Clinical Laboratory Improvement Amendments). Federal standards (42 CFR 493) governing US clinical laboratory testing, specimen handling, and quality control.

DEA (Drug Enforcement Administration). US federal agency regulating controlled substances under the Controlled Substances Act.

DSCSA (Drug Supply Chain Security Act). 2013 federal law (Pub L 113-54, Title II) mandating electronic, interoperable package-level tracking of prescription drugs across the US supply chain.

DUR (Drug Utilization Review). Pharmacist review of a prescription for clinical appropriateness, drug-drug interactions, therapeutic duplication, and patient-specific factors before dispensing.

EHR (Electronic Health Record). Digital patient health record system used by healthcare providers.

ETASU (Elements To Assure Safe Use). A subset of REMS requirements that impose specific conditions (e.g., prescriber certification, patient enrollment, laboratory testing) on how a drug is prescribed or dispensed.

FAA (Federal Aviation Administration). US federal agency regulating civil aviation, airspace, and aircraft certification.

FDA (Food and Drug Administration). US federal agency regulating pharmaceuticals, biologics, and medical devices.

FHIR (Fast Healthcare Interoperability Resources). An HL7 standard for healthcare data exchange, typically delivered via RESTful APIs.

GDP (Good Distribution Practice). FDA and international standards for maintaining pharmaceutical quality during transportation, storage, and distribution.

HIPAA (Health Insurance Portability and Accountability Act). US law (Pub L 104-191) governing privacy and security of protected health information.

HL7 (Health Level Seven International). Standards development organization for healthcare data interoperability; publisher of the FHIR standard.

IATA PI 650. International Air Transport Association Packing Instruction 650, which specifies packaging requirements for UN3373 (Category B) biological substances transported by air.

IoT (Internet of Things). Network of connected physical devices capable of collecting and exchanging data, including the sensor suite used in drone chain-of-custody systems.

LIS (Laboratory Information System). Software system used by clinical laboratories for specimen tracking, test ordering, result reporting, and chain-of-custody documentation.

MKT (Mean Kinetic Temperature). Weighted-average temperature calculation that captures the cumulative thermal effect of temperature variations over a transit or storage window. Used to assess whether a shipment remained within a product's stability budget.

NIOSH (National Institute for Occupational Safety and Health). US agency that maintains the *NIOSH List of Hazardous Drugs in Healthcare Settings*, which triggers USP <800> handling requirements.

NPI (National Provider Identifier). Unique 10-digit identifier issued by CMS to US healthcare providers and used in administrative and financial transactions.

OBRA '90 (Omnibus Budget Reconciliation Act of 1990). Federal law that established the requirement for pharmacists to offer counseling to Medicaid patients receiving new prescriptions; most states have since extended this requirement to all patients.

OPTN (Organ Procurement and Transplantation Network). The national US system governing organ allocation, transport, and outcomes tracking; operated under federal contract per 42 CFR Part 121.

PDD (Personal Delivery Device). Regulatory term for ground-based autonomous delivery robots. State definitions and requirements vary.

PHI (Protected Health Information). Individually identifiable health information regulated under HIPAA.

PMCID (PubMed Central Identifier). Unique identifier for articles archived in NIH's PubMed Central repository.

PT1000. Platinum resistance temperature detector with 1000 ohms nominal resistance at 0°C. Used for high-precision temperature measurement in pharmaceutical cold chain applications.

PV (Pharmacist Verification). The licensed pharmacist's review and approval of a prescription order against the dispensed product, distinct from prospective drug utilization review.

RBAC (Role-Based Access Control). Security model in which access permissions are granted to organizational roles rather than individual users.

Remote ID. Digital identification requirement for drones operating in US airspace under 14 CFR Part 89, functioning as a drone's license plate.

REMS (Risk Evaluation and Mitigation Strategy). FDA-mandated program for drugs with serious safety concerns, imposing distribution and use restrictions that may include ETASU.

RFID (Radio-Frequency Identification). Wireless technology for automatic identification and tracking of tags attached to objects.

UAS / UAV (Unmanned Aircraft System / Unmanned Aerial Vehicle). Aircraft operated without an onboard pilot; UAS refers to the complete system including aircraft, control link, and ground control station.

UN3373. United Nations classification code for Category B biological substances, governing packaging and transport of patient specimens and diagnostic samples that do not meet the higher-risk Category A threshold.

UNOS (United Network for Organ Sharing). Non-profit organization that operates the OPTN under federal contract.

USP (United States Pharmacopeia). Non-governmental standards-setting organization whose compendia (*USP-NF*) are enforceable under the Federal Food, Drug, and Cosmetic Act when referenced by FDA or state law. Chapters cited in this whitepaper include:

- **USP <659>**: Packaging and Storage Requirements
- **USP <797>**: Pharmaceutical Compounding, Sterile Preparations
- **USP <800>**: Hazardous Drugs, Handling in Healthcare Settings
- **USP <1079>**: Good Storage and Shipping Practices

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About AeroX

AeroX is a drone technology and consulting company focused on advancing safe, compliant, and scalable autonomous aerial operations for critical industries. Our work on chain-of-custody standardization reflects our commitment to ensuring that the promise of medical drone delivery is realized without compromising patient safety, regulatory compliance, or institutional trust.

For more information or to discuss how the AeroX Chain of Custody Framework applies to your organization, contact us at info@ncaerox.com.

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