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FDA AI Guidance 2026: Drug Manufacturing & Digital Health

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Executive Summary

The U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) is actively preparing new guidance documents for 2026 to address emerging technologies in drug development, specifically **artificial intelligence (AI) in pharmaceutical manufacturing** and **digital health technologies (DHTs) in drug development**. On January 6, 2025, FDA announced draft guidance on using AI to support regulatory decisions about a drug or biological product's safety, effectiveness, or quality (www.fda.gov). Similarly, the agency has begun issuing and planning guidances on digital health in clinical trials (e.g., a December 2023 guidance on remote data acquisition (www.fda.gov)) and is soliciting feedback on broader DHT uses via a March 2026 Request-for-Information (regulations.justia.com) (www.raps.org). CDER's 2026 guidance agenda (released February 2026) explicitly includes new items on digital health in clinical investigations and AI/ML in manufacturing (www.raps.org).

This comprehensive report examines the background, current status, and future directions of these initiatives. We review historical FDA activities and regulations (including 21st Century Cures Act and FDA's FRAME initiative) that shape today's framework, survey both industry and regulatory perspectives, and analyze data on technology adoption. Key guidance documents, workshops, and publications are detailed, alongside case studies illustrating AI and digital health in pharmaceuticals. We examine stakeholder feedback (e.g., a May 2025 report on AI in manufacturing (aapsopen.springeropen.com)), and compare international efforts (such as ICH Q13 for continuous manufacturing and the EU's AI Act). The report also discusses challenges (data integrity, validation, equity) and forward-looking topics (e.g., FDA's TEMPO pilot for digital devices (www.fda.gov)). We conclude with implications for sponsors, suggestions for regulatory engagement, and prospects for 2026 and beyond.

Introduction and Background

AI and Digital Health in Pharma: Definitions and Scope

Artificial intelligence (AI) refers to computer-based models that "make predictions, recommendations, or decisions influencing real or virtual environments" (www.fda.gov). Machine learning (ML), a subset of AI, uses data-driven algorithms to improve performance over time (www.fda.gov). In drug development, AI/ML can be embedded at multiple stages: identifying drug candidates, optimizing clinical trial designs, analyzing safety data, and automating manufacturing quality control. **Digital health technologies (DHTs)**, a related but distinct category, include mobile apps, wearables (heart-rate monitors, insulin pumps, etc.), and remote sensors that collect health data. When connected to drug development, DHTs can provide remote participant monitoring, novel clinical endpoints, or digital therapeutics that complement drugs. Both AI and DHTs offer opportunities to make drug development more efficient and patient-centered, but also pose unique regulatory challenges around data validity, bias, and integration with existing frameworks (jamanetwork.com) (www.fda.gov).

Over the last decade, innovation in these areas has accelerated. FDA's Digital Health FAQs explain how to market standalone medical software (Software as a Medical Device, SaMD) in the United States (FDA Digital Health FAQs). FDA maintains public pathway-specific databases for cleared, approved, and De Novo-authorized devices; totals depend on the regulatory pathway, product definition, and reporting period (FDA Digital Health FAQs). Likewise, AI/ML components are increasingly reported in FDA submissions: by 2021, more than 100 drug and biologic applications contained AI/ML elements (www.fda.gov), and CDER has seen "an exponential" rise in submissions using AI since 2016 (www.fda.gov). These trends underscore the need for regulatory policies that ensure patient safety while accommodating innovation.

Regulatory Framework: FDA Centers and Legislation

Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA's **Center for Drug Evaluation and Research (CDER)** oversees drugs and certain therapeutic biological products, while the **Center for Devices and Radiological Health (CDRH)** regulates most digital health devices (including many software-based medical devices). FDA's **Center for Biologics Evaluation and Research (CBER)** regulates biologics including vaccines, blood products, and cellular and gene therapies, as well as certain devices that

manufacture a biologic at the point of care (FDA jurisdiction). CDER and CBER share responsibility for therapeutic biologics (FDA biologics overview). The centers collaborate on AI and DHT issues, reflecting their convergence. For example, CDER and CDRH jointly contributed to the January 2025 draft guidance on AI for drug submissions (www.fda.gov). FDA's **Digital Health Center of Excellence (DHCoE)**, launched in September 2020, coordinates digital health work across FDA (FDA launch announcement).

Key legislative milestones have shaped this space. The 21st Century Cures Act (2016) amended the FD&C Act to **exclude certain software** from the device definition. Certain software functions may be excluded from the statutory device definition, and FDA applies a risk-based policy to qualifying low-risk general-wellness products; status depends on intended use and the applicable criteria (FDA General Wellness guidance). Some low-risk general-wellness products may fall outside the device definition or within FDA enforcement policy depending on intended use and other criteria; absence of disease-specific claims alone does not determine regulatory status (FDA General Wellness guidance). However, higher-risk digital health (like diagnostic software or apps driving treatment) remains in FDA's remit.

Similarly, government initiatives like the 2022 Food and Drug Omnibus Reform Act (FDORA) and Prescription Drug User Fee Act (PDUFA) VII include mandates for digital/trial modernizations.For instance, PDUFA VII requires FDA to publish a **framework for using DHTs in drug development**, establish a Digital Health Steering Committee, hold public meetings, and fund demonstration projects (www.fda.gov). The FDORA and infrastructure bills also encourage advanced manufacturing (including continuous and distributed manufacturing and AI-based methods) by launching centers of excellence and pilot programs (www.agencyiq.com) (www.fda.gov).

On digital health, FDA has so far issued multiple guidances: for example, FDA's 2019 Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act guidance explains the amended device definition and its effect on medical-device software guidances. In January 2026, FDA overhauled its General Wellness and CDS guidances (www.nixonpeabody.com), clarifying that many low-risk apps (including wearables that passively measure vital signs) need no pre-market review under certain conditions. FDA also maintains a "List of AI-Enabled Medical Devices" and numerous guidances on software validating, cybersecurity, interoperability, and AI/ML-specific issues (jamanetwork.com).

On the manufacturing side, CDER's **FRAME (Framework for Regulatory Advanced Manufacturing Evaluation)** initiative, begun in 2021, is explicitly focused on modern manufacturing technologies (continuous, distributed, point-of-care manufacturing) and AI/ML integration (www.fda.gov). FRAME has engaged stakeholders through discussion papers and workshops (e.g., on distributed manufacturing in 2022 and AI in 2023) and signals future guidance development (www.fda.gov).

Together, these legislative and policy actions show FDA's intent to modernize oversight for software, devices, and data-driven methods in line with technological advances, while still upholding safety and efficacy standards.

AI in Pharmaceutical Manufacturing

Current Landscape and Opportunities

AI/ML in manufacturing refers to using data-driven models to optimize production processes. Use cases include **process design/scale-up**, **advanced process control (APC)**, **fault detection**, and **trend analysis** (www.agencyiq.com) (www.fda.gov). In practice, AI can analyze large volumes of real-time sensor and process data to predict equipment failures (predictive maintenance), detect product quality deviations early, and adjust control parameters automatically. For example, *soft sensors* powered by ML can infer difficult-to-measure attributes (e.g., blend uniformity) from correlated signals (www.sciencedirect.com). A 2026 review notes that combining AI with Process Analytical Technology (PAT) and Quality-by-Design (QbD) enables anomaly detection and advanced control systems in both small-molecule and biologic plants (www.sciencedirect.com).

Digital “twins” – virtual replicas of production lines – are another example: they allow simulation of process changes without risking real batches. Industry conferences and trade publications frequently highlight AI applications in equipment monitoring, robotics, and supply chain logistics (www.sciencedirect.com). FDA describes advanced manufacturing technologies as having the potential to improve manufacturing and supply-chain reliability and timely access to quality medicines (FDA FRAME initiative).

From a quantitative perspective, investments in AI for pharma manufacturing are rapidly growing. A November 2021 National Academies report identified AI-based advanced process controls as a key innovation likely in the next 5–10 years (www.agencyiq.com). That report recommended FDA build expertise to oversee such technologies. Likewise, supply chain disruptions during COVID-19 underscored the need for agility (e.g., via distributed manufacturing and AI-driven forecasting) (www.agencyiq.com). FDA describes substantial experience reviewing regulatory submissions with AI components (www.fda.gov). In short, AI in manufacturing offers improved quality and reduced costs, but has been slow to deploy due to technical and regulatory hurdles.

Regulatory Initiatives and Guidance

FDA’s **FRAME Initiative** provides the primary regulatory context for AI in manufacturing. As of 2023, FRAME has prioritized AI alongside continuous and distributed manufacturing (www.fda.gov). In March 2023, CDER published a **discussion paper** “Artificial Intelligence in Drug Manufacturing” for public comment (aapsopen.springeropen.com) (www.fda.gov). This paper (linked from FRAME’s website) defines Industry 4.0 concepts and proposes areas where AI could apply (process scale-up, process control, monitoring, etc.) (www.agencyiq.com). It identifies five “areas of consideration” for regulatory policy, including cloud computing, IoT data management, oversight scopes, validation standards, and data integrity (www.agencyiq.com). The goal was to gather feedback on regulatory bottlenecks.

Following that, FDA held a **public workshop** on Sept 26–27, 2023 (joint with PQRI) to engage stakeholders on the regulatory framework for AI in pharmaceutical manufacturing (aapsopen.springeropen.com) (www.fda.gov). CDER leadership (Dr. Patrizia Cavazzoni) emphasized in remarks that AI/ML can bring “safe,

effective, and high-quality treatments to patients faster" (www.fda.gov), but also flagged ethical and data bias concerns (www.fda.gov). The workshop addressed topics like risk-based validation of AI/ML models, data governance, and integration into the pharma quality system (PQS).

In the wake of these activities, FDA collected stakeholder feedback. An open-access summary (AAPS Open, May 2025) synthesized public comments from the AI manufacturing discussion paper and workshop (aapsopen.springeropen.com). Key findings included industry desire for clear guidance and global harmonization: respondents emphasized good data management, model validation best practices, and uncertainty about integrating AI into existing Quality Systems (aapsopen.springeropen.com). They expressed concerns about explainability of complex models, use of third-party data, and meeting CGMP requirements with novel technologies. The consensus was that AI models need robust lifecycle plans and should align with current strategies for drug quality. This feedback is being used by FDA to shape further policy.

Building on stakeholder input, CDER's **2026 Guidance Agenda** (issued Feb 2026) lists draft guidances related to advanced manufacturing. Notably, it includes *"AI/ML Quality Considerations in Pharmaceutical Manufacturing"* under the Pharmaceutical Quality/CMC category (www.raps.org). This upcoming guidance will likely address how to ensure product quality when AI models are part of manufacturing controls. Also on the agenda is guidance on *"Distributed Manufacturing Application Content,"* reflecting interest in decentralized production (www.raps.org). While FDA cautioned that the agenda is not binding, these inclusions confirm that guidance on AI in manufacturing is imminent.

To date, FDA has not yet issued binding regulation on AI in manufacturing, but it has several related activities. For example, in January 2025, FDA issued a draft guidance on **"Considerations for Complying with 21 CFR 211.110"** (21 CFR 211.110 compliance) (www.fda.gov). FRAME's website also links to a Stakeholder Feedback report (Nov 2023). FDA issued the final ICH Q13 guidance on continuous manufacturing of drug substances and drug products in March 2023. FDA's collaboration with International groups (e.g., ICH's continuous manufacturing guideline) and acknowledgment of Industry 4.0 concepts suggest it is moving toward explicit policies. The planned 2026 AI manufacturing guidance will likely clarify verification of AI models, data integrity in cloud/IoT systems, and how CGMP inspections adapt to advanced data flows (www.agencyiq.com).

International and Industry Perspectives: Globally, pharma regulators similarly recognize AI's role. The ICH has begun updating guidelines (e.g., Q13 on continuous manufacturing) that are AI-enabled. Other regulators (EMA's advanced manufacturing working groups) are exploring analogous frameworks. Industry usually supports harmonized guidance; for instance, a global consortium (industry & academies) advocates for AI models consistent with QbD principles and risk-based validation. Many companies note that without clear FDA expectations, investment in AI is risky. Congress has also encouraged FDA technical capacity for overseeing these technologies (www.agencyiq.com). Thus, as guidance emerges in the U.S., it likely will align with international standards to facilitate global drug production.

Case Studies and Examples

While FDA's pipeline is primarily policy-focused, real-world examples illustrate AI's impact. In one case, a company implemented ML-driven process control in continuous manufacturing: by analyzing real-time spectra data, AI adjusted process parameters to maintain critical quality attributes within tighter limits

(www.sciencedirect.com). In another, a biologics manufacturer uses image-recognition AI to inspect cell culture bags for contamination, reducing manual inspection time. FDA's Emerging Technology Program accepts proposals for manufacturing technologies that are novel or designed to address specific patient needs (FDA ETP overview). In R&D, firms use AI for **digital twins** that simulate scale-up from lab to plant, though implementation is still emerging.

In regulatory submissions, manufacturers have started including AI data: for instance, some have proposed using AI to analyze near-infrared spectroscopy for blend uniformity, replacing time-consuming lab assays. FDA has reviewed such submissions using its emerging credibility framework (www.fda.gov) and has worked with sponsors via its Emerging Technology Program. These pilot programs demonstrate feasibility but also continuous monitoring needs: AI models may "drift" as processes change, so maintaining trust is an open concern. The forthcoming FDA guidance on credibility will directly address expectations for model validation, adaptation, and documentation (www.fda.gov).

Digital Health Technologies (DHTs) in Drug Development

Current Landscape and Opportunities

Digital health technologies (DHTs) include electronic sensors, computing platforms, and information technology that offer opportunities to obtain clinical trial data directly from patients (FDA DHT program) (jamanetwork.com). In drug development, DHTs offer new ways to measure patient outcomes. For example, wearable fitness trackers can record step count, sleep, and heart rate outside the clinic. Glucose data may instead come from a separate FDA-authorized glucose-measuring device, such as a CGM, whose data a smartwatch application can display (FDA safety communication) (jamanetwork.com). Smart inhalers or connected blood pressure cuffs relay data from home. DHTs also enable digital therapeutics (software that delivers treatment regimens, sometimes paired with drugs).

The FDA (and patients) view DHTs as a means to **decentralize trials** and capture richer endpoint data. A JAMA perspective by FDA scientists notes that DHTs can allow "more frequent or continuous data collection" and measure new concepts like tremors or gait that were previously hard to quantify (jamanetwork.com). For instance, a stroke trial might use smartphone-based hand-motion tests to assess recovery on a daily basis. The COVID-19 pandemic accelerated remote monitoring; many trials now incorporate DHTs to improve enrollment and retention. Studies show digital measures can be more patient-centric and inclusive, reaching (for example) rural patients or those with mobility issues (jamanetwork.com).

FDA data confirm this trend. FDA's AI-Enabled Medical Device List identifies devices authorized for marketing from public authorization records, but FDA states that the list is not comprehensive. Each authorization remains specific to a device and intended use (FDA AI-Enabled Medical Device List). In drug development, sponsors have submitted clinical trial protocols employing DHTs (for remote endpoints or digital endpoints,

such as seizure tracking via a video app). reSET-O is a prescription digital therapeutic cleared to increase treatment retention in clinician-supervised adults with opioid use disorder, as an adjunct to outpatient treatment including transmucosal buprenorphine and contingency management (FDA indications for use).

Despite enthusiasm, challenges exist. Many DHTs must be *validated* to ensure their measurements are reliable (e.g., is a wrist-worn heart monitor accurate enough for a regulatory endpoint?). DHT data also raise privacy and data management concerns. Importantly, DHTs often straddle drug and device regulation. For CDER, the key is often how digital data support a drug's safety/effectiveness claims, whereas CDRH classifies the software/device risk. FDA encourages sponsors to engage early on hybrid products. For example, a "digital pill" (ingestible sensor plus an antidepressant) is regulated as a combination product (the drug is CDER's lead with CDRH consulting) (jamanetwork.com) (www.fda.gov).

Regulatory Initiatives and Guidance

FDA has undertaken several initiatives to facilitate DHT use in drug trials. In March 2023, CDER/CDRH published a **Framework for Use of DHTs in Drug and Biologics Development** (as a PDUFA VII commitment) to outline future activities (public meetings, demonstration projects) (www.fda.gov). In December 2023, FDA finalized guidance **"Digital Health Technologies for Remote Data Acquisition in Clinical Investigations"** (www.fda.gov). This Level 1 guidance offers recommendations on selecting and verifying DHTs (both hardware and software) and using them to collect endpoint data. It notes that, if properly implemented, DHTs can **"improve the efficiency of clinical trials"** and broaden patient participation (www.fda.gov). FDA also provides supporting resources (FAQs, podcasts) on this guidance page.

Continuing these efforts, on March 31, 2026 FDA solicited public comment via a Federal Register Notice **"Advancing the Use of Digital Health Technologies in Clinical Investigations for Drugs and Biological Products"** (regulations.justia.com). The notice explains FDA's PDUFA VII commitment to establish a DHT framework and mentions the 2023 guidance. It acknowledges rapid tech advances (e.g., smartphone sensors, gamified pediatric apps) and explicitly seeks input on challenges and guidance needs for DHT-derived endpoints (regulations.justia.com). This RFI indicates FDA plans to issue new guidance documents based on stakeholder input. According to that notice, topics of interest include verification/validation of novel sensors, digitally derived endpoints in specific disease areas, and ideas for future public workshops (regulations.justia.com).

Before these recent efforts, FDA has taken other steps: In 2015 an FDA docket gathered input on new tech in trials. FDA launched the Digital Health Center of Excellence in September 2020 as an evolution of its existing digital health program (FDA launch announcement). FDA has also updated other guidances: for example, in January 2026 FDA replaced its 2019 General Wellness and 2022 CDS guidances with clearer versions (www.nixonpeabody.com), thereby reducing confusion for developers. Importantly, FDA emphasizes **cross-center work**: CDER, CDRH, and CBER collaborate on DHT issues. A 2025 JAMA article by FDA staff states that all Centers are committed to DHT inclusion, have held joint meetings, and even formed a DHT Steering Committee to align reviews of DHT data (jamanetwork.com).

In parallel, FDA's DHCoE is a resource for stakeholders. It has published indices of digital health guidance, hosts public workshops, and launched pilots. A notable example is the "TEMPO" pilot (Technology-Enabled Meaningful Patient Outcomes), announced Dec 2025 (www.fda.gov). In TEMPO, FDA (mainly CDRH) works

with CMS to expand access to certain digital devices for chronic diseases under a risk-based enforcement-discretion model. Participating manufacturers may request discretion for requirements such as premarket authorization, so devices in the pilot are not necessarily FDA-authorized. TEMPO illustrates FDA's interest in integrating DHTs into care delivery, which if successful could incentivize digital endpoints in drug trials as well.

Perspectives from Stakeholders

Industry generally welcomes FDA's DHT progress but asks for clarity. Sponsors want concrete guidelines on topics like how to statistically handle continuously streamed data, or how to qualify a digital endpoint. In the 2026 RFI, FDA specifically asks for feedback on what **guidance topics** would aid DHT adoption (regulations.justia.com), showing regulators acknowledge the need for detail. Patient and public advocacy groups also have interest: DHTs promise to make trials more accessible (e.g., for disabled or rural patients) (jamanetwork.com), but raise questions about digital equity and data rights. FDA's open call for input is partly to hear these perspectives.

Academic and consortia have similarly emphasized guidance needs. For example, literature on "digital endpoints" and "digital therapeutics" frequently calls for standardized validation frameworks and data standards. Internationally, regulators are exploring similar issues: the EMA has a pilot project on digital endpoints, and the EU's new Medical Device Regulation (MDR) updates software definitions. Notably, the U.S. focus on risk-based enforcement (as seen in the general wellness/CDS updates (www.nixonpeabody.com)) suggests FDA may lean toward flexibility for low-risk DHT uses, reserving strict review for when patient safety depends on them (e.g., an app that alerts acute events). The ongoing policy evolution reflects a balance between innovation and oversight.

Case Studies and Examples

Several real-world examples illustrate digital health in drug studies and treatment:

- **Decentralized Trials:** During the COVID era, many pharmaceutical companies rapidly adopted decentralized trial elements. For instance, symptom-reporting apps and home spirometers were used in vaccine and COPD studies, enabling remote monitoring.
- **Digital Therapeutics and Drug Combinations:** *Pear Therapeutics* developed reSET-O, a prescription mobile app for opioid use disorder, which was cleared by FDA's Center for Devices and Radiological Health (CDRH) through the 510(k) pathway (FDA clearance letter). The cleared indication is to increase treatment retention in clinician-supervised adults with opioid use disorder, as an adjunct to outpatient treatment including transmucosal buprenorphine and contingency management (FDA indications for use). Similarly, *Proteus Digital Health*'s aripiprazole (Abilify MyCite) system combined a drug pill with an ingestible sensor and smartphone app. These products show how drug outcomes increasingly tie to digital data.
- **Wearables as Endpoints:** DHTs can record participant data such as biomarkers, daily activities, sleep, and vital signs at home and in other everyday settings (FDA remote-data-acquisition guidance).

- **Aggregate Data in Biostatistics:** FDA's meeting in late 2022 showcased an example from oncology where digital images were used to identify tumor progression, augmenting radiologist reads. Another case is diabetes management: continuous glucose monitors (CGMs) are now routinely attached to many Type 1 diabetes drug studies, providing high-resolution glucose endpoints instead of once-daily labs.

These cases underline that DHTs can capture meaningful patient data. FDA's December 2023 guidance stressed that appropriate validation of each technology is essential (www.fda.gov). Sponsors are advised to consult both the Digital Health and Biostatistics divisions early when planning novel endpoints. For example, if using a smartwatch-based gait analysis in a Parkinson's study, sponsors should demonstrate that its digital endpoint correlates with clinical status and that data handling is secure and complete.

FDA CDER 2026 Guidance Agenda: AI in Manufacturing and Digital Health

FDA's 2026 Guidance Agenda (CDER), published February 2026, enumerates anticipated guidance topics organized by category (www.raps.org). Among the 81 listed items, two directly pertain to our topics of interest (see Table 1).

Table 1: Selected CDER 2026 Guidance Agenda Items Related to AI and Digital Health

Guidance Topic / Title	Category	Content / Focus	Status
Engagement with FDA about DHT use in drug development (topic summary)	Administrative	Guidance on engaging FDA in planning use of DHTs (wearables, apps, sensors) in trials (www.raps.org).	**New** (Draft) Planned 2026
AI/ML Quality Considerations in Pharmaceutical Manufacturing	Pharma Quality/CMC	Guidance on applying quality principles when AI/ML models are used in manufacturing processes (www.raps.org).	**New** (Draft) Planned 2026
Distributed Manufacturing Application Content	Pharma Quality/CMC	Guidance on regulatory content for distributed (networked) manufacturing applications (www.raps.org).	**New** (Draft) Planned 2026

Sources: CDER Guidance Agenda (Feb 2026) (www.raps.org); FDA FRAME Initiative documents (www.fda.gov).

The first entry (digital health in trials) appears in the **Administrative** section of the agenda. It explicitly refers to "engaging with the FDA to discuss the use of digital health technologies in clinical investigations" of drugs and biologics (www.raps.org). This aligns closely with the March 2026 RFI and signals that a focused guidance or Q&A document on DHTs in drug trials is forthcoming. FDA often issues such "how to meet with FDA" guidances to outline best practices for sponsors. We expect this guidance to cover topics such as how companies should notify FDA of planned DHT use, data standards, privacy oversight, and possibly defining contexts of use for digital endpoints.

The second entry (AI/ML in manufacturing) is under **Pharmaceutical Quality/CMC**. It specifically calls out AI/ML quality considerations (www.raps.org), potentially translating FRAME learnings into recommendations. FDA guidance generally is nonbinding; specific statutory or regulatory requirements remain distinct (FDA explanation of guidance). This would likely advise manufacturers on validating and verifying AI models (e.g., establishing performance metrics, ensuring data integrity) and on documenting controls. The frameworks already under consideration (the 2025 draft on AI credibility (www.fda.gov) and comment summaries (aapsopen.springeropen.com)) suggest the guidance will adopt a risk-based approach to model validation consistent with CGMPs. It may also address supply-chain aspects of third-party AI tools or cloud platforms. Given FDA's comment periods, this guidance could be released as a Draft Level 1 (by end 2026) or Final Level 1 (if feedback was already gathered via discussion papers).

The third listed item on distributed manufacturing is related to advanced manufacturing rather than AI per se, but it underscores FDA's attention to modern production models. Manufacturers should note that "distributed" technologies (e.g., modular plants, point-of-care mfg) could interface with AI (e.g., remote monitoring of multiple sites). We include it here since the pipeline documents it; FDA's interest in distributed systems may intersect with digital tools and AI that operate across networks.

Beyond these, CDER's agenda includes items tangentially relevant to digital innovation. For example, there's a planned guidance on national drug code (NDC) formatting (www.raps.org) which, while rooted in drug labeling, exemplifies the digital modernization of drug identification (NDC changes can affect barcoding and digital recordkeeping). FDA's final Clinical Decision Support Software guidance was issued on January 6, 2026, and re-issued on January 29, 2026. This article focuses on AI in pharmaceutical manufacturing and DHTs in drug development.

Importantly, CDER notes that its agenda is aspirational and may change (www.raps.org). Moreover, guidances outside CDER—such as CDRH's medical device AI guidances (updated draft in Jan 2025) or general FDA-DHCoE guidances—will also shape what sponsors must do with digital tech. Sponsors should therefore monitor not just CDER publications but also CDRH and cross-center policies. FDA's final guidance on predetermined change control plans for AI-enabled devices was issued in August 2025. Its recommendations apply to AI-enabled devices, including device constituent parts of device-led combination products, reviewed through the 510(k), De Novo, and PMA pathways (FDA final guidance).

Data Analysis and Evidence-Based Perspectives

Technology Adoption Metrics

Quantitative measures illustrate the rapid adoption of AI and DHT in the life sciences. For AI, public data is emerging. FDA reports that by early 2025, over 500 drug/biologic submissions since 2016 had *some* AI component (www.fda.gov). The JAMA report notes that the first drug/biologic application with AI was only in 2016, yet by 2021 "more than 100" had AI/ML (www.fda.gov). The *April 2025 JAMA* viewpoint highlights that

devices capturing digital biomarkers also proliferated: by mid-2025, FDA databases listed hundreds of AI-enabled and sensor-based products (jamanetwork.com). (FDA states that its AI-enabled medical device list is not comprehensive (FDA AI-enabled device list).)

FDA's DHT framework includes workshops and demonstration projects, engagement with interested parties, internal evaluation processes, shared learning, and guidance development (FDA DHT program).

Investments and Market Data: McKinsey expected life-science organizations to increase their generative-AI budgets (McKinsey).

Regulatory Submissions with AI/DHT

FDA identifies potential uses of AI in predicting patient outcomes, understanding predictors of disease progression, and processing large datasets, including real-world data and DHT data (FDA AI guidance announcement).

On digital health, FDA's tracking of "Digitally-derived Endpoints" is nascent, but pilot submissions have occurred. FDA does not use a single "digital therapeutic approval" category; software products are reviewed under the applicable device pathway. For example, reSET-O was cleared by CDRH through 510(k) (FDA clearance letter). Moreover, feedback from CDER's DHT pilot projects suggests a 2023–24 spike in requests by sponsors to include smartphone-captured endpoints (like voice-based depression scales) in protocols. FDA's FY2025 budget justification also mentioned a need to process "increasingly complex data streams" in support of new drug reviews (www.fda.gov), implicitly acknowledging the DHT trend.

Synthesis of Expert Opinions

Experts broadly agree that FDA is moving toward a more permissive, clear framework. Former FDA officials and regulatory experts have described 2026 as a "pivot point": Commissioner Makary's public remarks (Jan 2026) emphasize cutting "27 guidances … by 50%," streamlining rules on software and AI (www.nixonpeabody.com). Academic commentaries (e.g. *Nature Biomedical Engineering*, 2025) applaud FDA's stepped-up guidance planning but caution that some topics (like liability for AI errors) remain ambiguous. Industry associations (PhRMA, BIO) have issued white papers urging swift finalization of AI and digital guidances to not stifle innovation, noting that companies avoid investing in large-scale AI systems without regulatory clarity.

One nuanced viewpoint is that while FDA is signaling pro-innovation rhetoric, actual implementation lags. Observers note that many guidances are promised but are still years away (e.g., the policy for AI credibility is draft vs. final). Furthermore, some technology startups feel the pace is too slow; for instance, the Digital Therapeutics Alliance has lobbied for expedited pathways for drug–software combinations, similar to orphan drug vouchers. On the other hand, patient advocates and ethicists warn that under-tightening policies too much could risk data privacy or equity in AI models. FDA appears to be balancing these views through its stakeholder workshops and public comments.

Case Studies and Real-World Examples

CDER and Industry Perspectives: Duke Margolis Workshop (2022)

A major precursor to guidance was a Duke Margolis workshop (Nov 2022) co-sponsored by FDA. Experts from government, industry, and academia met to discuss AI in drug development and manufacturing. Post-workshop reports (Duke Margolis, Dec 2022) emphasize that **context of use** for AI models must be carefully defined, aligning with FDA's draft guidance principles (www.fda.gov). The workshop discussions underscored examples: using AI to predict patient support data (e.g., predicting who will respond to a therapy), versus using AI for batch release testing. These perspectives shaped FDA's risk-based approach: for high-impact uses (e.g., batch quality release), heavy validation and audit trails are expected. For more research-oriented uses (e.g., target identification), more flexibility is possible. Such case-driven differentiation is likely to appear in final guidance.

Medical Center Innovation: Remote Monitoring Programs

FDA recommends training trial participants and personnel on the appropriate use of DHTs. Usability-evaluation findings can inform device design, instructions, and training (FDA remote-data-acquisition guidance).

Regulatory Sandbox: Emerging Technology Program (ETP) Cases

FDA's Emerging Technology Program invites companies to propose manufacturing technologies that are novel or designed to meet specific patient needs. Early engagement is a hallmark of the program (FDA ETP overview).

International Collaboration: ICH Q13 (Continuous Manufacturing)

Although not AI-specific, ICH Q13 (finalized Nov 2022) is an example of harmonizing advanced manufacturing. It sets general expectations for continuous processing (sensor use, PAT). Novartis and other multinational companies were early adopters of continuous lines and were consulted in Q13 development. In parallel, U.S. FDA advanced life science consortia (e.g., ISPE, PQRI) have similar guidelines for continuous manufacturing and its digital control. For U.S. digital health devices, FDA's TEMPO pilot allows participating manufacturers to request enforcement discretion for certain requirements, including premarket authorization and investigational device requirements (FDA TEMPO announcement).

Implications and Future Directions

Industry Impact and Compliance

The forthcoming FDA guidances on AI and digital health are expected to significantly influence how drug companies operate. In manufacturing, companies investing in AI-driven control systems can consider guidance recommendations when planning their quality management systems; alternative approaches may be used if they satisfy applicable statutes and regulations (FDA explanation of guidance). This could involve establishing formal validation protocols for AI/ML models (analogous to analytic method validation) and defining procedures

for change control when models are updated (mirroring CDRH's evolving AI guidance). Pharma quality departments are already mobilizing to pilot such frameworks, anticipating FDA's insistence on data lineage, reproducibility, and CGMP alignment (www.agencyiq.com) (aapsopen.springeropen.com).

In clinical development, trial sponsors may need to submit specific plans for digital data acquisition. The planned guidance on DHT engagement suggests that sponsors should prepare documentation on device selection, data security, and statistical analysis. Indeed, FDA's Remote Data guidance encourages sponsors to "engage early" with review divisions when using novel DHTs (jamanetwork.com) (regulations.justia.com). Companies are likely to form dedicated "digital medicine" teams (a trend already under way) to navigate these regulations, akin to how they handle combinatorial products. Electronic data systems (EDC/CTMS) will also need updates to handle continuous streams of health data and ensure audit trails.

Patient and Public Health Considerations

From a public health perspective, these developments aim to **increase access and evidence**. Digital tools can make trials more inclusive (e.g., via home monitoring for patient groups who cannot travel) (jamanetwork.com). AI in manufacturing promises fewer drug shortages (through more efficient, flexible production) and potentially lower costs. However, there are also risks: reliance on new tech could introduce novel error modes (e.g., algorithmic bias in recruitment, cybersecurity vulnerabilities in networked factories). FDA guidance is expected to address these by requiring demonstration that new methods are at least as reliable as traditional ones. Notably, FDA explicitly mentions equity: its CDRH/CBER digital health framework talks about making trials representative of target populations (jamanetwork.com) and avoiding algorithmic discrimination (www.fda.gov). Guidance may thus include recommendations on validating AI algorithms across diverse demographic data sets.

Future Regulatory Evolution

Looking forward, FDA's statements indicate a commitment to updating the regulatory "toolkit." The Commissioner's remarks in January 2026 promise more streamlined AI and digital health policies (www.nixonpeabody.com). FDA's mention of 27 guidances to be cut by 50% implies consolidating overlapping rules – perhaps merging device and drug digital guidances into unified frameworks. The establishment of an FDA internal AI advisory body (revealed in 2024) also suggests ongoing cross-agency coordination. On the legislative side, Congress may further empower FDA: the FDORA creates new pathways (e.g., Centers of Excellence for manufacturing) that could fund expanded FDA capabilities in AI analytics.

Internationally, harmonization efforts like ICH's work on AI (proposed ICH guidance on AI/ML in drug development is rumored for ICH meetings) will shape FDA's approach. Conversely, the EU's AI Act (in force since August 2024, with high-risk rules for AI in medical devices applying from August 2, 2028 after the 2026 Digital Omnibus on AI (EUR-Lex)) classifies medical AI into risk categories; its framework may eventually influence FDA through mutual recognition or convergence discussions.

Finally, technological trends will not stand still. Emerging fields such as **federated learning** (AI trained across multiple sites without sharing raw data) may raise new regulatory questions about data privacy and validation. Likewise, digital health is moving towards **virtual reality (VR) therapeutics** and **metaverse health trials**,

scenarios FDA must anticipate. FDA's pipeline, by planning guidance in 2026 for current issues, lays groundwork but must remain agile. The Agency's practice of using public workshops and RFIs shows awareness that guidance must evolve as the science does.

Conclusion

Artificial intelligence and digital health are rapidly transforming the drug development landscape. FDA's CDER has acknowledged this transformation by planning targeted guidance for 2026 on these topics (www.raps.org). Over the past few years, FDA has laid critical groundwork – drafting AI frameworks for drug development (www.fda.gov), convening stakeholder workshops on AI manufacturing (aapsopen.springeropen.com), and issuing guidances on digital trial data (www.fda.gov). For DHTs in drug development, FDA encourages early engagement with the agency (FDA DHT program). CDER is not required to publish every guidance on its agenda (CDER 2026 guidance agenda).

The implications are profound. Pharmaceutical companies and device/developer partners must prepare now: they should inventory current AI and DHT uses, engage with FDA early (via pilots or formal meetings), and align internal processes with the concepts in these emerging guidances. Regulators and industry must also address challenges such as ensuring algorithmic fairness, maintaining data integrity in complex IT systems, and protecting patient privacy amidst new data streams.

Our analysis finds that FDA's approach is risk-based and iterative. The agency emphasizes enabling innovation — Commissioner Makary's remarks promise clearer, more efficient policies (www.nixonpeabody.com) — but always with safeguards. The public workshops and RFIs demonstrate a willingness to adapt guidance to real-world feedback (regulations.justia.com) (aapsopen.springeropen.com).

In sum, by 2026 the regulatory environment will be markedly more tailored to 21st-century technologies. The next-generation guidances will help ensure that AI and digital tools enhance, rather than complicate, drug quality and patient care. Stakeholders who stay informed and actively participate in FDA's evolving regulatory process will be best positioned to harness these technologies responsibly. As one FDA summary put it, incorporating DHTs and AI must be done with "human involvement" and "a risk-based approach" to **innovations and protecting public health** (www.fda.gov) (aapsopen.springeropen.com). The road ahead promises safer, more effective medicines developed more efficiently — but only if governed by clear, evidence-based policy.

References: Sources cited in this article include official FDA communications, peer-reviewed publications, regulatory reporting, law-firm commentary, and market research (www.fda.gov) (regulations.justia.com) (aapsopen.springeropen.com) (www.fda.gov) (jamanetwork.com) (www.raps.org) (see in-text citations). These include FDA press releases (e.g., Jan 6, 2025 AI guidance announcement (www.fda.gov)), FDA Voices articles (e.g., on AI in development and manufacturing (www.fda.gov)), regulatory news analyses (www.raps.org), and academic publications like JAMA Health Forum (jamanetwork.com) and AAPS Open (aapsopen.springeropen.com). Additional context comes from FDA framework pages and workshops (www.fda.gov) (jamanetwork.com).

Source links

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

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