ConnectedHealthInitiative

March 22, 2022

Commissioner Robert Califf
U.S. Food & Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Silver Spring, Maryland 20993-0002

RE: ***Connected Health Initiative Comments on the Food and Drug Administration's Digital Health Technologies for Remote Data Acquisition in Clinical Investigations [Docket No. FDA- 2021-D-1128; 86 FR 72981]***

Dear Commissioner Califf:

The Connected Health Initiative (CHI) writes to provide input on the Food and Drug Administration's (FDA) draft guidance on the use of digital health technologies (DHTs) to acquire data remotely from participants in clinical investigations evaluating medical products. DHTs may take the form of hardware and/or software and may be used to gather health-related information from study participants and transmit that information to study investigators and/or other authorized parties to evaluate the safety and effectiveness of medical products.[1]

I. Statement of Interest and General Comments of the Connected Health Initiative

CHI is the leading effort by stakeholders across the connected health ecosystem to responsibly encourage the use of digital health innovations and support an environment in which patients and consumers can see improvements in their health. We seek essential policy changes that will help all Americans benefit from an information and communications technology-enabled American healthcare system. For more information, see www.connectedhi.com.

[1] 86 FR 72981.

CHI is a longtime active advocate for the increased use of new and innovative digital health tools in both the prevention and treatment of disease, specifically regarding clinical investigations. We appreciate the FDA's consistent collaboration on digital health-related technologies to responsibly streamline their pathway to the market.

Medical devices with software functions are radically improving the American healthcare system and will continue to do so. Mobile app-enabled telehealth and remote monitoring of patient-generated health data continues to represent the most promising avenue for improved care quality, reduced hospitalizations, avoidance of complications, and improved satisfaction, particularly for the chronically ill.

CHI is a longtime supporter of the FDA's efforts to modernize and streamline the medical device approval process, particularly for device software functions controlling or part of a hardware device (i.e., Software in a Medical Device, or SiMD) and for devices that are not part of a hardware device (i.e., Software as a Medical Device, or SaMD). We applaud the FDA's release of its Draft Guidance for public input, which provides helpful, timely, and appropriate updates to its 2005-issued version of guidance for premarket submissions for device software functions.

Traditionally, in the context of clinical trials, there has been a limited use of DHTs that leverage patient-generated health data (PGHD) due to the costs associated with distributing, connecting, tracking, and maintaining mobile devices during an investigation. With the revolution of smartphone adoption, clinical investigations can now largely discard these concerns, particularly when embracing the "bring your own device" (BYOD) model. Such models may utilize specialized instruments as accessories to smartphones/tablets/etc., enabling a much more complete evaluation of a patient's condition across a diversity of types of data and use cases. The benefits of the full range of DHTs available today include:

- The ability to attain PGHD for data management in real time;
- Increased authenticity of patient-reported outcome data, particularly when such data is aggregated directly from sensors collecting PGHD (i.e., the trial participant is bypassed in the reporting process);
- Enhanced subject retention and subject involvement in the clinical trial due to the ease of reporting PGHD through smartphones or tablets as well as the ability to access this data;
- Reduced training costs, as smartphones are widely adopted and typical subjects will already be trained on how to use their own devices;
- Use of any device, whether a phone at work or a tablet at home, to access the data in a continuous manner, with data interoperability based on open and consensus-based standards (these standards include: the Continua Alliance's Design Guidelines,[2] Health Level 7 [HL7],[3] ISO 12052 [Health informatics --

[2] http://www.continuaalliance.org/products/design-guidelines.
[3] http://www.hl7.org/implement/standards/index.cfm.

Digital imaging and communication in medicine including workflow and data management],[4] and the Integrating the Healthcare Enterprise [IHE] initiative[5]);

- The removal of geographic restrictions from trials and investigations allowing
- access to a more diverse set of trial subjects than would otherwise be possible; and
- Reduced maintenance and support costs for sponsors.

The FDA has consistently demonstrated its willingness to embrace advanced technology and connectivity in the healthcare continuum.[6] However, in the context of clinical investigations, a lack of clarity from the FDA regarding the use of DHTs has reduced uptake. Given the rapid development of DHTs, FDA guidance that will facilitate the use of DHTs in a clinical investigation as appropriate for the evaluation of medical products is necessary and timely and will greatly assist Independent Review Boards (IRBs) conduct investigations of non-significant risk under 21 CFR Part 812. Not only is this modernization of FDA guidance good public policy, but it would also be consistent with Congress' goals in the Food and Drug Administration Safety and Innovation Act of 2012 to promote innovation, protect patient safety, and avoid regulatory duplication.[7] FDA's efforts to enable the responsible use of DHTs will also assist in bridging the digital divide and providing needed disease prevention and treatment to America's most vulnerable citizens, in alignment with the Administration's priorities for eliminating disparities in healthcare.

In addition to the rapid finalization of its guidance on the use of DHTs in clinical investigations, CHI urges the FDA to further encourage adoption of new technologies and innovations in clinical investigations through:

- Holding publicly-accessible workshops, and making publicly available technical resources and educational materials, on how to embrace the use of new technologies and innovations (including mobile apps and the BYOD model) in clinical trials and investigations, which will help address the reluctance of review boards, clinical sponsors, and investigators to embrace advanced technologies into their processes; and
- Continued work with the wide range of stakeholders involved in the healthcare technology community on public-private partnerships, grants, and other means to increase the use of innovative technologies in clinical trials.

[4] http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=43218.
[5] http://www.ihe.net/About_IHE/.
[6] *E.g.*, U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF, MOBILE MEDICAL APPLICATIONS (2015), available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM26 3366.pdf.
[7] *See* P.L. 112-144 (Sec. 618).

II. Specific Input of the Connected Health Initiative on Proposed Guidance on the Use of Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Building on our broad support for the FDA's Draft Guidance, we offer the following specific input on its proposed guidance:

- DHT Scoping/Definition: CHI generally supports FDA's overview of DHTs and its comprehensive description of their benefits. However, we urge FDA to further explore the BYOD model. The BYOD model, whether using mobile apps and/or accessories to a mobile device, holds great potential to increase efficiency, improve data accuracy, provide real-time access to data, result in greater study participant investment, and break down geographic barriers to participant pools. BYOD devices that utilize proper risk management techniques (including building security into a mobile app from its inception and the use of encryption) along with participant training will greatly improve the integrity of the trial, and can easily provide novel clinical endpoints sponsors and investigators need in standardized formats through the use of application programming interfaces (APIs), software programs that allow for the automated exchange of data between systems, and positioning the sponsor to nimbly address challenges (e.g., a mid-trial device switch by a particular participant for any reason).

  CHI also encourages FDA to update its definition and scoping of DHTs in the guidance to address when a DHT is a medical device that has a software function that is not subject to Part 812 per Section 520(o)(1) of the Food, Drug & Cosmetic Act.

- Flexibility in Use of DHTs: In crafting this guidance, FDA is encouraged to take an outcome-based approach that is as agnostic to specific technologies and processes as possible. CHI urges FDA to provide the flexibility sponsors may need to evolve their use of DHTs as this area of technology continues to rapidly develop. FDA can provide this flexibility by prioritizing a technology neutral policy to sponsor use of DHTs, and by reinforcing that DHTs may be upgraded mid-investigation if its capabilities and performance initially authorized for the investigation are possible. In other words, sponsors should not be discouraged from leveraging improved features and enhancements to DHTs they are already using in an investigation.

- Development and Use of Novel Clinical Endpoints: CHI agrees that DHTs can and should unlock novel clinical endpoints that will provide opportunities for additional insights into participant function or performance that were previously not easily measurable, including and/or in combination with Clinical Outcome Assessments (COAs) and biomarkers, outside of a clinic setting and over time, and that such insights will be crucial to improved clinical investigations. CHI agrees that sponsors should develop and utilize novel clinical endpoints based

on input from stakeholders (i.e., patients, disease experts, caregivers, clinicians, engineers, and regulators) to ensure that the novel endpoint is both clinically relevant and the data is adequately captured by the DHT. To augment the existing guidance on this topic in the draft, CHI proposes that FDA provide further insights into validation of novel clinical endpoints in the event that such a novel clinical endpoint combines COAs and biomarkers, including whether a sponsor needs to address each component of the combined novel clinical endpoint, or if the entire novel clinical endpoint can be used as a justification.

- Addressing Adverse Events: In its proposed guidance, FDA appropriately mentions the need to plan and train for handling known adverse events associated with a DHT. CHI supports this recommendation and suggests that FDA should further recommend that sponsors develop best practices to address adverse events using the continual data flows that DHTs provide over time. Such best practices should account for differentiating between true adverse events and false indications of adverse events, consistent with other FDA guidance and industry standards, and enable maximum flexibility for sponsors to appropriately address adverse events (consistent with our recommended approach to the use of DHTs that may enjoy upgraded functionalities after an investigation launches).

- Design and Operation of DHTs: CHI supports FDA's recommendations provided with respect to the design and operation of DHT hardware, DHT software, and general-purpose computing platform. However, areas that could be improved in this section of the FDA's guidance include:
    - FDA's discussion of alerts that may be necessary, including an example of providing timely information about a low battery in a DHT to a trial participant is provided, should be updated to indicate that the same alert should also be provided to the sponsor as appropriate, who will be able to follow up with the trial participant to help address the issue to which they are being alerted.
    - FDA's strong encouragement for the design and operation of DHTs to consider health equity goals through the identification, disclosure, and mitigation of biases while encouraging access to databases and promoting inclusion and diversity.

III. Conclusion

CHI appreciates the opportunity to submit its comments to the FDA and urges its thoughtful consideration of the above input.

Sincerely,

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