FDA MyStudies App

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Medications in Pregnancy SIG webinar
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Disclosure and Disclaimer

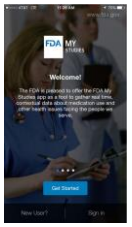
- David Martin received funding from the Patient Centered Outcomes Research Trust Fund to develop the FDA My Studies Mobile App
- No conflicts of interest to disclose
- The views expressed are those of the author and should not be construed as FDA's views or policies
- The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services

Overview

- Opportunities for Mobile Technology
- Description of FDA My Studies system
- FDA Guidance related to informed consent, authenticity, integrity, and confidentiality
- Implications of the FDA My Studies pilot
- Access to FDA My Studies documentation and code
- Next steps

Two big opportunities

- **Patient-Centric Interaction**
  - Direct capture of the patient perspective
  - 24 hour convenience
  - Electronic transmission enables data to be captured from geographically dispersed patients



- **Unobtrusive measurement**
  - Biosensors can be worn or attached to patient
  - Continuous monitoring for rare events (e.g., seizures, arrhythmias)
  - Capture real life situations (stress, sleep, exercise, eating)

Commitments to Evaluate RWE

21st Century Cures

"FDA shall establish a program to evaluate the potential use of real world evidence (RWE) to support:

- **A new indication for an approved drug**
- **Post-approval study requirements**

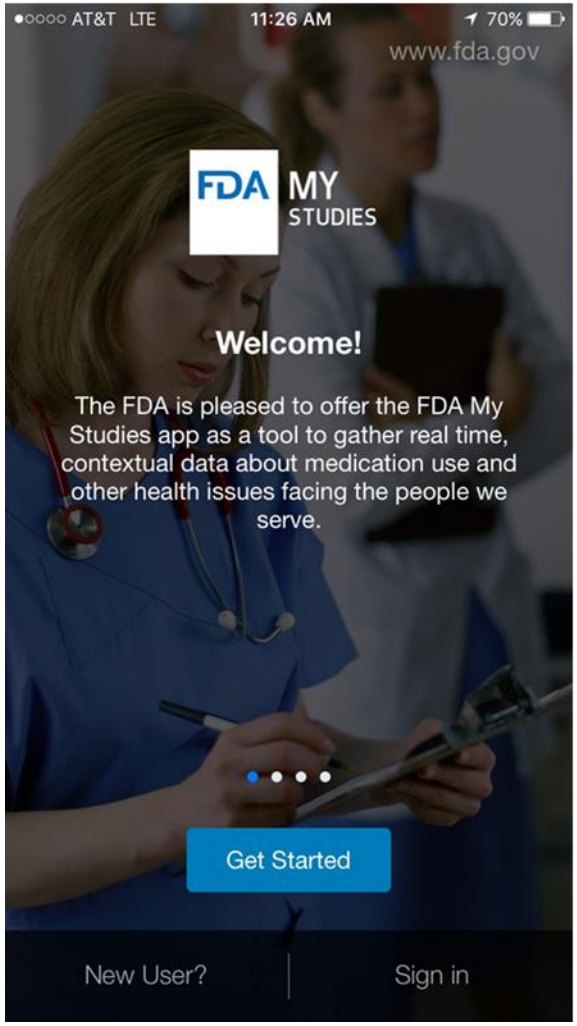
- **Real-World Data (RWD)** are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources
- **Real-World Evidence (RWE)** is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD

RWD include data derived from *electronic health records* (EHRs), *claims and billing data*, data from product and disease *registries*, patient-generated data including in home-use settings, and data gathered from other sources that can inform on health status, such as mobile devices.

Endpoints in FDA Registrational trials 2007-2015

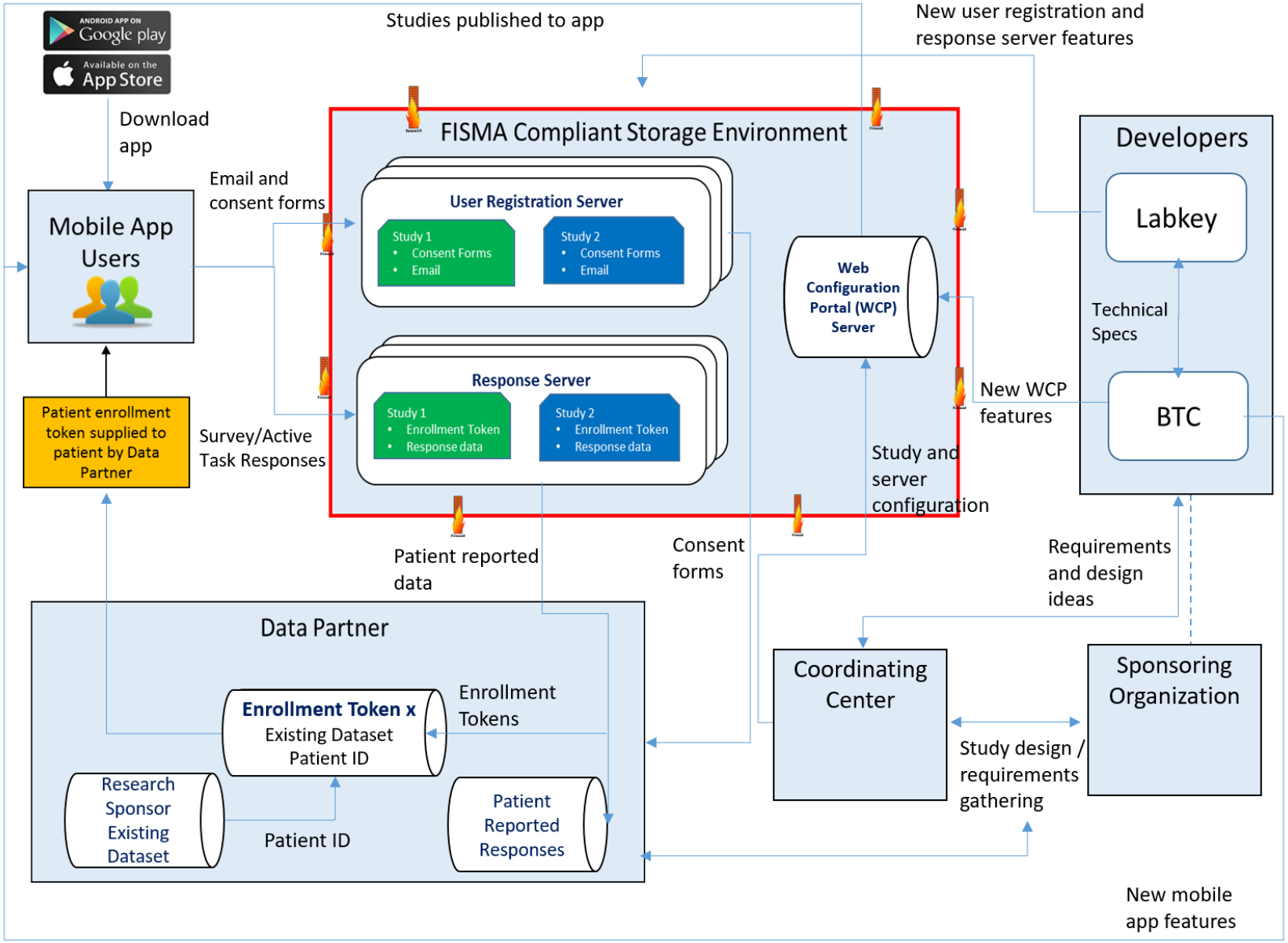
Type of Endpoint	% of NDA	Examples of Endpoints Measured
Chemistry data	11	HBA1c, pregnancy test, GFR
Hematology	6	Severe neutropenia Apheresis yield > 5 million CD34+ cells/kg
Pathology	2	Increase/decrease of parabasal cells; biopsy proven acute rejection, clearing of anterior chamber cells
Microbiology	6	Sustained virological response, plasma viral load, conversion to negative sputum
Imaging +/- (survival, clinical signs)	17	Bone mineral density; vertebral fractures, spleen volume, progression free survival
Physiological/ functional measurement	9	6 minute walk, normal sinus rhythm, FEV1, sleep studies
Clinical event /clinical sign	19	Death, hospitalization, MACE, MS relapse, Lice free head
CRO/PRO	30	Toronto western spasmodic torticollis rating scale, Hamilton depression rating scale, Rheumatology scale ankylosing spondylitis scale, psoriasis severity index, seizures, sleep, prostate symptom score

FDA My Studies

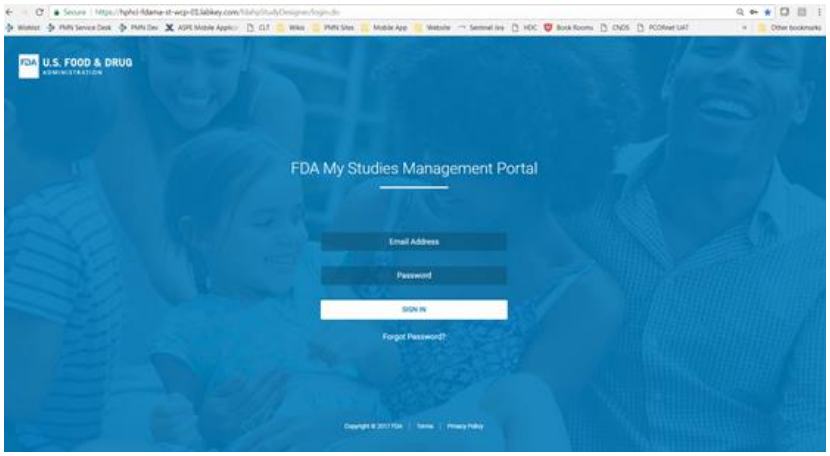


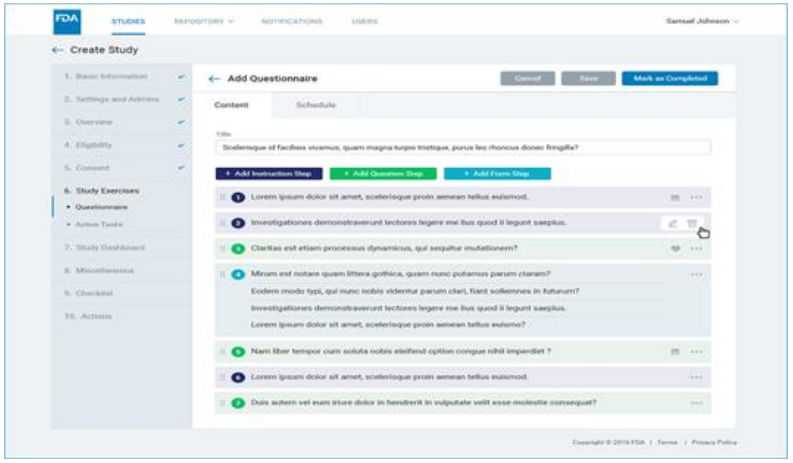
- Mobile App
  - Standard frameworks - ResearchKit (iOS), ResearchStack (Android)
  - Gateway capability
- Web-based configuration portal
- Secure Storage Environment
  - FISMA complaint
  - Partitioned for distributed research
  - Responses can be downloaded in broadly compatible formats (e.g., for use in SAS, Excel, etc.)

Supporting Multisite & Distributed Studies



Reusable Infrastructure

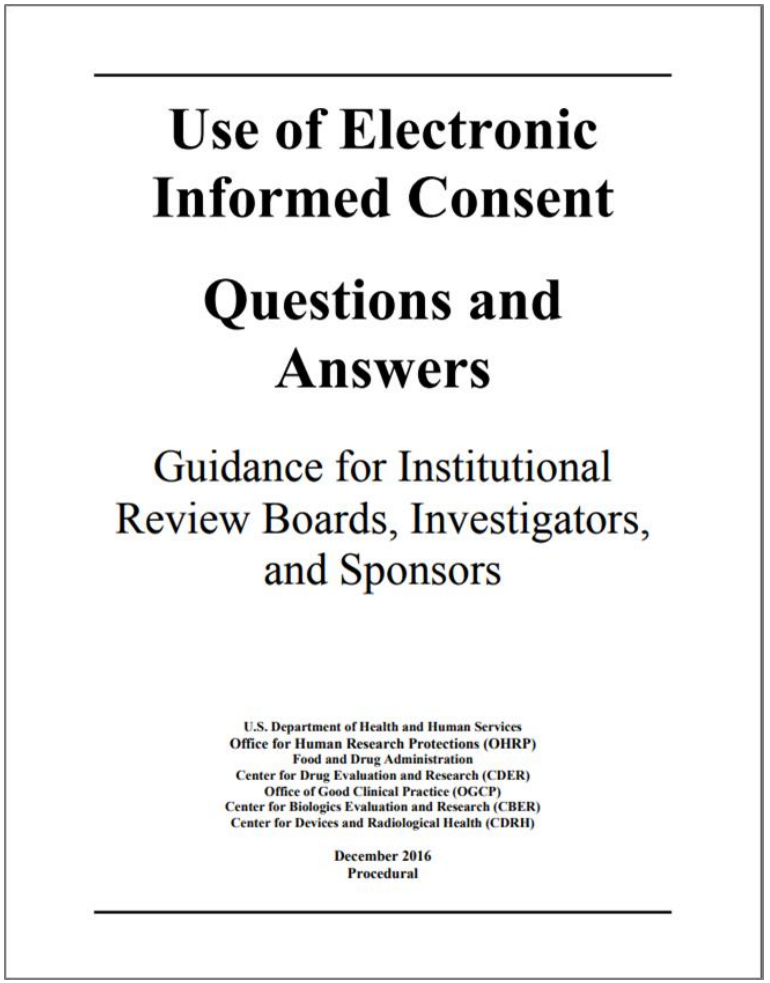




- Configure Study Elements (including questions and active tasks)
  - Custom recurrence and frequency
  - Logical branching
- Create and Manage Resources and Notifications
  - Flexible notifications
  - Study Dashboards
  - Create patient enrollment tokens

Informed Consent

- Can be obtained from patient remotely
- Method needed to ensure the person signing the consent is the person in the study
- May use audio visual presentation
- Must have a process to address patient's questions
- Must provide a suitable record to patient
- FDA needs to be able to inspect it



Use of Electronic Informed Consent

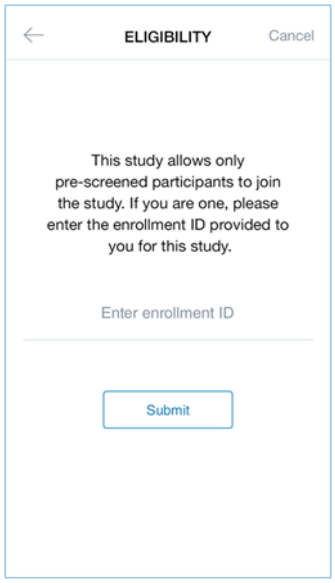
Questions and Answers

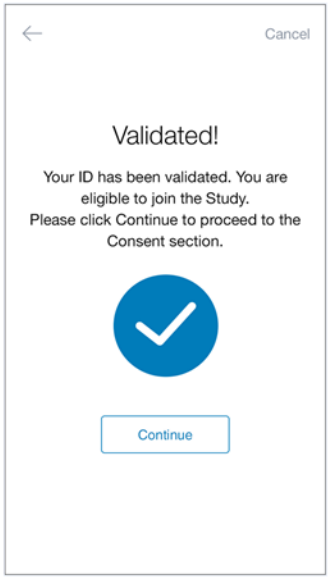
Guidance for Institutional Review Boards, Investigators, and Sponsors

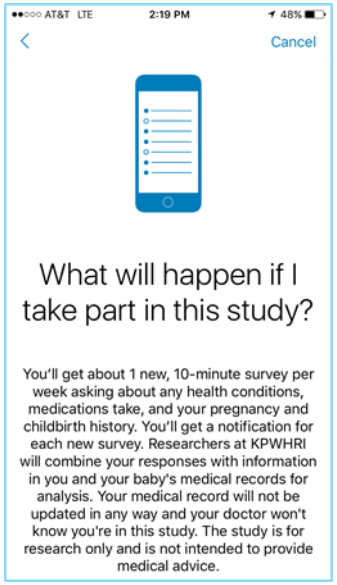
U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Good Clinical Practice (OGCP)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

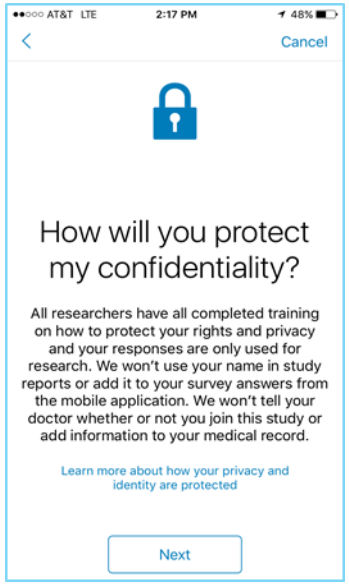
December 2016
Procedural

Enrollment and Consent



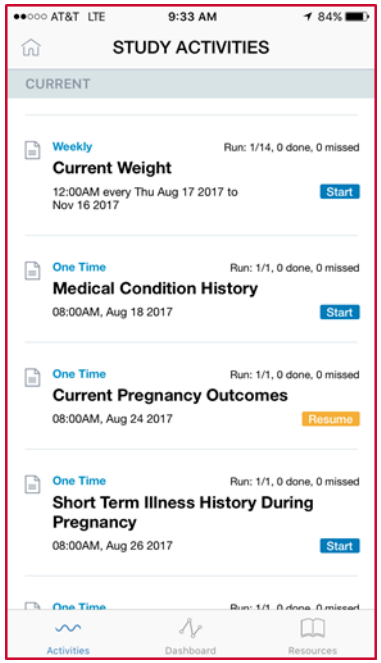


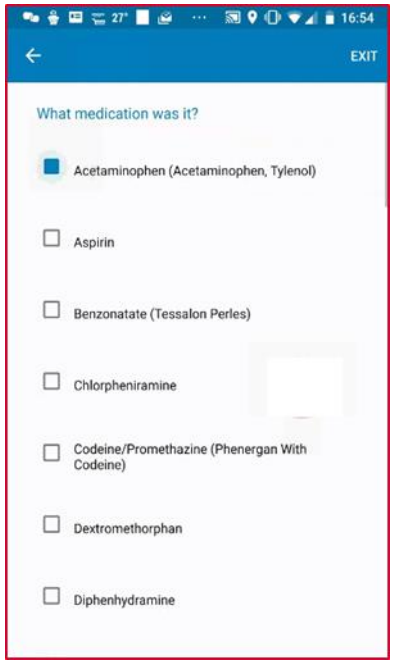


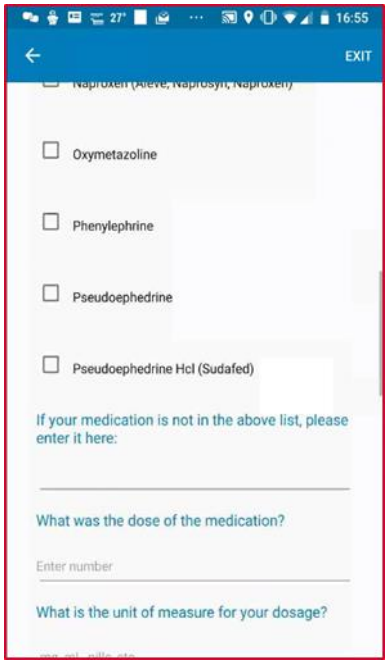


- Pre-select a cohort from electronic health data
- Recruit and distribute enrollment tokens for pre-selected cohorts
- Participants download the app in iOS or Android app stores
- Participants review eligibility information and provide informed consent through the app

Engagement

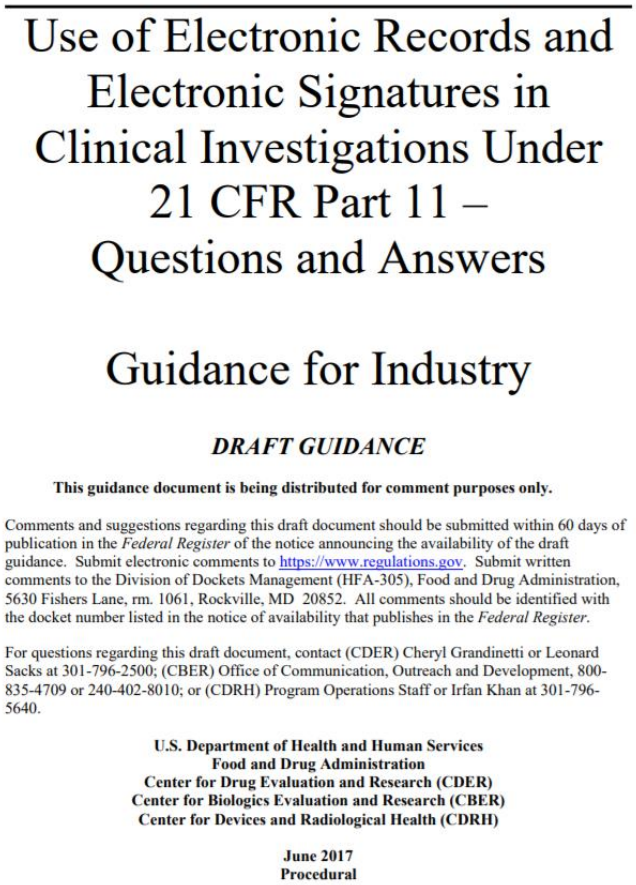






- Participants respond when they choose within the study schedule
- Responses are securely transmitted to the Response Server
- Dashboard displays progress
- Configurable notifications

21 CFR Part 11 and Mobile Technology



Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Cheryl Grandinetti or Leonard Sacks at 301-796-2500; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Program Operations Staff or Irfan Khan at 301-796-5640.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

June 2017
Procedural

- Goals: Ensure authenticity, integrity, and confidentiality
- Refers to portable electronic technology used in clinical investigations that allows for off-site and remote data capture from study participants
  - Includes mobile platforms, mobile applications, wearable biosensors and other remote and ingestible sensors, and other portable and implantable electronic devices
- The recommendations apply to technology that is provided by the sponsor or owned by the study participant

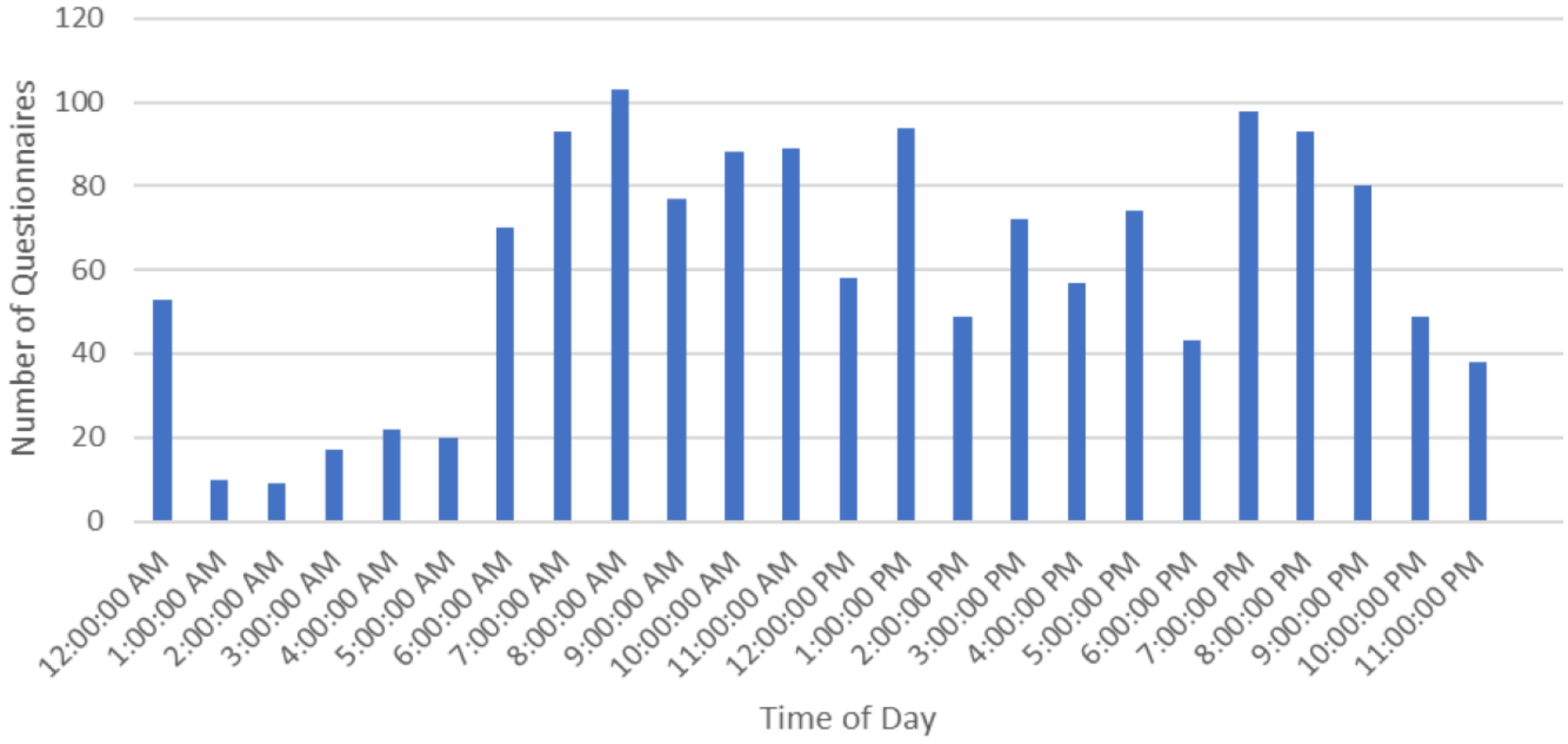
Audit Trails

- The mobile technology should record the date and time that the data are captured and this information should be transmitted or recorded in the durable database
- The first durable database should capture
  - Date and time that the data enter the durable database
  - Data originator for each data element
    - Patient
    - Mobile Technology (e.g., biosensor)
    - EHR
- An audit trail should track modifications to the data and include data element identifiers that reflect the date, time, and data originator and the reason for the change
  - Modified or corrected data should not obscure previous entries

Pilot Study

- Kaiser Permanente Washington
  - About 680,000 members and 6,000 births per year
  - Participant in Sentinel and PCORnet
- 1,070 randomly selected pregnant women (based on electronic health record data) received an invitation letter with the participant enrollment token
  - 64 consented to participate in the study
    - 4% response for mail-only group and 8% response for phone call follow-up group
    - Compares to 1% "activation rate" noted in another Sentinel Initiative (FDA-Catalyst) study involving mailings from data partners and no financial incentives
- Patients contributed to questionnaire design

FDA My Studies Pilot: 24 hour Engagement Pattern



Implications of My Studies

- Mobile technology can expand the depth and diversity of pharmacoepidemiology data
  - Women provided sensitive information including continued alcohol, smoking, and illicit drug use during pregnancy
  - Aggregate use reported through app vs. secondary electronic health data
    - OTC: 13x
    - Rx: 60%
    - Women provided reasons for discontinuation
- Patient-centric interaction can present challenges
  - One erroneous free text medication input
  - Four live births not reported

Implications of My Studies

- Mobile Technology can operate successfully within a distributed clinical research environment
  - Linking data from mobile technology to distributed pharmacoepidemiology data or trial data is feasible
  - My Studies App and data storage environment can support a 21 CFR Part 11 compliant study
  - Institutional review boards willing to review
- Recruitment strategies and incentives remain important
- Patients should be involved in application development as well as questionnaire design
- Open source and reusable infrastructure reduces “up front” investment but may impose constraints

FDA MyStudies: now open source

U.S. Department of Health and Human Services

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FDA's MyStudies Application (App)

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The U.S. Food and Drug Administration (FDA) is posting computer code and a technical roadmap that will allow researchers and developers to customize and use the FDA's newly created MyStudies app. The FDA MyStudies App is designed to facilitate the input of real world data directly by patients which can be linked to electronic health data supporting traditional clinical trials, pragmatic trials, observational studies and registries. It was developed by the FDA and private sector partners, but open source code and technical documentation are being released to the public, so the app and patient data storage system can be reconfigured by organizations conducting clinical research. The app bore the FDA brand while its functionality was tested in a pilot study, but it can now be rebranded by researchers and developers who would like to customize and rebrand the app.

The FDA MyStudies App has several important features, including:

- The data storage environment is secure and supports auditing necessary for compliance with 21 CFR Part 11 and the Federal Information Security Management Act, so it can be used for trials under Investigational New Drug oversight.
- The app is configurable for different therapeutic areas, and health outcomes, which reduces software development hurdles for non-FDA users.
- The data storage environment is partitioned to support multi-site trials or "distributed database" studies.
- The code for MyStudies will be open source so software developers can improve upon its capabilities.

Open source code is being released for two versions of the app. One is built on Apple's ResearchKit (iOS) framework, and the other is built on the open source ResearchStack framework, which runs on Google's Android. (The original FDA-branded app is not currently in app stores because it was removed after being tested in a pilot study.)

- https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm625228.htm
- https://www.fda.gov/Drugs/ScienceResearch/ucm624785.htm
- https://github.com/PopMedNet-Team/FDA-My-Studies-Mobile-Application-System

Links to technical documents

MyStudies App Technical Documents

- Open Source Code and Technical Documentation for the FDA MyStudies App on GitHub
- MyStudies Mobile App Quick Overview for Research
- The FDA MyStudies App: A Patient Centered Outcomes Research Trust Fund Enabler For Distributed Clinical Trials And Real World Evidence Studies
- Appendices

Upcoming Releases

Additional open source code built on the Apple ResearchKit (iOS) framework and the ResearchStack framework for Google's Android operating system will be released over the next several calendar quarters. These enhancements will simplify configuration for researchers and improve the experience for participants. Additional details can be found in the Mobile App Quick Overview for Research document. Please see the Sentinel website for more information on the "FDA-Catalyst MyStudies App Alignment with Pragmatic Trials and/or Registries" project.

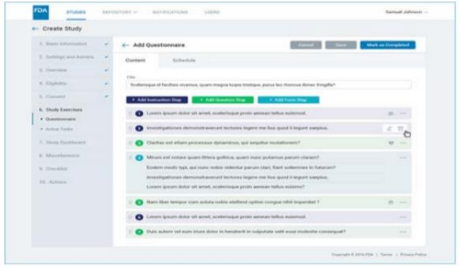
Quick overview and report

Mobile App Quick Overview for Research

Architecture

- Mobile App
  - Standard frameworks - ResearchKit (iOS), ResearchStack (Android)
  - Optional gateway capability

- Web-based configuration portal
  - Configure Study Elements (including questions and active tasks)
    - Custom recurrence and frequency
    - Logical branching
  - Create and Manage Resources and Notifications
    - Flexible notifications
    - Study Dashboards
  - Create patient enrollment tokens



Sentinel

THE FDA MYSTUDIES APP: PATIENT CENTERED OUTCOMES RESEARCH TRUST FUND ENABLER FOR DISTRIBUTED CLINICAL TRIALS AND REAL WORLD EVIDENCE STUDIES

COLLECTION OF PATIENT-PROVIDED INFORMATION THROUGH A MOBILE DEVICE APPLICATION FOR USE IN COMPARATIVE EFFECTIVENESS AND DRUG SAFETY RESEARCH

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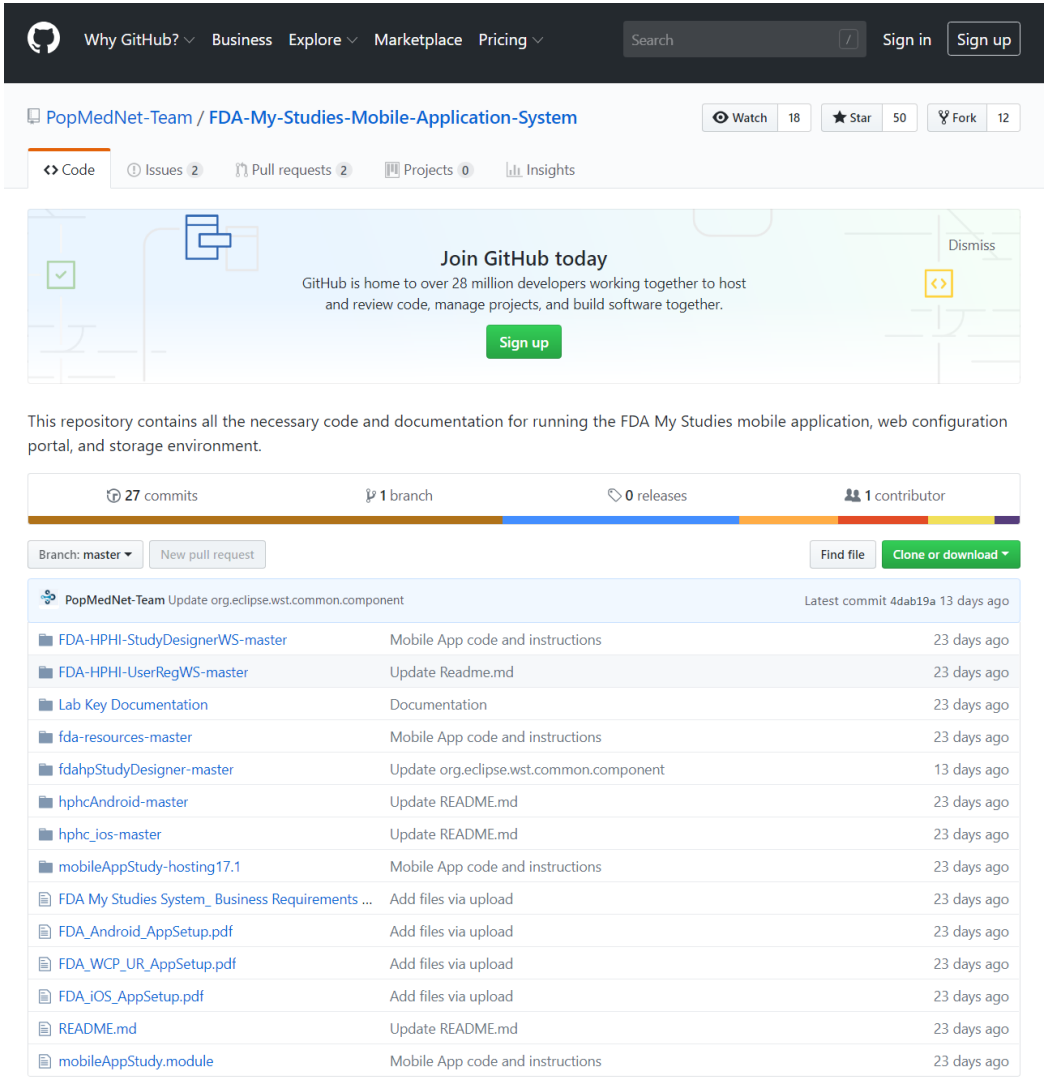
October 10, 2018

The Sentinel System is sponsored by the U.S. Food and Drug Administration (FDA) to proactively monitor the safety of FDA-regulated medical products and complements other existing FDA safety surveillance capabilities. The Sentinel System is one piece of FDA's Sentinel Initiative, a long-term, multi-faceted effort to develop a national electronic system. Sentinel Collaborators include Data and Academic Partners that provide access to healthcare data and ongoing scientific, technical, methodological, and organizational expertise. The Sentinel Coordinating Center is funded by the FDA through the Department of Health and Human Services (HHS) Contract number HHSF223201400030I. This project was funded by the Office of the Secretary PCORTF under Interagency Agreement #750115PE060034 with the FDA.

GitHub repository



Next Steps

- Learn from experience supporting a registry and clinical trial
- Public meeting or webinar oriented at end users and developers
- Updates to open source FDA MyStudies app

Questions/ Comments

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