503A / 503B Analytical Testing Obligations

Side-by-side comparison · USP chapters · 21 CFR regulatory citations · 21 CFR Part 11 applicability

Testing dimension		503A Compounding pharmacy · Patient-specific Rx required		503B Outsourcing facility · Full CGMP · FDA-registered	
Status key: REQUIRED CONDITIONAL BEST PRACTICE NOT REQUIRED					
GOVERNING FRAMEWORK	**Regulatory standards**	USP <795> (non-sterile) and <797> (sterile). State board rules may impose additional requirements beyond USP minimums.	21 U.S.C. §503A	REQUIRED	Full CGMP compliance required. FDA-regulated manufacturer in all practical respects. Subject to FDA inspection on a risk-based schedule; initial inspection typically within months of registration. 21 CFR Parts 210 & 211
FINISHED PRODUCT TESTING	**Identity testing**	Required when state board mandates or when BUD extension is sought. Not universally mandated by USP alone for all preparations.	USP <795> / State boards	CONDITIONAL	Required for every batch before distribution. Must use a validated analytical method (HPLC or equivalent). 21 CFR 211.165(a)
FINISHED PRODUCT TESTING	**Potency / assay**	Required for high-risk sterile preparations; for non-sterile preparations, requirement is state board-dependent. Not universally mandated.	USP <797> / State boards	CONDITIONAL	Required for every batch. Method must be validated per 211.194. Acceptance criteria pre-defined in approved specification. 21 CFR 211.165 & 211.194
FINISHED PRODUCT TESTING	**Sterility testing**	Required for high-risk Category 3 CSPs (Compounded Sterile Preparations) per revised USP <797> (2023).	USP <797> (2023 rev.)	CONDITIONAL	Required for every sterile batch. 14-day incubation per USP <71>. Positive result triggers formal OOS investigation. 21 CFR 211.167 / USP <71>
FINISHED PRODUCT TESTING	**Bacterial endotoxin (BET)**	Required for high-risk sterile CSPs administered parenterally. LAL or recombinant Factor C assay per USP <85>.	USP <85> / USP <797>	CONDITIONAL	Required for all parenteral sterile products, every batch. Limit = K/M (dose-based calculation per USP <85>). 21 CFR 211.167 / USP <85>
FINISHED PRODUCT TESTING	**Particulate matter**	Not explicitly required under 503A for standard CSPs. Good practice for large-volume parenterals.	USP <797> (advisory)	BEST PRACTICE	Required per USP <788> (sub-visible) and visual inspection. Limits depend on injection route and volume. 21 CFR 211.167 / USP <788>
FINISHED PRODUCT TESTING	**Container-closure integrity**	Not required. Good practice for sealed sterile containers.	—	BEST PRACTICE	Required for sterile products. Validated method required (HVLD, dye ingress, or headspace analysis). 21 CFR 211.167
IN-PROCESS CONTROLS	**In-process testing**	Not formally mandated. Good practice to check pH, appearance, and fill weight during sterile compounding.	USP <797> (advisory)	BEST PRACTICE	Mandatory. Representative samples tested at critical manufacturing steps. Results recorded in batch production record contemporaneously. 21 CFR 211.110
STABILITY & BUD	**Stability programme**	Required only if assigning a BUD beyond USP <795>/<797> category defaults. Real-time data must support the extended claim.	USP <795> / <797> (2023)	CONDITIONAL	Full ICH Q1A-aligned programme mandatory for every product. Real-time and accelerated studies. Expiry dates are data-derived. 21 CFR 211.166 / ICH Q1A

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Testing dimension		503A Compounding pharmacy · Patient-specific Rx required			503B Outsourcing facility · Full CGMP · FDA-registered
STABILITY & BUD	**Beyond-use / expiry dating**	Category-based default BUDs per USP <795>/<797>. Limits tightened under 2023 revisions.	USP <795> / <797> (2023)	REQUIRED	Expiry date must be justified by stability data for every SKU. Not convention-based or assumed. 21 CFR 211.137
METHOD VALIDATION	**Analytical method validation**	Not required for 503A. Compendial methods may be used without formal validation in most jurisdictions.	–	NOT REQUIRED	Required for all methods used in finished product release and stability testing. Must demonstrate specificity, linearity, accuracy, precision, and robustness. 21 CFR 211.194(a)
OOS & DEVIATIONS	**OOS investigation procedure**	Not explicitly mandated by USP or most state boards. Having a written OOS procedure is best practice.	–	BEST PRACTICE	Mandatory two-phase investigation: laboratory investigation first, full-scale if root cause not identified. Full documentation required throughout. 21 CFR 211.192
OOS & DEVIATIONS	**Deviation & CAPA system**	Not required. Some state boards encourage written deviation procedures.	–	BEST PRACTICE	Required. Every departure from approved procedure must be investigated, root-caused, and formally closed. CAPA required for systemic issues. 21 CFR 211.192 & 211.22
ENVIRONMENTAL MONITORING	**Environmental monitoring (EM)**	Required for sterile compounding areas. Viable + non-viable air, surface, and personnel sampling per ISO classification.	USP <797> (2023 rev.)	REQUIRED	Required. EM programme must be validated. Excursions trigger investigation. Results must be trended over time. 21 CFR 211.42 / USP <797>
ENVIRONMENTAL MONITORING	**Media fill / process simulation**	Required periodically per USP <797> for sterile compounding personnel. Failure requires investigation and requalification.	USP <797> (2023 rev.)	REQUIRED	Required. Frequency determined by facility risk assessment. Failure requires root cause investigation before aseptic processing can resume. 21 CFR 211.113 / USP <797>
CONTRACT TESTING	**Contract lab use**	Permitted. COA review recommended. No formal vendor qualification required by USP or most state boards.	USP <797> (advisory)	CONDITIONAL	Permitted with formal vendor qualification file: audit, quality agreement, method transfer, and ongoing performance monitoring. Raw data access rights must be contractually secured. 21 CFR 211.22 & 211.84
ELECTRONIC RECORDS	**21 CFR Part 11 compliance**	Not mandated for 503A. Strongly recommended for sterile compounding to ensure contemporaneous and attributable records.	–	BEST PRACTICE	Mandatory for all CGMP records. Requires: audit trails, unique user IDs, controlled electronic signatures, and validated system (IQ/OQ/PQ). Spreadsheets do not comply. 21 CFR Part 11
ELECTRONIC RECORDS	**Data integrity (ALCOA+)**	Best practice. Attributable, legible, contemporaneous, original, accurate records expected but not explicitly enforced at federal level.	FDA DI Guidance 2018	BEST PRACTICE	Mandatory. FDA investigators specifically assess ALCOA+ compliance during inspections. Spreadsheets and paper reconstructions are common 483 observation triggers. 21 CFR Part 11 / FDA DI Guidance
ADVERSE EVENTS	**Adverse event reporting**	Serious adverse events reported to state board of pharmacy. FDA MedWatch reporting is voluntary for serious events.	State board rules	CONDITIONAL	Mandatory MedWatch reporting to FDA for all serious adverse drug experiences within 15 calendar days of awareness. 21 U.S.C. §353b(b)(5) / 21 CFR 310.305