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FDA PreCheck Type V DMF: A Digital-Thread Blueprint

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In this article

Executive Summary

FDA PreCheck is a voluntary pilot for new pharmaceutical manufacturing facilities in the United States and insular areas. It is not a new approval pathway, a substitute for current good manufacturing practice (CGMP), or a promise of a favorable inspection or application outcome. FDA selected **seven companies** for the initial cohort on **June 29, 2026**, after receiving **more than 80 requests** during the February 1 to March 1 window (www.fda.gov). Participation is voluntary, and selection does not guarantee expedited review, approval, or inspection outcomes (www.fda.gov).

The program has two linked phases. **Phase 1, Facility Readiness**, couples a Pre-Operational Review (POR) with a facility-specific **Type V Drug Master File (DMF)**. **Phase 2, Application Submission**, begins with pre-submission interactions before the first New Drug Application (NDA), Abbreviated New Drug Application (ANDA), or Biologics License Application (BLA) using the facility (www.fda.gov). The POR moves through design review, pre-construction review, equipment installation and qualification review, and pre-production review. A POR site visit is expressly **not an inspection** (www.fda.gov).

The implementation problem is therefore not merely document assembly. It is lifecycle configuration management. The facility team needs a digital thread that binds each reviewed requirement to a controlled design baseline, installed asset, qualification result, quality-system control, FDA interaction, and DMF section. NIST describes a digital thread as information flow along the product lifecycle (www.nist.gov) and calls for authorization, authentication, and traceability of trustworthy lifecycle data (www.nist.gov), while ICH Q10 treats knowledge management as a systematic approach (database.ich.org). Together, those ideas support a practical architecture: federated systems of record, immutable identifiers, versioned baselines, bidirectional trace links, and risk-based change impact.

The Type V DMF should be managed as the regulatory view of that thread, not as the master copy of every engineering record. FDA says it can centralize POR-reviewed facility information, but detailed PreCheck-specific content and procedures were still forthcoming as of September 2026 (www.fda.gov). “Qualify once, reference many” is a potential reuse model, not a guarantee: one Type V DMF may be referenced in multiple

applications (www.fda.gov). A defensible 90-day start establishes ownership, identifiers, baseline rules, a traceability pilot, change workflow, DMF publishing map, and evidence-based readiness dashboard before project data fragment across contractors and platforms.

Introduction and Background

The FDA PreCheck question for a facility leader is deceptively simple: what information should be captured now so the facility can support early FDA engagement and later product applications without reconstructing its history? The answer spans facility engineering, chemistry, manufacturing, and controls (CMC), quality, validation, regulatory operations, and information technology and operational technology (IT/OT). Each function owns part of the evidence, but FDA's model expects the physical build and the Type V DMF to evolve together.

The policy context is material. FDA reported that, as of 2025, approximately **53% of brand drug products** and **69% of generic drug products** were manufactured outside the United States (www.fda.gov). USP separately estimated that India and the European Union supplied **51% of U.S. prescription API volume** in 2025 (qualitymatters.usp.org). GAO reported that India and China together represented nearly **40% of foreign establishments** manufacturing drugs for the U.S. market in January 2024 (files.gao.gov). Executive Order 14293, issued May 5, 2025, cited industry estimates that new capacity may take **five to 10 years** to build (www.whitehouse.gov). BLS projects sector employment to rise by **19,000** from 2024 to 2034 (www.bls.gov). PreCheck addresses regulatory engagement inside that larger capital timeline. It cannot remove construction, technology-transfer, qualification, or application dependencies.

This report translates FDA's four POR elements into an information architecture. It distinguishes official requirements and program statements from editorial implementation choices. The suggested identifiers, scores, service levels, and 90-day sequence are **not FDA requirements**. They are governance patterns intended to make reviewed claims reproducible.

IntuitionLabs is an adjacent life-sciences consultancy, not a PreCheck program or facility-software provider. Its relevant perspective is that authoritative enterprise sources should retain identity, permissions, retrieval, citations, and accountable operation (intuitionlabs.ai). That framing is complementary to the regulatory analysis: the objective is controlled evidence flow, regardless of which validated applications implement it.

What FDA PreCheck and the Type V DMF Are

Program scope and boundaries

PreCheck eligibility was limited to new facilities in the United States and insular areas (www.fda.gov). Applicants needed to commit to a future original NDA, ANDA, or BLA, or qualifying supplement associated with the facility. The initial cohort comprises Amneal Pharmaceutical, Cellares, Eli Lilly, FUJIFILM Biotechnologies, Kriya Therapeutics, Kyowa Kirin, and Regeneron (www.fda.gov). This article does not imply that any organization outside that cohort receives pilot benefits.

Several boundaries matter in planning:

- **Voluntary status:** PreCheck participation is not mandatory for later product approval.
- **No outcome guarantee:** Selection does not assure faster review, approval, or inspection results.
- **Facility focus:** Phase 1 advances understanding of facility design, equipment, qualification, and the Pharmaceutical Quality System (PQS), not product approval.
- **Existing pathways:** Phase 2 uses established interactions connected to an NDA, ANDA, or BLA.
- **Visit distinction:** A POR site visit can inform readiness but is not an inspection.
- **Pilot evolution:** FDA says the approach may be tailored to participants, so teams should version assumptions and decisions.

FDA describes Phase 1 as having two integrated components, the POR and Type V DMF. Phase 2 then uses the resulting facility knowledge in application-focused engagement. FDA says these engagements aim to enable earlier inspection timelines in the review cycle (www.fda.gov). “Earlier” describes the aim, not a committed schedule.

Type V DMF in this setting

A DMF allows confidential information to support another submission by reference. A parallel European master-file procedure explicitly protects confidential manufacturer know-how (www.ema.europa.eu), although it does not define U.S. Type V practice. Type V covers FDA-accepted reference information outside the standard subject matter of Types II through IV. Under 21 CFR 314.420, FDA ordinarily neither independently reviews nor approves or disapproves a DMF (www.ecfr.gov) (www.govinfo.gov). PreCheck is notable because FDA intends to actively assess participating Type V DMFs (www.fda.gov).

Ordinary procedural controls still provide the conservative baseline:

- **Letter of intent:** For Type V information outside Types II through IV, 21 CFR 314.420(a)(5) directs the prospective holder to first submit a letter of intent to FDA's DMF staff (www.ecfr.gov) (www.govinfo.gov).
- **Authorization:** The holder places a letter of authorization in the DMF before FDA may use its information for a referenced application (www.govinfo.gov).
- **Maintenance:** FDA's general guideline calls for an annual report on the original submission anniversary (www.fda.gov).
- **Change notice:** A holder must notify each affected referencing applicant or sponsor of pertinent changes (www.govinfo.gov).
- **Biologics reference:** 21 CFR 601.2(g)(4) permits a BLA to incorporate master-file information that is not drug-substance, intermediate, or drug-product information (www.ecfr.gov).

The crucial uncertainty is content granularity. FDA had not yet issued detailed PreCheck Type V DMF content and submission procedures by the publication date. The Common Technical Document (CTD) is organized into **five modules** (admin.ich.org), and ICH M4 calls for quality information in a structured format

(database.ich.org). Those standards provide publishing context, not an announced PreCheck Type V table of contents. A team should therefore separate an **official minimum** from its **working information model**, maintain a decision log, and be ready to remap rather than hard-code an unannounced dossier structure.

The Four-Element Digital Thread

The digital thread should connect intent, execution, evidence, and regulatory representation. NIST emphasizes authorization, authentication, and traceability of trustworthy product data across the lifecycle (www.nist.gov). In pharmaceutical facilities, that translates into persistent identifiers for rooms, systems, utilities, equipment, requirements, hazards, tests, deviations, and approved claims.

Table 1 maps each official POR element to a practical artifact chain. FDA identifies Element 1 as design review of facility and PQS concepts (www.fda.gov); the remaining rows follow the sequence on the same official structure page. The DMF destinations are proposed working modules, not FDA-prescribed sections.

POR element	Controlled artifacts	Accountable owner	System of record	Proposed Type V DMF view
1. Design Review	Design basis, process flow, contamination-control concept, PQS concept, critical requirements, open assumptions	Facility engineering with Quality and CMC approval	Requirements repository plus controlled document management	Facility narrative, layouts, intended operations, PQS design
2. Pre-Construction Review	Approved-for-construction baseline, resolved FDA comments, design qualification, risk assessments, interface register	Engineering design authority	Document management, building information modeling (BIM), requirements tool	Final design baseline and disposition of reviewed changes
3. Equipment Installation and Qualification Review	Asset register, specifications, installation evidence, calibration, commissioning, qualification protocols and reports	Validation lead with system owners	Asset/BIM data, commissioning and qualification platform	Equipment and utility design, installation, qualification summary
4. Pre-Production Review	Turnover status, deviations, corrective and preventive action (CAPA), training, procedures, release-to-operate decision	Site Quality head	Quality management system (QMS), learning system, validation repository	Constructed and qualified state, PQS readiness, remaining commitments

The table exposes an important design rule: the dossier is a governed projection of source evidence. It should not become a parallel engineering database. ISO 19650-1 offers a useful, non-FDA information-management pattern involving exchange, recording, versioning, and organization across actors (committee.iso.org). Industry Foundation Classes (IFC) can make built-asset information machine interpretable, but IFC use is an implementation option, not a PreCheck requirement (www.buildingsmart.org). COBie is another optional handover pattern that can carry as-built, operations, maintenance, and commissioning information (nibs.org).

Element 1: turn concepts into traceable requirements

Element 1 is review of facility and PQS design concepts. The deliverable is not a presentation deck alone. It is an approved concept baseline whose claims can be decomposed into requirements and verification methods.

- **Assign stable IDs:** Give every critical requirement, room, utility, equipment class, and PQS capability a nonsemantic identifier.
- **Record provenance:** Store author, approver, effective date, source, rationale, and supersession relationship.
- **Link risks:** Connect each critical requirement to contamination, cross-contamination, process, data, or operational risks.
- **Declare verification:** Specify whether design review, inspection, test, analysis, or qualification will prove the requirement.

ICH Q9(R1) says risk evaluation should be based on scientific knowledge (database.ich.org) and that the formality of quality risk management should be commensurate with risk (database.ich.org). It also identifies effective knowledge management as one way to reduce uncertainty (database.ich.org). These principles justify more rigorous traceability for high-impact controls without requiring equal detail for every drawing attribute.

Element 2: freeze the reviewed construction baseline

Element 2 reviews final design after necessary modifications and before construction. The information architecture needs an explicit **reviewed baseline** and a mechanism to distinguish it from later approved changes. A transmittal date or folder label is too weak because it does not reveal object-level differences.

- **Snapshot the baseline:** Capture document revisions, BIM model version, asset list, requirement set, risk register, and unresolved decisions.
- **Preserve comments:** Link FDA questions and meeting minutes to their responses and affected requirements.
- **Control interfaces:** Track boundaries among process equipment, utilities, automation, building systems, and procedures.
- **Calculate change impact:** Identify affected requirements, rooms, assets, tests, DMF claims, and applications before approval.

EU GMP Annex 15, useful as lifecycle validation context rather than a U.S. PreCheck mandate, says the user requirements specification should remain a point of reference through the validation lifecycle (health.ec.europa.eu). It also expects planned changes that may affect quality to be formally documented and impact-assessed (health.ec.europa.eu) (health.ec.europa.eu). NIST's information-security vocabulary similarly defines configuration change control as tracking, reviewing, approving or rejecting, and logging changes (nvlpubs.nist.gov).

Element 3: connect installed state to qualification evidence

Element 3 reviews equipment design and installation plans. The digital thread now has to prove that the installed object corresponds to the reviewed design and that qualification evidence corresponds to that object.

- **Resolve identity:** Map vendor tag, engineering tag, enterprise asset ID, automation object, and qualification system ID.
- **Capture configuration:** Record model, materials, firmware or software, critical settings, calibration range, and utility connections.
- **Link evidence:** Bind requirements to protocol steps, raw observations, deviations, approvals, and final reports.
- **Retain exceptions:** Keep failed or repeated tests visible through their approved resolution, without overwriting history.

FDA's process-validation guidance defines validation as activities across the product and process lifecycle (www.fda.gov). It says Stage 2 covers facility design and qualification of equipment and utilities, as well as process performance qualification (www.fda.gov). ICH Q10 also identifies development, technology transfer, and process validation as knowledge sources (database.ich.org). That makes a requirement-to-qualification link more than a convenient dashboard relation. It is the evidence path from intended state to demonstrated state.

Element 4: reconcile the pre-production truth

Element 4 assesses construction, installation, and readiness for production. Readiness should be computed from approved evidence, then reviewed by accountable people. It should not be inferred from percent-complete schedules alone.

- **Reconcile as-built state:** Compare the approved construction baseline with installed and qualified configuration.
- **Close critical exceptions:** Show deviations, CAPAs, temporary controls, and commitments with owners and dates.
- **Verify PQS operation:** Connect procedures, trained roles, change control, deviation handling, supplier controls, and management review.
- **Publish the regulatory view:** Regenerate DMF content from approved sources and reconcile it against the prior submission.

WHO recommends documenting data flows and data-process maps for data-integrity risk assessment (cdn.who.int). It also expects a selected computerized system to be suitable and validated for intended use (cdn.who.int). OECD places data governance across the full lifecycle (www.oecd.org). These are useful governance tests, not claims that WHO or OECD guidance defines PreCheck.

Systems of Record, Traceability, and Control

A federated architecture

No single platform normally owns all facility truth. A practical architecture assigns authoritative records and connects them through identifiers and controlled interfaces:

- **Document management:** Approved specifications, narratives, drawings, protocols, reports, meeting minutes, and DMF renditions.
- **Requirements management:** Requirements, rationales, source citations, risks, verification methods, and trace links.
- **BIM and asset information:** Spaces, systems, assets, attributes, connections, and model revisions.
- **Commissioning and qualification:** Test plans, execution data, exceptions, approvals, and turnover packages.
- **QMS:** Changes, deviations, CAPAs, effectiveness checks, and quality decisions.
- **Regulatory information management and publishing:** Submission metadata, sequences, lifecycle operations, letters of authorization, and application references.
- **Integration and analytics:** Read-only joins, data-quality rules, lineage, and readiness measures.

Metadata cannot be treated as optional plumbing. MHRA calls metadata an integral part of the original record (assets.publishing.service.gov.uk). OECD says metadata provide meaning, context, and structure (www.oecd.org). FDA's ALCOA formulation includes contemporaneous recording, an original or true copy, and accuracy (www.fda.gov). Although these documents apply in their own contexts, the technical point is general: without metadata, a test result or drawing cannot reliably establish which configuration it represents.

Minimum traceability model

Table 2 shows a minimum relation set. Each row is a relationship to govern, not necessarily a separate database table.

From object	Required link	To object	Control question
FDA interaction	addresses / modifies	Requirement or decision	What changed because of the engagement?
Requirement	mitigates / verifies by	Risk and test	Why is it critical, and how is it proven?
Design object	realizes	Requirement	Which drawing, model object, or specification implements it?
Installed asset	conforms to	Design object and approved change	Is the field state equal to the accepted baseline?
Test result	verifies	Requirement and asset configuration	What exact state passed, when, and under whose approval?

From object	Required link	To object	Control question
Deviation or CAPA	affects / resolves	Test, requirement, asset, and claim	Does the exception change readiness or submitted information?
DMF claim	summarizes / cites	Approved source evidence	Can the claim be regenerated and defended?
Application reference	authorizes / consumes	DMF version and sections	Which applicant may rely on which facility baseline?

The model makes completeness measurable. A requirement is not “complete” merely because its text is approved. It is complete when the approved design realizes it, the installed state is reconciled, required testing is approved, exceptions are dispositioned, and any regulatory claim points to that evidence. ICH Q9(R1) also emphasizes integrity of data used in risk-based decisions (database.ich.org).

Electronic controls should preserve history. Under 21 CFR 11.10, closed systems must be validated for accuracy, reliability, and consistent intended performance (www.ecfr.gov), and record changes must not obscure previously recorded information (www.ecfr.gov). EU GMP Annex 11 similarly offers useful lifecycle context by requiring user requirements to remain traceable (health.ec.europa.eu) and system descriptions to include data flows and interfaces (health.ec.europa.eu). WHO adds that audit trails should remain enabled throughout the data lifecycle (cdn.who.int).

Governing the Type V DMF Baseline and Change

Baseline, amendments, and reference reuse

The DMF baseline should have a release manifest containing the submission sequence, effective date, source-object versions, approvals, unresolved commitments, affected sections, and a cryptographic or repository checksum for each rendered file. The manifest permits reconstruction even when source systems continue to evolve. ICH Q12 provides an analogous lifecycle principle by stating that its Product Lifecycle Management document should be updated as needed (database.ich.org). ICH Q10 likewise says product and process knowledge should be managed from development onward (database.ich.org).

The operating model should distinguish four states:

- **Working:** Authoring content linked to current source evidence.
- **POR-reviewed:** Content corresponding to the latest FDA engagement and disposition set.
- **Submitted:** The immutable DMF sequence actually transmitted.
- **Current effective:** The submitted baseline plus accepted amendments and active commitments.

FDA says DMF holders are responsible for keeping their files current, and it plans additional information for PreCheck maintenance and updates. ICH Q10 supports the surrounding discipline: product and process knowledge should be managed from development onward (database.ich.org), quality risk management should

evaluate proposed changes (database.ich.org), and an effective change system should guard against unintended consequences (database.ich.org). ICH Q12 adds that robust change management is necessary across multiple sites, including outsourced sites (database.ich.org).

Reference reuse needs an application map, not only letters of authorization. For each NDA, ANDA, BLA, supplement, or associated Type II DMF, the holder should record applicant, product, authorization scope, Type V DMF version, referenced sections, application milestone, and change-notification contact. The current CTD model intends Modules 2 through 5 to be common across regions (admin.ich.org), while the latest eCTD v4.0 package was endorsed in June 2026 (admin.ich.org). Those submission standards do not decide PreCheck scope, but they reinforce the value of structured lifecycle metadata. FDA's "qualify once, reference many" phrase describes possible efficiency. It does not mean that one facility review eliminates product-specific CMC assessment or future inspection.

Change-impact workflow

A controlled change should pass through the following sequence:

1. **Identify:** Assign the change an ID and describe current state, proposed state, reason, and affected effective date.
2. **Traverse:** Query linked rooms, assets, requirements, risks, tests, procedures, training, DMF claims, and application references.
3. **Score:** Apply an editorial impact score for product quality, patient risk, validated state, regulatory representation, construction rework, and application dependency.
4. **Decide:** Route to Engineering, Quality, CMC, Validation, Regulatory, and cybersecurity owners according to affected objects.
5. **Execute:** Update designs and physical configuration under approved work orders, with test evidence and exception control.
6. **Reconcile:** Compare implemented state with the approved change and update the trace graph.
7. **Publish:** Determine whether POR communication, Type V DMF amendment, referencing-applicant notice, or application update is needed.
8. **Verify:** Confirm downstream consumers received the update and close only after evidence is approved.

MHRA says organizations remain responsible for the systems they use and the data generated (assets.publishing.service.gov.uk). It also recommends that third-party agreements address data ownership, governance, and accessibility (assets.publishing.service.gov.uk). OECD describes the lifecycle as beginning with data generation and recording (www.oecd.org). That is especially relevant when design firms, equipment vendors, commissioning providers, and cloud platforms participate in the thread.

Readiness dashboard and governance

A readiness dashboard should expose evidence quality, not manufacture a single reassuring percentage. Suggested measures include:

- **Baseline coverage:** Critical objects included in the current approved baseline divided by expected critical objects.
- **Trace completeness:** Critical requirements with approved design, asset, verification, and DMF links divided by all critical requirements.
- **Configuration reconciliation:** Installed critical assets matching approved configuration divided by inspected critical assets.
- **Qualification closure:** Required test steps approved with no unresolved critical exception divided by required steps.
- **DMF currency:** Submitted claims confirmed against current approved source records divided by claims sampled.
- **Change latency:** Median elapsed time from impact identification to approved regulatory disposition.
- **Reference coverage:** Referencing applications mapped to effective DMF sections and contacts divided by active references.
- **Data quality:** Required metadata fields passing completeness, uniqueness, validity, and referential-integrity rules.

These are editorial examples. Thresholds and service levels should be risk-based and approved by the facility's governance body. WHO's data-integrity guidance expects audit trails to remain enabled throughout the data lifecycle (cdn.who.int). NIST calls for authorization, authentication, and lifecycle traceability of trustworthy product data (www.nist.gov). FDA similarly says relationships between data and metadata should be preserved securely and traceably (www.fda.gov).

Accountability should be explicit. Engineering owns design configuration. Asset and automation owners own installed configuration. Validation owns verification strategy and evidence. Quality approves GxP decisions and release of the validated state. Regulatory operations owns DMF lifecycle and authorization records. CMC owns alignment with product applications. IT/OT owns validated platforms, integrations, security, and retention. A data steward owns identifiers, metadata quality, and cross-system reconciliation. The site governance board owns priority and unresolved cross-functional risk. ISO's exchange, recording, versioning, and organization model offers a neutral vocabulary for these responsibilities (committee.iso.org).

Implementation Guidance: A 90-Day Start

A new facility should establish the thread before construction volume overwhelms manual reconciliation. *Table 3* gives an editorial 90-day sequence. It is a planning example, not an FDA deadline.

Period	Decisions and work products	Exit evidence
Days 1 to 30: govern	Name accountable owners; inventory systems and contractors; define identifiers; classify critical information; establish baseline, signature, retention, and access rules	Approved governance charter, object dictionary, system-of-record map, and current-state data-flow map

Period	Decisions and work products	Exit evidence
Days 31 to 60: connect	Configure the minimum trace model; map POR artifacts to proposed DMF views; pilot requirements through one critical utility or process train; define change-impact rules	Working trace graph, sampled source-to-claim path, gap register, and approved change-routing matrix
Days 61 to 90: operate	Rehearse a design change; generate a DMF section from controlled sources; test reference mapping; launch dashboard and review cadence; document validation strategy	Approved pilot evidence, reconciled baseline, dashboard with drill-down, and prioritized scale plan

The sequence deliberately starts with ownership and semantics, not a platform purchase. NIST's 2024 roadmap found life-sciences digital-thread implementations fragmented across disparate systems and terminology (nvlpubs.nist.gov). Its target capability is to collect, access, associate, and share reliable contextual data across sources (nvlpubs.nist.gov). In the roadmap survey, about **40%** of participants were most familiar with Industry 4.0, although the cited passage does not provide a pharmaceutical-only sample size (nvlpubs.nist.gov). A small, end-to-end pilot reveals identifier conflicts and ownership gaps before enterprise rollout.

Selection criteria for enabling technology should include:

- **Open interfaces:** Documented APIs, bulk export, event handling, and durable identifiers.
- **Lifecycle control:** Versioning, effective dating, supersession, electronic signatures, and audit trails.
- **Trace queries:** Bidirectional navigation from regulatory claim to source evidence and back.
- **Data portability:** Preservation of value, meaning, context, and relationships during migration.
- **Least privilege:** Role-based access that separates authoring, approval, administration, and consumption.
- **Validation fit:** Evidence that the configured intended use can be specified, tested, released, and maintained.
- **Supplier controls:** Contractual access to metadata, audit history, retention, and exit data.
- **Human review:** Clear decision points where qualified people approve interpretation and regulatory disposition.

EU GMP Annex 11 states that migration should preserve both data value and meaning (health.ec.europa.eu). OECD describes data governance as spanning the whole data lifecycle (www.oecd.org). buildingSMART's IFC model illustrates how machine-interpretable information can support workflow automation (www.buildingsmart.org). These principles argue against point-to-point exports that lose context after handover.

For an adjacent advisor such as IntuitionLabs, the useful role is architecture, integration, governance, and measured adoption, not regulatory decision-making. Its first-party description includes data pipelines, integration, warehousing, and business intelligence (intuitionlabs.ai). Facility and Quality leadership must retain accountability for the records, validated state, and submissions.

Data Analysis and Evidence

The available evidence supports urgency and disciplined experimentation, but not a quantified promise of faster facility approval. The strongest program numbers are **more than 80 requests** and **seven initial participants** (www.fda.gov), a selection ratio below **8.75%** if every request is treated as a unique eligible candidate. FDA did not characterize that calculation as an acceptance rate, so it should not be used to predict future selection. The wider manufacturing economy is not a proxy for pharmaceuticals, but Commerce estimated domestic content at **80% of U.S. manufacturing gross output** in 2022 (www.commerce.gov).

The domestic-manufacturing context is also quantitative. FDA stated that only **9% of active pharmaceutical ingredient manufacturers** were in the United States as of 2025 (www.fda.gov). USP's separate volume estimate assigns **35%** to India and **16%** to the European Union (qualitymatters.usp.org). GAO counted **1,065 drug-manufacturing inspections in fiscal 2023**, a **40% increase** from fiscal 2022 (files.gao.gov). FDA says application-based inspections occur for about **20% of application reviews** (www.fda.gov). None of these figures establishes a PreCheck time saving. They show the scale and selectivity of the regulatory operating environment.

Application timing provides another boundary. FDA's general goal is action within **six months** for Priority Review versus **10 months** for standard review (www.fda.gov). PreCheck does not convert an application to Priority Review and does not change those general definitions. Its stated Phase 2 aim is more efficient facility evaluation and earlier inspection timing within existing pathways.

Digital adoption evidence is promising but immature. A 2026 industry study analyzed **26 responses** (strathprints.strath.ac.uk); the paper reports **92%** for digital CMC tools (strathprints.strath.ac.uk). The small sample limits generalization. ISPE's survey series reports nearly **3,200 accumulated respondents**, including **418 respondents** in its 2023 sample (ispe.org) (ispe.org). Manufacturing, Quality, and Engineering together represented about **75%** of that 2023 sample (ispe.org). A pharmaceutical digital-twin scoping review selected only **nine publications** (journals.sagepub.com), with **four of nine, or 44%**, focused on drug manufacturing (journals.sagepub.com). That evidence supports pilot-based learning rather than assuming a mature benchmark market.

For facility leaders, the defensible business case is therefore operational: reduce duplicate transcription, shorten impact analysis, expose missing evidence earlier, and make a submitted claim reproducible. Benefits should be measured locally against a baseline such as hours to trace a claim, percentage of reconciled critical assets, change-cycle time, number of orphan records, and time to assemble an amendment. BLS's projected rise from **350,500** sector jobs in 2024 to **369,500** in 2034 supplies workforce context, not a digital-thread benefit estimate (www.bls.gov). No public source reviewed for this report establishes a universal return on investment or a guaranteed PreCheck schedule reduction.

Implications and Future Directions

PreCheck creates a strong incentive to treat facility knowledge as a maintained regulatory asset. ICH Q10 calls knowledge management a systematic approach (database.ich.org) and connects transferred knowledge to control strategy and validation (database.ich.org). The immediate implication is organizational. Engineering

handover cannot be the moment when Quality and Regulatory first encounter facility metadata. Those functions need shared identifiers and decision rights from concept design onward.

The second implication is architectural. A **digital twin** is a virtual representation of a physical or perceived real-world entity, concept, or notion in NIST's definition (csrc.nist.gov). NIST's broader digital-thread formulation concerns information flow along the product lifecycle (www.nist.gov). A twin may aid visualization or simulation, but the PreCheck need is broader: a digital thread must also connect quality decisions, records, and regulatory representations. Buying a 3D model without governance does not solve the traceability problem.

The third implication is regulatory adaptability. FDA may specify Type V DMF content, submission procedures, and maintenance expectations as the pilot develops. The June 2026 eCTD v4.0 package shows that submission standards also evolve (admin.ich.org). A modular content model can absorb that guidance. A rigid document hierarchy tied to unconfirmed assumptions will create rework. Teams should monitor FDA's program pages, preserve every mapping decision, and treat schema changes as controlled changes.

The fourth implication concerns reuse. A facility-level source can reduce repeated submission of product-agnostic information, but every reference still needs authorization, scope, version, and change-notification governance. Codified DMF practice permits incorporation only when the holder authorizes it in writing (www.govinfo.gov). ICH Q12 separately emphasizes change management across multiple sites, including outsourced sites (database.ich.org). Reuse increases the value of consistency while increasing the blast radius of an uncontrolled change. The better the reuse map, the faster a holder can identify affected applications.

Finally, data governance should be designed for long-lived facilities, not only a pilot milestone. OECD's lifecycle begins with generation and recording and continues through later phases (www.oecd.org). Its guidance also says governance applies across the whole lifecycle (www.oecd.org). WHO recommends mapping data flows for risk assessment (cdn.who.int). Retention, format migration, supplier exit, cybersecurity, and obsolescence therefore belong in the initial architecture.

Frequently Asked Questions (FAQs)

Does every new U.S. pharmaceutical facility need a PreCheck Type V DMF?

No. PreCheck is voluntary and participation was limited to selected pilot facilities. FDA also states that DMFs are not required by statute or regulation (www.fda.gov). Ordinary regulation says FDA does not independently review or approve DMFs as a general rule (www.govinfo.gov). Nonparticipants should not represent themselves as receiving PreCheck benefits. They can still apply the underlying disciplines of lifecycle validation, configuration control, and traceable facility information.

Is a PreCheck site visit an inspection?

No. FDA explicitly says the POR site visit is not an inspection. FDA may use applicable compliance-program and inspection-manual expectations to form a readiness assessment, but that does not transform the visit into an inspection or guarantee a later outcome.

What should the Type V DMF contain?

FDA describes it as the central repository for facility information reviewed during the POR, but detailed PreCheck-specific content and procedures were still forthcoming as of September 19, 2026. The CTD's five-module organization (admin.ich.org) is context, not the missing Type V specification. EMA's separate active-substance procedure follows CTD Module 3.2.S (www.ema.europa.eu), which illustrates that a master-file structure must be explicitly defined. A working model should cover facility description and layouts, reviewed design decisions, major systems and equipment, qualification summaries, PQS design and readiness, change history, commitments, and controlled references to source evidence, while remaining adaptable to later FDA instructions.

Can one Type V DMF support several applications?

Potentially. FDA says a single Type V DMF can be referenced by multiple applications. The holder still needs authorization and lifecycle controls, and each application retains product-specific content and assessment. “Reference many” should be implemented as a governed application-to-section map, not interpreted as automatic acceptance.

Is a digital twin required?

No public FDA PreCheck material reviewed here requires a digital twin, BIM platform, IFC, or a particular vendor. The needed capability is traceable, controlled, current information. IFC can enable machine interpretation and workflow automation (www.buildingsmart.org), but that does not make it a regulatory requirement. A twin may be one interface to that information, while authoritative evidence remains distributed across validated systems of record.

How should a team measure readiness?

Use drillable evidence measures, not a single project-completion percentage. Track critical-requirement trace completeness, installed-to-approved configuration reconciliation, qualification exception closure, DMF claim currency, change latency, and application-reference coverage. Define thresholds through documented quality risk management, with effort commensurate with risk (database.ich.org).

Is a “facility master file” a separate PreCheck submission?

No separate artifact is assumed here. “Facility master file” is treated as search shorthand for the facility-specific Type V DMF and its linked source records. The controlled submission remains distinct from the broader engineering and quality systems that supply its evidence.

Conclusion

FDA PreCheck changes the timing and structure of engagement for selected new U.S. facilities, but it does not change the need for sound engineering, validated systems, CGMP readiness, or complete product applications. Its defining information challenge is to keep the POR and Type V DMF synchronized while the facility progresses from concept through construction, qualification, and pre-production.

The most durable response is a governed digital thread. Stable identifiers connect reviewed intent to design objects, installed assets, tests, exceptions, quality decisions, DMF claims, and authorized application references. Federated systems remain authoritative for their own records, while controlled metadata and trace links make the full evidence path reproducible.

Leaders should begin with ownership, semantics, and baselines. Within 90 days, a facility program can approve a system-of-record map, pilot one end-to-end trace, rehearse a change, generate a controlled DMF view, and expose evidence quality in a readiness dashboard. That foundation does not guarantee PreCheck selection or regulatory outcomes. It does make facility knowledge easier to assess, update, reuse, and defend as FDA's detailed Type V DMF procedures evolve.

Source links

Links cited in this article, in order of first appearance. Full addresses are provided for readers using extracted text.

1. https://www.fda.gov/news-events/press-announcements/fda-selects-seven-participants-precheck-pilot-program-advance-us-drug-manufacturing
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