

December 28, 2015

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

**RE: Comments of ACT | The App Association regarding the Food and Drug Administration's Request for Comments, *Using Technologies and Innovative Methods To Conduct Food and Drug Administration-Regulated Clinical Investigations of Investigational Drugs; Establishment of a Public Docket* (Docket No. FDA-2015-N-3579)**

Dear Acting Commissioner Ostroff:

ACT | The App Association writes to provide input to the Food and Drug Administration (FDA) in response to its request for comments on the scope and direction of the use of technologies and innovative methods in the conduct of clinical investigations.<sup>1</sup> ACT | The App Association represents more than 5,000 app companies and technology firms that create the apps used on mobile devices around the globe. As the world has quickly embraced mobile technology, our member companies have been creating innovative solutions across modalities and segments of the economy, with no stronger an example than healthcare. ACT | The App Association is spearheading the Connected Health Initiative, an effort to clarify outdated health regulations, incentivize the use of remote patient monitoring, and ensure the environment is one in which patients and consumers can see improvement in their health.<sup>2</sup> This coalition of leading mobile health companies and key stakeholders urge Congress, the FDA, the Center for Medicare & Medicaid Services (CMS), and other key policymakers to adopt policies that encourage mobile health innovation while keeping sensitive health data private and secure.

ACT | The App Association appreciates the FDA's examination of the changing and increasingly intricate clinical trial enterprise and its crucial role in medical product development. As the FDA is aware, advanced technological advances in software applications can vastly improve many facets of clinical trials, from assisting in participant recruitment and continued engagement, to better collecting data, to supervising clinical trial sites and investigators. While mobile apps hold the potential to revolutionize the effectiveness of clinical investigations, these

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<sup>1</sup> See *Using Technologies and Innovative Methods To Conduct Food and Drug Administration-Regulated Clinical Investigations of Investigational Drugs; Establishment of a Public Docket*, 80 Fed. Reg. 66543 (Oct. 29, 2015) (RFC).

<sup>2</sup> "Connected Health Initiative." Available at: <http://connectedhi.com>.

solutions are unlikely to be leveraged to their full potential without FDA clarity around use of advanced data collection and communication methods, including the integration of Bring Your Own Device (BYOD) models.

## **I. General Views of ACT | The App Association on the Benefits of Mobile Apps in Clinical Trials**

The integration of remote monitoring of patient-generated health data (PGHD) has been – and continues to be – proven as an integral aspect of any healthcare system. The demonstrated benefits of remote patient monitoring (RPM) services include improved care, reduced hospitalizations, avoidance of complications and improved satisfaction, particularly for the chronically ill.<sup>3</sup> A particularly compelling example of the use of virtual chronic care management is by the Department of Veterans Affairs, which resulted in a substantial decrease in hospital and emergency room use.<sup>4</sup> Telemedicine tools, wireless communication systems, portable monitors, and cloud-based patient portals that provide access to health records are all emerging technologies that are revolutionizing remote patient monitoring (including asynchronous technologies) and the medical care industry, representing a significant opportunity.<sup>5</sup> There is also a growing body of potential cost savings to providers, noted most recently by a study predicting that remote monitoring will result in savings of \$36 billion globally by 2018, with North America accounting for 75% of those savings.<sup>6</sup> RPM has the potential to positively engage patients when addressing chronic and persistent disease states to improve management of chronic conditions.

With 60% of the population already using mobile apps to help track their conditions and make informed choices about their health,<sup>7</sup> mobile-app enabled telehealth and remote monitoring of PGHD continues to represent the most promising avenue for improving care quality while lowering costs despite significant statutory and regulatory burdens remain in place that prevent these innovations from being utilized. As notable examples, Section 1834(m) of the Social Security Act has resulted in significant restrictions on telehealth services;<sup>8</sup> further, remote

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<sup>3</sup> See Hindricks, et al., *The Lancet*, Volume 384, Issue 9943, Pages 583 - 590, 16 August 2014 doi:10.1016/S0140-6736(14)61176-4. See also U.S. Agency for Healthcare Research and Quality (“AHRQ”) Service Delivery Innovation Profile, Care Coordinators Remotely Monitor Chronically Ill Veterans via Messaging Device, Leading to Lower Inpatient Utilization and Costs (last updated Feb. 6, 2013), available at <http://www.innovations.ahrq.gov/content.aspx?id=3006>.

<sup>4</sup> Darkins, *Telehealth Services in the United States Department of Veterans Affairs (VA)*, available at <http://c.ymcdn.com/sites/www.hisa.org.au/resource/resmgr/telehealth2014/Adam-Darkins.pdf>.

<sup>5</sup> Kalorama Information, *Advanced Remote Patient Monitoring Systems*, 8th Edition (2015), available at <http://www.kaloramainformation.com/redirect.asp?progid=87656&productid=9123949>.

<sup>6</sup> Juniper Research, *Mobile Health & Fitness: Monitoring, App-enabled Devices & Cost Savings 2013-2018* (rel. Jul. 17, 2013), available at [http://www.juniperresearch.com/reports/mobile\\_health\\_fitness](http://www.juniperresearch.com/reports/mobile_health_fitness).

<sup>7</sup> *Get Mobile, Get Healthy: The Application of Health & Fitness Report*, Mobiquity (2014), available at <http://www.mobiquityinc.com/mobiquity-white-papers?ref=mHealth-report-2014>.

<sup>8</sup> See 42 CFR § 410.78.

patient monitoring, independent of telehealth services, is unreasonably restrained by CMS' decision to bundle it with other codes, resulting in a lack of reimbursement for remote patient monitoring. As a result, Medicare coverage for telehealth is astonishingly low,<sup>9</sup> while support for RPM is non-existent and denies reasonable reimbursement for the monitoring of patient-generated health data (PGHD). The same technologies that enable telehealth and RPM – such as electronic health records with view, download and transmit capability enabled through the use of application programming interfaces (APIs)<sup>10</sup> – are poised to provide similar benefits to the clinical trial process. Because technologies that integrate patient-generated health data (PGHD) into the continuum of care generally will also benefit the clinical trial process, we urge FDA to recognize the broad transformative nature of these advances and to ensure that regulation of such technologies does not restrict the associated benefits to any particular aspect of the healthcare system.

Traditionally, in the context of clinical trials, there has been a limited use of mobile apps that leverage PGHD due to the high costs associated with distributing, connecting, tracking, and maintaining mobile devices to trial participants. With the revolution of smartphone adoption, which has occurred more quickly than any other technology in history, clinical trial sponsors can largely discard these concerns, particularly when embracing the BYOD model. Such a model may utilize specialized instruments as accessories to smartphones/tablets/etc.

While much progress remains to be made in the clinical trial context, promising (and foundational) examples of advanced telehealth and RPM technologies being used in clinical trials exist, including:

- ACT | The App Association member Rimidi<sup>11</sup> uses both the BYOD model as well as connected glucometers in a clinical trial they have launched to better understand and improve the treatment of diabetes. Physicians are using the Rimidi platform to monitor their patient's glucose levels, as well as to help their patients determine the correct balance of insulin more efficiently.

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<sup>9</sup> According to CMS, Medicare telemedicine reimbursement totaled a mere \$13.9 million in Calendar Year 2014. See <http://ctel.org/2015/05/cms-medicarereimburses-nearly-14-million-for-telemedicine-in-2014/>.

<sup>10</sup> CMS defines an API as “a set of programming protocols established for multiple purposes...[that] may be enabled by a provider or provider organization to provide the patient with access to their health information through a third-party application with more flexibility than often found in many current ‘patient portals.’” CMS further explains that “[i]f the provider elects to implement an API, the provider would only need to fully enable the API functionality, provide patients with detailed instructions on how to authenticate, and provide supplemental information on available applications which leverage the API.” 80 FR 16753.

In practice the software application developer community relies on APIs to establish interoperability in a safe and secure manner across contexts. APIs are not just technical specifications regulating how data can be exchanged on a network, but should be understood as a technique for governing the relations these networks contain.

<sup>11</sup> <http://www.rimidi.com/>.

- Apple's ResearchKit<sup>12</sup> is an open source software framework that makes it easy for researchers and developers to create apps that could improve medical studies. The software leverages built-in sensors measuring touch, movement and sound, and significantly expands the scale of data collected in clinical research. The sheer number of iPhones being used across the globe opens up new possibilities for researchers. Until now, taking part in a medical study has usually required traveling to a hospital or facility to complete tasks and fill out questionnaires. With ResearchKit, an individual can use their iPhone to perform activities and generate data anywhere, providing a source of information that is more objective.

The ResearchKit framework provides templates for app developers to generate an electronic consent flow and obtain the participant's signature on the consent document. The ResearchKit framework can also be used to generate a signed PDF of the consent form and provide the signed form to the user.

Several of the world's leading medical institutions are already using ResearchKit to gain further insight into diseases. They have created apps to research new ways to diagnose autism, track an epileptic seizure, map air quality for asthmatics, track the health of diabetics, and study the longterm impacts of chemotherapy for those with breast cancer. The University of Rochester and Sage Bionetworks developed the mPower app using ResearchKit and the iPhone's gyroscope, touch screen and other features to precisely measure data such as dexterity, balance, memory, and gait. This information could help researchers better understand how various symptoms are connected to Parkinson's disease. And Stanford Medicine and the University of Oxford have collaborated to create the MyHeart Counts app. It uses surveys and tasks to help researchers more accurately evaluate how participants' activity, measured on an iPhone, and lifestyle relate to their risks of cardiovascular disease. By identifying these correlations, researchers can begin to better understand how to keep hearts healthier and gives participants a much more objective Lifetime Risk Estimate for cardiovascular disease. Over 10,000 participants signed up for the MyHeart Counts app medical trial within the first 24 hours after it debuted.

- Intel, through a partnership with the Michael J. Fox Foundation for Parkinson's Research, utilizes sensors in wearable devices (such as smart watches and fitness trackers) to collect and analyze real-time measurements of movements.<sup>13</sup> The study of this data helps researchers understand and detect the progression of Parkinson's and aids in symptom management.

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<sup>12</sup> <http://www.apple.com/researchkit/>.

<sup>13</sup> <http://www.intel.com/content/dam/www/public/us/en/documents/white-papers/using-wearable-technology-mjff.pdf>,

- In early 2015, Novartis selected Qualcomm Incorporated as a partner in its Trials of the Future program to collect and aggregate medical device data during clinical trials.<sup>14</sup> Further, using devices enabled by Qualcomm Incorporated mobile broadband and wireless technologies, innovative clinical trials are occurring through the Scripps Translational Science Institute<sup>15</sup> that include:

### **DigMed2 – Using wireless monitoring to understand the body’s response to meditation**

The practice of meditation has been part of human society for at least 5,000 years. This long history of meditation practice has persisted with the belief in its beneficial effects on the mind and body. There is no doubt that there is a strong mind-heart connection, although it remains poorly understood, especially in a medical or biological sense.

Many of the body’s interactions are thought to be regulated by the autonomic nervous system, which evidence suggests can be influenced by meditation. Despite that, widespread acceptance of meditation as being important for improving wellness is hindered by the limited data available defining its benefits. We hope that with the Digital Medicine in Meditation research study we will help to scientifically illuminate some of the benefits of meditation. Scripps Translational Science Institute (STSI) is excited to collaborate with the Chopra Center on this project. With STSI’s experience and expertise in digital and personalized medicine we hope to offer advanced insight into the body’s response to meditation by wirelessly and unobtrusively monitoring heart and brain activity during meditation.

This study took place during the Seduction of Spirit retreat at the Chopra Center, November 3-9, 2013.

### **Wired for Health – Wireless monitoring for disease wellness and prevention**

The Scripps Wired for Health Study aims to evaluate the impact of using a smartphone enabled “Wireless Monitoring System” in conjunction with a disease wellness and prevention program on the healthcare costs and resource utilization of chronically ill individuals with diabetes, hypertension, and cardiac arrhythmia.

Consisting of a combination of current wireless medical devices designed for use in the management of these conditions, a smartphone, and an online software platform to analyze disease data and enable care coordination; our Wireless Monitoring System

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<sup>14</sup> See *Qualcomm Announces Strategic Collaboration with Novartis to Optimize Global Clinical Trials*, available at: [http://www.qualcomm.com/images/pdf/press/QCL\\_Novartis%20press%20release\\_V2\\_forCorp%20CORP%20EDITS\\_FINAL\\_v2cleanPDF.pdf](http://www.qualcomm.com/images/pdf/press/QCL_Novartis%20press%20release_V2_forCorp%20CORP%20EDITS_FINAL_v2cleanPDF.pdf) (Jan. 5, 2015).

<sup>15</sup> Information on these digital health clinical studies is publicly available at: [http://www.stsiweb.org/translational\\_research/digital\\_medicine/digmed2\\_index/](http://www.stsiweb.org/translational_research/digital_medicine/digmed2_index/).

(wireless monitoring) will augment an existing outpatient Disease management program offered by Health Comp.

### **Comparative Effectiveness of Pocket Mobile Echocardiography vs. Transthoracic Echocardiography**

A new hand held pocket echo device (GE Vscan) has now become available to clinicians, with limited data available comparing the effectiveness of this device as a screening tool when compared to traditional transthoracic echocardiography (TTE).

The investigators are evaluating the effectiveness of this hand-held echo (HHE) device in detecting cardiac pathology in a both an inpatient and outpatient clinical setting as compared to a comprehensive TTE evaluation.

### **GIRAFFE Study – Genomic Risk Markers for Atrial Fibrillation Following Extended Cardiac Rhythm Monitoring**

Multicenter (17 sites), nationwide study of an anticipated ~1500 individuals presenting with symptoms suggestive of, but not yet diagnosed as Afib. Receive a Zio patch for 2 weeks rhythm monitoring plus genetic testing to identify novel markers for Afib risk.

### **Scanadu SCOUT™ – Scanadu Consumer Health Outcomes Study**

Evaluate the real-world use of the Scanadu Scout™ by a cohort of self-selected investors in an earlier crowdfunding campaign on Indiegogo for the Scanadu Scout™, through a prospective observational study. Using validated survey tools and through the remote tracking of frequency of use and physiological measurements from the Scanadu Scout™ device and app.

Participants will receive web-based surveys at 4 time points: baseline, 3, 12 and 18 months.

### **Wearable Sensors for Objective Measures of PTSD**

A pilot study in collaboration with the Navy to intensively monitor sleep quality, activity and ANS function of 40 servicemen/women dx with PTSD who are already scheduled to take part in a 10 week residential treatment program using an innovative wristband sensor that continuously monitors measures of stress, activity and sleep quality. The hope is to acquire data that in the future will permit markedly improved diagnosis and treatment of PTSD sufferers.

### **Pilot Study of the MultiSense Patch in the Home Diagnosis of Sleep Apnea**

To compare multiple biometric parameters tracked by the MultiSense™ to gold standard monitoring in an accredited sleep lab using polysomnography. Home monitoring will explore potential findings supportive of sleep apnea while monitoring at home during routine sleep over 5 to 7 nights. Enrolling 10 adults already scheduled for a medically indicated sleep study will help us to make these determinations. Subjects will wear the device, which is the size of a Band-Aid, via adhesive to their chest over a period of 10 days. Subjects will go about their normal daily activities and return the device via mail once completed.

### **Pilot Study of the Quanttus Device for Monitoring Patients with Heart Failure**

The study proposes to utilize a novel, wearable device, Quanttus Device, developed by Quanttus, Inc. which has multiple sensors embedded in a “wrist-watch” in order to explore its monitoring capabilities in individuals with congestive heart failure.

### **Self-Directed Biological Transformation Initiative – SBTI**

This is a follow-up study of the DigMed2 study in collaboration with the Chopra Center, as well as UCSD, UCSF, Harvard and Mt. Sinai Hospital of New York. Individuals attending a “Perfect Health” retreat will undergo extensive testing and monitoring before and after the retreat in order to identify novel biomarkers of stress and its improvement. For the mobile health arm of the study, individuals will wear a MultiSense wireless patch for one week before and one month after the retreat.

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The FDA has demonstrated its willingness to embrace advanced technology and connectivity in the healthcare continuum.<sup>16</sup> However, in the context of clinical trials, a lack of clarity from the FDA regarding the use of mobile devices and apps has reduced uptake. For example, the FDA’s most recent final guidance related to clinical trials was released in 2009; further, the vast majority of guidance documents available from the FDA were released before the year 2000. As noted above, leaps in technological advancement (and unprecedented uptake by the American population) have taken place in the last 15 years which should be embraced in clinical trials. 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

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<sup>16</sup> *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/UCM263366.pdf>.

Innovation Act of 2012 to promote innovation, protect patient safety, and avoid regulatory duplication.<sup>17</sup>

ACT | The App Association applauds the FDA for requesting information on these issues through the RFC, and provides answers to specific questions posed by the FDA below.

## **II. Responses of ACT | The App Association to Specific Questions Posed by the FDA**

1. What technologies, communication infrastructure, or innovative methods are being used to conduct clinical investigations? FDA is aware of several groups conducting and interested in conducting clinical investigations using mobile technology and remote methods for data collection. FDA requests feedback on experiences with implementing such methods or models (for example, lessons learned), as well as information supporting the use of any suggested technologies, methods, or models, including any characteristics that would make the technology more or less desirable for use in clinical trials.

Clinical trial challenges prevail that are unconnected to the use of connected technology (e.g., challenges in attaining consent and enrollment, language barriers, etc.), but the use of mobile apps offers opportunities to reduce such barriers. As discussed above, the smartphone revolution has brought about an entire economy for mobile applications, of which healthcare is a significant segment, and which offers numerous benefits to clinical trial sponsors and investigators. Aside from reducing costs and complications related to the management of dedicated connected devices in clinical trials, further benefits of integrating mobile apps into clinical trials 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

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<sup>17</sup> See P.L. 112-144 (Sec. 618).

standards (these standards include: the Continua Alliance's Design Guidelines,<sup>18</sup> Health Level 7 [HL7],<sup>19</sup> ISO 12052 [Health informatics -- Digital imaging and communication in medicine including workflow and data management],<sup>20</sup> and the Integrating the Healthcare Enterprise [IHE] initiative<sup>21</sup>);

- The removal of geographic restrictions from studies; and
  - Reduced maintenance and support costs for sponsors.
2. What are ways FDA could encourage adoption of these technologies and innovative methods in the conduct of clinical investigations?

ACT | The App Association urges the FDA to encourage adoption of new technologies and innovations in clinical investigations through:

- Holding a series of publicly-accessible workshops, and make 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;
  - Working 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; and
  - Undertaking a concerted to update key clinical trial guidance documents for stakeholders as soon as practicable.
3. Identify any clinical, cultural, business, regulatory, or other barriers perceived by stakeholders that serve as a disincentive to the use of technology to facilitate the conduct of clinical investigations.
- a. What challenges do stakeholders anticipate in adoption of these technologies or methods? Are there challenges in complying with regulatory requirements surrounding the conduct of clinical investigations that use such technologies or methods?

ACT | The App Association does not believe that the uptake of these technologies in clinical trials itself is a serious issue because of the benefits noted above. However, challenges in compliance with regulatory requirements have, and will continue to, present themselves to clinical investigators when they must continue to rely on guidance that may date back into the

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<sup>18</sup> <http://www.continuaalliance.org/products/design-guidelines>.

<sup>19</sup> <http://www.hl7.org/implement/standards/index.cfm>.

<sup>20</sup> [http://www.iso.org/iso/iso\\_catalogue/catalogue\\_tc/catalogue\\_detail.htm?csnumber=43218](http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=43218).

<sup>21</sup> [http://www.ihe.net/About\\_IHE/](http://www.ihe.net/About_IHE/).

1990's. Therefore, a major discouragement in uptake will continue to be the lack of clarity in the FDA's guidance for clinical investigations. We strongly urge the FDA to, in crafting this guidance, take an outcome-based approach that is as agnostic to specific technologies and processes as possible.

- b. What are the perceived barriers or challenges to obtaining and documenting informed consent or obtaining institutional review board review, approval, and oversight for clinical investigations utilizing these technologies or methods?

ACT | The App Association has observed several key barriers to the use of connected technology in clinical investigations. These barriers include:

- A reluctance for review boards, clinical sponsors, and investigators to embrace advanced technologies into their processes due to a lack of training and awareness of their benefits;
  - An assumed digital illiteracy of potential study participants;
  - Language barriers for particular demographics.
4. FDA is interested in obtaining information on potential trial participant acceptance, privacy, and human subject protection issues that may occur as a result of the use of technologies and innovative methods for the conduct of clinical investigations. In particular, FDA is interested in assessing potential trial participants' interest, tolerance, concerns, and willingness to participate in clinical investigations that involve nontraditional settings or utilize new technologies. FDA is also interested in identifying the factors that affect trial participant awareness, acceptance, enrollment, and retention for these investigations.
    - a. Are there specific patient groups or therapeutic areas that could particularly benefit from these types of technologies or methods?

Based on the above, effectively, any patient group or therapeutic area for which a clinical trial would be conducted which would benefit from increased efficiency, improved data accuracy, real-time access to data, and greater study participant investment would benefit from the use of mobile apps and/or the BYOD model.

- b. What new opportunities for the conduct of clinical investigations are created through the use of continuous or intermittent remote monitoring and data collection?

As discussed above, the use of remote monitoring of PGHD in clinical trials will create new efficiencies in trials, improve the quality of data, present data on a real-time basis to enable better analysis, increase study participant engagement and investment in the trial, and will remove geographic limitations that once hampered studies.

- c. What are some of the anticipated risks to trial participants that may occur as a result of the use of these technologies or off-site methods in clinical investigations?

Trial participants will face the same risks they face today by engaging in clinical studies. Traditionally, a participant will submit their data in-person (or in paper form), with it then being entered into a database. Using RPM, such data is transmitted directly to the clinical investigator and enters a similar database. Potential risks in the latter model would include:

- *Data integrity and related participant privacy impacts.* This risk is taken very seriously by the app industry, and ACT actively works to ensure that developers take data integrity and privacy expectations into consideration as early as possible in the development cycle through such measures as training and the appropriate use of access controls and encryption, as well as serving as an interface for this community with regulators and lawmakers.
- *Loss of connectivity.* This is a risk largely applicable to particularly rural areas of the United States, and can be addressed by ensuring retention of untransmitted data on a device until it is verifiably transmitted to the clinical investigator.

- d. What are some of the anticipated benefits to trial participants that may occur as a result of the use of these technologies or off-site methods in clinical investigations?

ACT | The App Association anticipates that the main benefit to trial participants will be greater convenience in their participation in the study. This ease in participation is related to improved participant pools through willingness to enroll and meaningfully participate, and more accurate clinical trial results.

- e. Are there perceived challenges to participation in clinical investigations utilizing these types of technologies or methods because of concerns regarding inadvertent disclosure of trial participants' information or breach of privacy? Are there concerns relating to the integrity of data collection or encryption or the secure transmission of information?

In the view of ACT | The App Association, the risks of inadvertent disclosure in clinical trials using mobile apps (and even the BYOD model) are no greater than in existing clinical trials where trial sponsors and investigators take great precautions to maintain the integrity of their systems and the privacy of trial participants, as long as adequate risk management techniques (including encryption) are employed. ACT | The App Association urges that the FDA provide guidance to clinical trial sponsors and investigators in updated guidance.

- f. Are there unique considerations for ensuring integrity of the source data, for example, authenticity and reliability?

ACT | The App Association is not aware of unique concerns related to the integrity of source data due to the use of new technologies in clinical trials. Such concerns exist in any clinical

trial. As discussed above, the use of RPM technologies in clinical trials will improve data authenticity and reliability, among other benefits.

g. How should validation of participant-operated mobile devices be addressed?

Trial sponsors and investigators should work to ensure that study participants are fully aware and consenting to such validation processes, and that these participants are trained on how to use the mobile device, any accessories to a BYOD device, and any mobile apps, required for the study to succeed. Validation of devices for integrity is possible today and is done in the mobile context across use cases. ACT | The App Association urges that the FDA provide guidance to clinical trial sponsors and investigators in updated guidance.

h. What are the challenges presented when data are collected using the Bring Your Own Device (BYOD) model? BYOD in clinical investigations refers to the practice of trial participants using their own devices, such as smartphones or tablets, for data collection. For example, participants in a clinical investigation may use their own computer devices to access and respond to study-related questionnaires. What are the perceived barriers to pooling data collected from different devices provided by individual trial participants, as well as pooling data from the BYOD model with data collected at the investigational site or on paper forms? How should situations such as mid-study user device switches be handled?

As discussed above, the BYOD model, whether through the use of 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. ACT | The App Association is aware of the following perceived challenges (and related solutions):

- BYOD devices may be perceived as more susceptible to data leakage and/or damage to a participant's privacy. This is a misperception, as a mobile app used for the purposes of the clinical trial that utilizes proper risk management techniques (including building security into a mobile app from its inception and the use of encryption) along with participant training, will ensure the integrity of the study.
- BYOD devices may be perceived to lend to the creation of data inputs to the clinical investigator that are not 'equivalent,' or of the same format, creating difficulties in processing and analysis. This, too, is a misperception, as the mobile app will dictate the shape and form data is submitted to the clinical investigator regardless of the BYOD device used, at the discretion of the trial sponsor. In other words, the clinical sponsor will have the ability to ensure that data stored in standardized formats through the use of APIs, software programs that allow for the automated exchange of data between systems. The trial sponsor is therefore well-positioned to address a mid-trial device switch by a particular participant.

ACT | The App Association urges that the FDA provide clarity consistent with our response to this question to clinical trial sponsors and investigators in updated guidance.

- i. What are the challenges or special considerations with recruiting and/or retaining potential trial participants with low levels of computer literacy or individuals who may have limited or no access to mobile technologies, computer devices, or the Internet? How can these challenges or special considerations best be addressed?

ACT | The App Association believes that trial sponsors can best address digital literacy issues with trial participants through training and responsiveness to questions about how to use the advanced technologies in the trial that may be asked. We urge the FDA to provide guidance to clinical trial sponsors and investigators in updated guidance.

ACT | The App Association appreciates the opportunity to submit comments to FDA on the scope and direction of the use of technologies and innovative methods in the conduct of clinical investigations, and looks forward to the opportunity to meet with you and your team to discuss these issues in more depth. Thank you for your consideration.

Sincerely,

A handwritten signature in black ink that reads "Morgan Reed". The signature is written in a cursive style and is set against a light gray rectangular background.

Morgan Reed  
Executive Director  
ACT | The App Association