



Framework for the Use of Digital Health Technologies in Drug and Biological Product Development

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Table of Contents

Introduction	2
Definitions	3
Scope	3
Background	5
Regulatory Background	5
Current Landscape of DHTs	6
Addressing Challenges Related to the Use of DHTs in Regulatory Decision-Making for Drugs.....	8
Internal Programs.....	8
1. DHT Steering Committee.....	8
2. Technical Expertise and Training	9
a. Verification and Validation	9
b. Use of a Participant's Own DHT or General-Purpose Computing Platform	10
c. Upgrades and Updates of DHTs in Drug Development	10
d. Artificial Intelligence and Machine Learning.....	10
e. Technical Consultation of Experts and Staff Training	11
3. Consistency of Evaluations Across Review Divisions.....	11
4. Statistical Considerations in the Analysis of DHT-Derived Data	11
5. IT Capabilities.....	11
External Programs	12
1. FDA Meetings With Sponsors.....	12
2. Drug Development Tool Qualification Program	12
3. Guidance	13
4. Public Meetings	14
5. Demonstration Projects	15
6. External Organizations	16
Conclusion.....	17



Introduction

The Prescription Drug User Fee Act VII (PDUFA VII) commitment letter represents the product of discussions between the Food and Drug Administration (FDA), regulated industry, and public stakeholders, as mandated by Congress.¹ The performance and procedural goals and other commitments specified in the PDUFA VII commitment letter apply to aspects of the human drug² review program that are important for facilitating timely access to safe, effective, and innovative new medicines for patients. The commitment letter includes goals relating to the use of digital health technologies (DHTs) to support drug development and review.³ Among other activities relating to the use of DHTs, under section IV.C.1 of the commitment letter, FDA has established a Framework for the Use of DHTs in Drug and Biological Product Development to guide the use of DHT-derived data in regulatory decision-making for drugs (hereinafter “Framework”).

This document outlines the Framework that FDA will use to implement a multifaceted DHT program for drugs. The DHT program will include workshops and demonstration projects; engagement with stakeholders; establishment of internal processes to support the evaluation of DHTs for use in drug development; promotion of shared learning and consistency regarding DHT-based policy, procedure, and analytic tool development; and publication of guidance documents. This document is not a guidance document and does not propose or establish policies.

¹ PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027, available at <https://www.fda.gov/media/151712/download>.

² For the purposes of the Framework, the terms *drug* or *drugs* include human drugs and biological products unless otherwise noted.

³ See section IV.C of the PDUFA VII commitment letter, “Enhancing Use of Digital Health Technologies to Support Drug Development and Review.”

Definitions

For the purposes of the Framework, DHTs are systems that use computing platforms, connectivity, software, and/or sensors for health care and related uses. They include technologies intended for use as a medical product, in a medical product, or as an adjunct to other medical products (devices, drugs, and biologics). DHTs may also be used to develop or study medical products. There is a large spectrum of DHTs available for potential use to support drug development and review, some of which meet the definition of a device under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and others that do not.⁴ DHTs may take the form of hardware and/or software. DHTs often consist of sensor hardware that allows for continuous or intermittent recording of physiological and/or behavioral data (e.g., blood pressure, physical activity, glucose levels). DHTs can also be software applications that are run on general-purpose computing platforms (e.g., mobile phone, tablet, or smart watch). These DHTs may be used to administer electronic clinical outcome assessments, including electronic patient-reported outcome and electronic performance outcome instruments. Some DHTs consist of hardware and software (e.g., a continuous glucose monitoring device that includes a sensor and a mobile application), both of which are necessary to achieve the DHT's intended function or functions.

Scope

The Framework includes the following activities outlined in the PDUFA VII commitment letter:

- Establishing a steering committee, including members from the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), the Oncology Center of Excellence (OCE), the Office of the Commissioner, and the Center for Devices and Radiological Health (CDRH) and its Digital Health Center of Excellence (DHCoe),⁵ to ensure consistent policy across FDA regarding the use of DHT-derived data in regulatory decision-making for drugs
- Convening public meetings or workshops with key stakeholders, including patients, biopharmaceutical companies, DHT companies, and academia, to gather input into issues related to the use of DHTs in regulatory decision-making
- Identifying demonstration projects to inform methodologies for efficient DHT evaluation

⁴ See section 201(h) of the FD&C Act for the definition of a device. How to determine whether a DHT proposed for use meets the definition of a device under the FD&C Act is outside the scope of this Framework. For further information about FDA digital health regulatory policies, see <https://www.fda.gov/medical-devices/digital-health-center-excellence/ask-question-about-digital-health-regulatory-policies>.

⁵ For further information about the CDRH DHCoe and available resources, see <https://www.fda.gov/medical-devices/digital-health-center-excellence>.

- Publishing guidance documents for drugs on the use of DHTs in traditional and decentralized clinical trials (DCTs) and in other areas as identified through stakeholder engagement
- Publishing guidance on regulatory considerations for prescription drug use-related software that includes information about software that is disseminated by a drug applicant for use with a prescription drug or biologic product that may be described in labeling, including prescribing information
- Enhancing consistency across centers with regards to the development, use, and review of DHTs and associated endpoints through building technical expertise and review capacity, providing staff training in evaluation of DHTs, and developing statistical methodology regarding DHT-derived clinical endpoints
- Enhancing IT capabilities to support the review of DHT-generated data



Background

Regulatory Background

In December 2021, FDA published the draft guidance for industry, investigators, and other stakeholders *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations*.⁶ This guidance outlines recommendations intended to facilitate the use of DHTs in clinical investigations, as appropriate, for the evaluation of medical products. These recommendations address selection of suitable DHTs, verification and validation of DHTs, and use of DHTs to collect data for trial endpoints. The guidance also addresses some of the risks associated with the use of DHTs in clinical investigations and their management. As noted, this is a draft guidance. When final, draft guidances will represent FDA's current thinking on their respective topics.

Many of the DHTs that can be used as tools to support drug development were originally developed and used as medical devices or general wellness products, and FDA (more specifically, CDRH and its DHCoE) has provided guidance on a number of topics relating to such products. This includes guidances that address mobile medical applications,⁷ general wellness,⁸ third-party off-the-shelf software used in medical devices,⁹ clinical evaluation of software as a medical device,¹⁰

⁶ [Digital Health Technologies for Remote Data Acquisition in Clinical Investigations | FDA](#)

⁷ [Policy for Device Software Functions and Mobile Medical Applications | FDA](#)

⁸ [General Wellness: Policy for Low Risk Devices | FDA](#)

⁹ [Off-The-Shelf Software Use in Medical Devices | FDA](#)

¹⁰ [Software as a Medical Device \(SAMD\): Clinical Evaluation | FDA](#)

information used to review medical device software,¹¹ considerations for changes to medical device software,¹² device interoperability for information sharing across systems,¹³ multiple function device products,¹⁴ and cybersecurity considerations for medical devices.¹⁵

Building on its longstanding commitment to advancing innovative approaches to DHTs, FDA issued a discussion paper in 2019¹⁶ and an Action Plan¹⁷ in 2021 focused on artificial intelligence (AI)-enabled medical devices to provide a holistic approach to the subset of DHTs that are enabled by machine learning. FDA has also published guidance to support patient-focused drug development,¹⁸ which may include the use of DHTs. In addition, FDA has hosted numerous workshops¹⁹ and patient engagement advisory committee²⁰ meetings on DHT-related topics and has engaged in stakeholder outreach activities through participation in public-private partnerships (e.g., the Medical Device Innovation Consortium),²¹ as well as collaborative communities²² with a DHT focus.

Current Landscape of DHTs

DHTs include technologies such as wearable, implantable, ingestible, and environmental sensors and software applications on mobile phones, among others. Advances in sensor technology, general-purpose computing platforms, and methods for data capture, transmission, and storage have revolutionized the ability to remotely obtain and analyze clinically relevant information from individuals. DHTs used for remote data acquisition are playing a growing role in health care and offer important opportunities in clinical research. DHTs can support traditional site-based clinical trials and enable the conduct of DCTs, which are clinical investigations where some or all trial-related activities occur at locations other than traditional clinical trial sites. DHT software can also be disseminated for use with a prescription drug.

Using the power of modern communication technology, miniaturization of electronic sensors, and mobile computing platforms, digital health technologies offer extraordinary opportunities to gather clinical data directly from patients.

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¹¹ [Content of Premarket Submissions for Device Software Functions | FDA](#)

¹² [Deciding When to Submit a 510\(k\) for a Software Change to an Existing Device | FDA](#)

¹³ [Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices | FDA](#)

¹⁴ [Multiple Function Device Products: Policy and Considerations | FDA](#)

¹⁵ [Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions | FDA](#)

¹⁶ [Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning \(AI/ML\)-Based Software as a Medical Device \(SaMD\) - Discussion Paper and Request for Feedback | FDA](#)

¹⁷ [Artificial Intelligence and Machine Learning \(AI/ML\) Software as a Medical Device Action Plan | FDA](#)

¹⁸ [Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments | FDA](#)

¹⁹ For example, [Public Workshop - Evolving Role of Artificial Intelligence in Radiological Imaging](#), [Virtual Public Workshop - Transparency of Artificial Intelligence/Machine Learning-enabled Medical Devices](#), and [Virtual Public Meeting - Patient-Generated Health Data Throughout the Total Product Life Cycle of Medical Devices](#)

²⁰ [CDRH Patient Engagement Advisory Committee | FDA](#)

²¹ <https://mdic.org>

²² [Collaborative Communities: Addressing Health Care Challenges Together](#)

Compared to scheduled trial visits, which require a participant to travel to a site, the use of DHTs to remotely collect data from trial participants may allow for more frequent or even continuous data collection, with reduced burden on trial participants. The technology exists to allow data derived from DHTs to be transmitted directly to investigators, sponsors, and/or other authorized parties, with the capability to maintain blinding or masking when appropriate. By reducing the burden on trial participants, DHTs may increase trial recruitment rates, help retain participation over longer periods of time, and increase participant diversity. Remote data collection may also prove useful in situations where face-to-face care or interaction is limited or unavailable (e.g., during a pandemic).

DHTs may also provide opportunities to collect data directly from trial participants who are performing daily activities (e.g., ambulation, sleep, everyday tasks) wherever the participants may be (e.g., home, school, work, outdoors). Moreover, DHTs may facilitate the collection of information from participants who are unable to report their experiences (e.g., infants, cognitively impaired individuals). These features may provide a broader picture of how participants feel or function in their daily lives by providing ways of measuring clinical characteristics or clinical events (e.g., hypertensive events, tremors, or acute hypoglycemia) that would otherwise be unavailable or impractical without the use of DHTs.

However, to use any measurement of clinical characteristics or clinical events as endpoints in clinical investigations intended to support drug development, approaches are needed to determine the clinical meaning and significance of these measurements to patients, caregivers, and healthcare providers. In addition, while remote data acquisition may increase opportunities for individuals to participate in clinical investigations remotely, it may raise issues including data privacy and confidentiality concerns.



Addressing Challenges Related to the Use of DHTs in Regulatory Decision-Making for Drugs

The successful utilization of DHTs to support drug development and review will depend on FDA and other stakeholders addressing the challenges discussed throughout the Framework. This Framework includes programs to support DHT-related activities within FDA (internal programs) and programs to engage industry and other stakeholders (external programs) in the development and use of DHTs.

Internal Programs

FDA has established the DHT Steering Committee which will utilize this Framework to develop internal programs to build review capacity and expertise and will help ensure consistent review policies regarding the use of DHTs for drug development.

1. DHT Steering Committee

The DHT Steering Committee will oversee the implementation of the PDUFA VII commitments related to evaluating DHT-based measurements in human drug development to support new drug applications, biologics license applications, supplements to those applications, and drug safety monitoring by helping to ensure that DHT-based data are fit for the intended purpose. The DHT Steering Committee has overseen the design of the Framework and will serve as the guiding body on activities and policy development related to DHTs. The DHT Steering Committee will also serve as a forum for shared

communication about DHT use in drug development as well as provide recommendations to promote consistency across centers regarding DHT-based policies, procedures, and analytic tools development.

The DHT Steering Committee consists of senior staff from CDER, CBER, and CDRH, including the DHCoE, as well as OCE and the Office of Clinical Policy and Programs. The DHT Steering Committee will do the following:

- Make recommendations and support implementation of PDUFA VII commitments regarding DHTs (e.g., public meetings, guidance documents, demonstration projects, technology needs, training)
- Gather information about the present state of DHTs, including specific challenges in their use
- Make policy recommendations impacting the use and evaluation of DHT-based measurements in human drug development
- Oversee activities to assist organizational units with consistent approaches to the review of drug submissions that contain DHT-derived data
- Oversee and coordinate DHT-related drug development working groups and teams across CDER and CBER, as appropriate
- Engage with external stakeholders on DHT-related issues in human drug development

More information about the DHT Steering Committee and its work will be published on the FDA website.

2. Technical Expertise and Training

The Agency will build on its technical expertise and develop training within the human drugs and biological products programs to enhance internal knowledge regarding the use of DHTs in drug development. Areas of focus will include the following:

a. *Verification and Validation*

Verification and validation are processes to ensure DHTs are accurate and reliable and meet intended users' needs. For the purposes of this Framework, verification is confirmation by examination and provision of objective evidence that the physical parameter that the DHT measures (e.g., acceleration, temperature, pressure) is measured accurately and precisely. Validation is confirmation by examination and provision of objective evidence that the selected DHT appropriately assesses the clinical event or characteristic in the proposed participant population. Verification is often viewed as part of the validation process. Usability and interoperability studies may be included as part of validation. Assessment of DHT verification and validation requires domain-specific expertise, including in statistics, mathematics, and general-purpose computing platforms.

b. *Use of a Participant’s Own DHT or General-Purpose Computing Platform*

FDA will build on its expertise in general-purpose computing platforms (e.g., mobile phones or smartwatches) to address participants’ use of their own DHTs in a clinical investigation. Challenges in the evaluation of personal DHTs or general-purpose computing platforms may relate to consistency, accuracy, and/or precision. Minimum technical specifications (e.g., for operating systems, storage capacity, and sensor performance) and performance specifications (e.g., accuracy and precision for measuring specified clinical events or characteristics) will be important to ensure the measurements are consistent across different protocol-specified DHTs.

c. *Upgrades and Updates of DHTs in Drug Development*

During clinical investigations, new models of DHTs may become available, and existing DHTs may require software updates. FDA will build its expertise in understanding the impact of updates or changes to DHTs. Technical experts and statisticians across centers will collaborate and assess whether there is a meaningful difference in results observed before and after the updates to a DHT and how the differences impact interpretability of those results in their context of use.

d. *Artificial Intelligence and Machine Learning*

AI is a branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviors such as learning, making decisions, and making predictions. The subset of AI known as machine learning (ML) allows models to be developed by training algorithms through analysis of data, without models being explicitly programmed.²³ AI can use different techniques, including models based on statistical analysis of data and knowledge-based systems that primarily rely on rules (e.g., if-then statements and ML). DHTs may incorporate the use of AI algorithms that have the potential to transform health care by deriving new and important insights from the vast amount of data generated by DHTs. There are numerous possibilities to incorporate DHTs using AI algorithms into drug development, including participant recruitment, site selection, clinical trials data collection and analysis, and safety monitoring. FDA intends to build on its domain-specific expertise in data science, informatics, statistics, and mathematics to help ensure the appropriate application of AI technology in the context of DHTs used for drug development.

²³ See International Medical Device Regulators Forum, Machine Learning-enabled Medical Devices: Key Terms and Definitions, available at <https://www.imdrf.org/sites/default/files/2022-05/IMDRF%20AIMD%20WG%20Final%20Document%20N67.pdf>.

e. *Technical Consultation of Experts and Staff Training*

To facilitate our work in the areas described above, FDA intends to enhance our relevant expertise through hiring new staff, training existing staff, and consulting with internal and external experts, as appropriate. The DHT Steering Committee will support development of a training program for drug reviewers to enhance their expertise in the review of submissions that include information relating to the use of DHTs.

3. Consistency of Evaluations Across Review Divisions

A single DHT measurement may be used for studies of different diseases and different drugs. For example, actigraphy is widely used to evaluate functionality and may be used in a broad range of conditions, including cardiorespiratory diseases, neuromuscular diseases, and psychiatric diseases. Review divisions and centers should have consistent approaches to the review and evaluation of submissions that contain DHT-related data. The DHT Steering Committee will help facilitate consistent approaches to the review and evaluation of such submissions.

4. Statistical Considerations in the Analysis of DHT-Derived Data

Although use of DHTs in clinical investigations has increased, few clinical investigations have used sensor-based DHTs to support primary or secondary endpoints. The use of DHT-derived endpoints presents unique statistical considerations for FDA during their review. These considerations are related to data quality; technical data specifications; provenance (i.e., understanding the lineage of the data); definitions used (e.g., activity counts, steps, calories); techniques and algorithms used for processing, summarizing, and analyzing DHT data; and treatment of missing data. Existing and novel statistical methods for validating DHT-derived data need to be assessed. FDA will leverage its statistical expertise to address novel analytical considerations for endpoints derived from DHT data. In addition, FDA will consider developing technical data specifications to facilitate submission of readily analyzable DHT-derived data supporting drug development.

5. IT Capabilities

Large DHT-generated datasets introduce new challenges regarding the ability to receive and analyze data to support a regulatory decision. Through PDUFA VII, FDA will enhance its IT capabilities to support the review of DHT-generated data. This work will be coordinated with other IT capability development activities across the Agency.

- FDA will enhance its internal systems to support review of DHT-related submissions, including capturing key information about clinical trials utilizing DHTs to support tracking the number and rate of change of DHT-related submissions. To facilitate tracking, CDER and CBER plan to request that sponsors and applicants identify when submissions contain

information related to the use of DHTs. FDA will develop internal systems to monitor trends in submissions containing DHT-related data.

- FDA will establish a secure cloud technology to enhance its infrastructure and analytics environment that will enable FDA to effectively receive, aggregate, store, and process large volumes of data from drug trials conducted using DHTs. FDA will utilize the cloud environment to meet review needs across CDER and CBER.
 - After establishing the cloud environment, FDA will pilot a secure, cloud-based mechanism to support submission and review of DHT-generated datasets.
- FDA will work to enhance, recommend, and implement standards that reduce the handling necessary to make DHT data analyzable. CDER and CBER intend to collaborate with the DHCoE to promote the development and adoption of data standards for DHT-generated datasets.

External Programs

The Framework describes a range of activities for FDA to engage with external stakeholders, such as sponsors, patient advocacy groups, DHT companies, clinical investigators, international regulatory bodies, and professional societies. Such activities can help FDA better understand the challenges and opportunities associated with DHTs and will include holding public meetings, running demonstration projects, and publishing guidance on the use of DHTs to support drug development and review.

1. FDA Meetings With Sponsors

Engagements between sponsors and FDA regarding the use of DHTs may occur at different stages of drug development and may include meetings with the DHT Steering Committee, Critical Path Innovation Meetings, pre-IND meetings, pre-submissions meetings, IND and NDA review meetings, and related meetings and communications.²⁴ Topics for discussion may include the regulatory status of DHTs, development of trial endpoints, selection of DHTs for clinical investigations, and verification and validation of DHTs.

2. Drug Development Tool Qualification Program

FDA has qualification programs that are intended to support the development of tools for use in assessing medical products and that provide another avenue for sponsors and other stakeholders to engage with the Agency. Developers of DHTs may choose to pursue qualification of DHTs as drug development tools

²⁴ Sponsors should follow each FDA center's procedures for engaging with the Agency in the context of a development program. For drugs and biological products, see the web page for Critical Path Innovation Meetings, available at <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/critical-path-innovation-meetings-cpim>; the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (December 2017); and the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of Biologics License Applications (BLA) Products* (June 2018). For further information about FDA digital health regulatory policies, see <https://www.fda.gov/medical-devices/digital-health/ask-question-about-digital-health-regulatory-policies>.

(DDTs)²⁵ for a specific context of use. A qualified DHT may be relied upon in multiple clinical investigations to support premarket submissions for drugs (if qualified as a DDT) where the context of use is the same (e.g., measurement of a specific outcome in a specific disease population), without having to repeat studies that supported the qualification, provided that the qualification has not been rescinded or modified. FDA's DDT Committee reviews requests for DHTs seeking qualification as a DDT. The DDT Committee and the DHT Steering Committee will work together to help ensure alignment and avoid overlap of responsibilities.

3. Guidance

To facilitate the appropriate use of DHTs in drug development, FDA has published draft guidances that, when finalized, will reflect FDA's current thinking on a number of DHT topics, and the Agency plans to develop additional guidance documents.

Draft guidance for industry, investigators, and other stakeholders

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations (December 2021)

This draft guidance outlines proposed recommendations intended to facilitate the use of DHTs in clinical investigations, as appropriate, for the evaluation of medical products. These recommendations address the following topics:

- Selection of DHTs that are suitable for use in clinical investigations
- Verification and validation of DHTs for use in clinical investigations
- Use of DHTs to collect data for trial endpoints
- Identification of risks associated with the use of DHTs during clinical investigations
- Management of risks related to the use of DHTs in clinical investigations

Draft guidance for industry *Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers (March 2023)*

Part 11 is intended to ensure the authenticity, integrity, and confidentiality of electronic records from their point of creation to their modification, maintenance, archiving, retrieval, or transmission. The draft guidance addresses commonly asked questions about the applicability of part 11 to electronic records, electronic signatures, and electronic systems used in clinical investigations, including use of DHT-derived data. The draft guidance proposes recommendations related to access controls, data provenance and traceability, secure data transfers, and archiving of derived data related to DHT use in clinical trials.

New capabilities for measuring function and symptoms continuously and in routine life settings could enable significant improvements in the degree to which data reflect the actual status of the research participant.

**Robert M. Califf, M.D.,
Commissioner U.S. Food and Drug Administration**

²⁵ See CDER's web page for Drug Development Tool (DDT) Qualification Programs, available at <https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tool-ddt-qualification-programs>.

Draft guidance for industry, investigators, and other stakeholders
Decentralized Clinical Trials for Drugs, Biological Products, and Devices

FDA plans to publish this draft guidance in 2023. This guidance will include recommendations to clarify and advance the use of decentralized clinical trials to support the development of drugs and devices.

Draft guidance for industry *Regulatory Considerations for Prescription Drug Use-Related Software* (targeted for publication by end of fiscal year 2023 per commitment letter)

As stated in the PDUFA VII commitment letter, prescription drug use-related software is software that is disseminated by a drug applicant for use with a prescription drug or biologic product or with a drug- or biologic-led combination product. This draft guidance will cover how such software may be described in labeling, including in the Prescribing Information, when the software is distributed with a drug or integrated as part of a drug- or biologic-led combination product, as well as when the software is distributed by an applicant independent of an approved product.

Additional DHT-related guidances

The DHT Steering Committee will address areas where additional guidance may be beneficial. Consistent with good guidance practices, guidance topics will be informed by stakeholder engagement, including interactions with sponsors, DHT companies, and patient advocacy groups. Public meetings and demonstration projects will also serve to identify topic areas of public health importance. As stated in the PDUFA VII commitment letter, beginning in fiscal year 2024, FDA will publish additional draft guidances in identified areas of need informed by stakeholder engagement.

4. Public Meetings

By the end of the second quarter of fiscal year 2023, FDA will convene the first of a series of five public meetings or workshops with key stakeholders, including patients, biopharmaceutical companies, DHT companies, and academia, to gather input on issues related to the use of DHTs in regulatory decision-making related to drug and biological product development. The meetings and workshops will be designed to address the following topics:

- *Understanding priorities for the development of DHTs to support clinical investigations*

The public meeting will explore improving patient access, increasing diversity, and facilitating engagement through remote trial-related measurements. It will also cover patient and industry perspectives, opportunities for remote data acquisition (e.g., actigraphy) from trial participants, and the use of DHTs to measure clinical outcomes.

- *Identifying approaches to DHT verification and validation*

The public meeting will explore approaches to verification and validation of various types of technologies for different patient populations and diseases. Such approaches may be helpful to demonstrate that the clinical event or characteristic to be assessed (e.g., step count or heart rate) is consistently and appropriately measured in the population of interest.
- *Understanding DHT data processing and analysis to inform the need for novel analytical techniques*

The public meeting will consider statistical challenges and issues related to the use and analysis of DHT-derived data. Challenges addressed at the meeting could include aggregation, analysis, interpretation, and reporting of continuously measured DHT data as well as handling of associated missing data.
- *Addressing the regulatory acceptance of safety monitoring tools that utilize AI and ML-based algorithms for pharmacovigilance purposes (e.g., continuous data streams from DHTs)*

The public meeting will cover AI for detecting adverse events (e.g., seizures, hypoglycemia) using DHTs and issues related to source data and algorithms.
- *Understanding emerging issues*

Over the next few years, as new issues emerge and as FDA learns more about the challenges related to the use of DHTs in clinical investigations and regulatory decision-making, a final public meeting topic will be determined to enhance FDA's ability to support drug development programs that use DHTs.

5. Demonstration Projects

FDA will identify at least three issue-focused demonstration projects to inform methodologies for efficient DHT evaluation in drug development. These projects may involve engagement with researchers from academia, the biopharmaceutical industry, patient groups, and other stakeholders. They will cover key issues to inform regulatory policy development and provide regulatory advice. The focus of these projects may include validation methods for specific technologies, endpoint development, analytic approaches to missing data, use of multi-channel inputs to characterize an endpoint, evaluation of continuous data versus discrete measurements, use and limitations of DHTs in DCTs, and other related issues.

6. External Organizations

Development of DHTs is a rapidly growing commercial enterprise involving, among others, technology companies, manufacturers of medical devices, and manufacturers of consumer technologies that measure health and wellness. Many developers have emerged that are focused on advancing the use of DHTs in clinical research, including external organizations such as public-private partnerships, consortiums, professional organizations, and trade groups. FDA will look to continue engagement with such external organizations to facilitate meeting the objectives included in this Framework.

FDA has participated in several forums organized by the National Academies of Sciences, Engineering, and Medicine; the Drug Information Association; the Heart Failure Collaboratory; and other professional bodies addressing the use of DHTs in drug development.



Conclusion

DHTs may provide opportunities for more efficient drug development. DHTs and DHT-derived data can be important tools in supporting timely access to safe, effective, and innovative new medicines for patients. DHTs can be used to increase decentralization of trial-related activities, improve patient access to trials, increase trial diversity, and promote retention by facilitating remote trial-related measurements. In addition, DHTs can facilitate direct collection of information from participants who are unable to report their experiences (e.g., infants, cognitively impaired individuals). Further, they may allow for development of novel endpoints, which can provide a broader picture of how participants feel or function in their daily lives. Despite the potential advantages of DHTs, many challenges arise when incorporating DHTs and DHT-derived data into regulatory decision-making. This Framework outlines a multifaceted approach to collaboratively address these challenges with our stakeholders. Through these joint efforts, we intend to advance the development of drugs and promote the public health.

Integrating research and clinical care with access to digital information presents enormous potential to benefit the research enterprise and health outcomes.

**Robert M. Califf, M.D.,
Commissioner U.S. Food and Drug Administration**



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