Clinical Researcher
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The Nuts and Bolts of Clinical Trials

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Clinical Researcher—April 2019 (Volume 33, Issue 4)

PEER REVIEWED

An Overview of the Prospects for Using Wearables to Improve Clinical Trials

Geoffrey Gill, MS

Drug development costs today have spiraled out of control. A report from Tufts in 2016{1} estimated the cost of introducing a new drug at $2.6 billion. On the other side, a 2018 report from Deloitte{2} estimated that the return on investment for new drug development had dropped from 10.1% in 2010 to 1.9%. Clinical trials are the key driver of cost and return, not only because they are very expensive to conduct, but also because their results are not always accurate—causing pharmaceutical companies to invest in late-stage clinical trials for drugs that never get to market or are not sufficiently differentiated to capture high returns if they do get to market.

Wearables are a key feature of one of the few promising approaches for revolutionizing clinical trials and addressing these issues. The reality is that most approaches to improve clinical trials are designed to make the existing processes more efficient, but wearables can fundamentally improve how outcomes are measured by providing a continuous stream of objective data. Furthermore, these data are consistent across geographies and can be available in near real time, allowing for compliance monitoring and management in a timely fashion.

These factors are becoming increasingly important as trials become more global. Current measures like patient-reported outcomes or in-clinic tests are often subjective, sporadic, variable across regions, and prone to inaccuracies, which can lead to faulty conclusions. By changing the outcome measures, wearables are moving the goal posts and providing the potential for significantly reduced sample sizes, shortened trials, and better clinical data to differentiate the drug.

Regulatory Support

If wearables can solve all these problems, why are they currently used in less than 1% of trials?{3} The issue is not U.S. Food and Drug Administration (FDA) approval; the FDA has provided strong indications that it supports the use of real-world data. FDA Commissioner Dr. Scott Gottlieb has stated that leveraging real-world data to improve regulatory decisions is a key strategic priority for the FDA. In December 2018, the FDA also introduced a new strategic framework to advance use of real-world evidence to support development of drugs and biologics.{4}

It is also pretty clear that wearables do not need to be approved as a medical device to be used in a trial. The *Clinical Trials Transformation Initiative (CTTI) Recommendations: Advancing the Use of Mobile Technologies for Data Capture & Improved Clinical Trials* explicitly state that "Mobile technologies for data capture in clinical trials do not typically need to be approved or cleared as a medical device."{5} Furthermore, wearable devices from several companies, including Actigraph, MC10, AliveCor, and Apple have received FDA approval and been used in clinical trials. However, FDA approval of a wearable as a medical device does not necessarily translate to FDA acceptance of use of the metrics it generates to define an endpoint.

Wearables Challenges

Most of the wearables on the market today have their own proprietary algorithms with no clinical validation or access to the raw data on which they were based, making the use of these data problematic. Proving to the FDA that a clinical trial is measuring real-world data that correspond to patient outcomes is difficult or impossible without raw data. Furthermore, without raw data, analyses cannot be upgraded as new algorithms are validated. There is no way to determine whether an anomalous reading is real or indicative of an issue. Without raw data, there is no way to build a real knowledge base that can be used going forward.

Then there is the challenge of including another technology in the trial—sites and participants are already overburdened, and asking participants to remember to charge a device or manage uploads or wear a bulky and/or uncomfortable wearable will often result in compliance issues, creating a whole new failure mode for the trials. Relying on the sites to manage this process will be costly and further stretch resources.

Running clinical trials is already difficult and expensive. Adding another element increases effort, cost, and the risk of failure—even if it is relatively easy to manage. No wonder the penetration of wearables in clinical trials is so low.

Still, something must be done to address this challenge, because wearables represent one of the best opportunities to truly revolutionize the clinical trials industry. Some sponsors hope that wearables companies will address all of these issues alone, but as a matter of economics, that is unlikely to happen—there are literally thousands of potential applications for wearables in clinical trials.

For example, they can be used to study a broad range of complex musculoskeletal or neurological conditions, such as Alzheimer's disease, Parkinson's disease, epilepsy, and cancer. The cost of developing and validating algorithms for all these applications is prohibitive, especially since the market for wearables for clinical trials is relatively small and low margin. To put this in perspective, my firm projects that the total potential market for wearables in clinical trials will be approximately $1 billion annually, which is less than half the cost of bringing one

drug to market. It is unrealistic to expect the wearables industry to make the investments necessary if the pharmaceutical industry won't.

Wearables Opportunities

Still, there is hope. The pharmaceutical industry can leverage years of work and experience garnered from using wearable sensors in other fields, particularly in academic and consumer neuroscience settings.

Many academic researchers are using wearables to conduct studies that could be relevant for clinical trials. For example, researchers at Boston University are currently using wearable sensors to study the effect of physical activity on cognition. Participants undergo a battery of cognitive tests at the start of the study and then their activity is monitored during waking hours for the next 12 weeks using a wearable device that collects all of the raw accelerometer data. Fifty percent of the participants are encouraged to exercise with weekly "coaching calls" and other methods; the remainder receive no additional assistance. At the end of the study, participants undergo a second battery of cognitive tests. If this study produces positive results, it will provide validation that improving activity levels will help improve cognitive results, enabling a potential outcome measure using wearables.

This type of work is being done by literally thousands of researchers around the world. In many, if not most, cases the algorithms are publicly available and independently verified. For example, there is a public domain activity and sleep algorithm based on accelerometry, GGIR,{6,7} that has more than 80 peer-reviewed articles that rely on the method.{8} Although not all academic research is so well documented and validated, much work has been done and it provides a major platform on which to build validated metrics. Leveraging this invaluable resource will require both access to the raw data and transparency on the part of the wearable supplier.

Experiences from consumer neuroscience (sometimes called neuromarketing) can teach us a great deal about developing scalable systems for collecting data. Neuroscience studies need to be completed in days or weeks, not months, at a fraction of the cost of a clinical trial. In one example, a company incorporated wearable sensors into market research kiosks in six malls and movie theaters around the country. This approach enabled nontechnical staff to collect about 15

minutes of medical quality electrocardiograph and galvanic skin response data from participants while they were viewing content specifically selected for the individual. The raw data were sent automatically to a central server for analysis. If certain sites were not meeting their quota for participants, that quota could be reallocated to other sites in real time. That system could collect data from 1,000 people in a weekend, at a cost of less than $50 per participant.

Another opportunity to address these challenges is for pharmaceutical companies to collaborate on algorithm development and agree on appropriate industry outcome measures. Although intellectual property is generally highly valued in the pharmaceutical arena, these algorithms and outcome measures could be cooperatively developed in a precompetitive environment; all companies would benefit from these improvements. There is a growing movement in the industry in this direction and it should be encouraged as much as possible.

Pharmaceutical companies will need to partner with wearables companies. Wearables companies will not be able to accomplish these goals on their own.

Assessing Partnership Potential

There are a several important attributes that pharmaceutical companies should look for in a wearables partner. First, it's critical that they gain access to the raw sensor data; without those data, it will be impossible to move forward on a larger scale. Algorithms from academic studies and other pharma companies will depend on it, as will continued progress.

Second, the data need to be collected as completely as possible. To meet this challenge, the sensors and systems must encourage compliance by putting the minimum burden on participants and sites. The system should have robust tracking features to allow the sponsor or contract research organization to monitor trial progress and take corrective action as issues arise. The system should also include multiple failsafe mechanisms to prevent data loss at all stages of data capture.

Third, the wearables company should be committed to openness and industry collaboration. It will be difficult, if not impossible, for proprietary algorithms to be accepted as validated outcome measures. Even if they are accepted for a specific application, they will not be able to be

extended by the industry. Although it may be difficult for some companies to accept, the wearables industry will need to compete on other dimensions if the use of wearables in clinical trials is to grow.

Finally, pharmaceutical companies should also seek wearables companies who have an extendible platform. A single partner enables more efficient implementation of different sensors into a company's systems, but more importantly, it takes time, effort, and trust to build a productive collaborative relationship. It is difficult to achieve that with many different partners.

Conclusion

There are many challenges to improving clinical trials through the use of wearables, but by leveraging work done in academia and other industries and taking a collaborative approach, they can play a role in fueling the industry's goals of getting better drugs to market cheaper and faster. In the end, that is what it is all about.

References

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2. Deloitte Center for Health Solutions. 2018. Unlocking R&D productivity: measuring the return from pharmaceutical innovation 2018. https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/measuring-return-from-pharmaceutical-innovation.html

3. Based on an internal Shimmer analysis of ClinicalTrials.gov data in 2018.

4. Statement from FDA Commissioner Scott Gottlieb, MD, on FDA's new strategic framework to advance use of real-world evidence to support development of drugs and biologics. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm627760.htm

5. *CTTI Recommendations: Advancing the Use of Mobile Technologies for Data Capture & Improved Clinical Trials.* 2018. https://www.ctti-clinicaltrials.org/files/mobile-devices-recommendations.pdf

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7. Sabia S, van Hees VT, Shipley MJ, Trenell MI, Hagger-Johnson G, Elbaz A, Kivimaki M, Singh-Manoux A. 2014. Association between questionnaire- and accelerometer-assessed physical activity: the role of sociodemographic factors. *Am J Epidemiol* 179(6):781–90. doi: 10.1093/aje/kwt330. Epub. PMID: 24500862. https://www.ncbi.nlm.nih.gov/pubmed/24500862

8. See https://github.com/wadpac/GGIR/wiki/Publication-list for a list of references.

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PEER REVIEWED

Revisiting the Form FDA 1572

The U.S. Food and Drug Administration's (FDA's) Form FDA 1572 is one of the many important regulatory documents submitted to the agency in connection with clinical trials. Many common mistakes are made when filling out and maintaining the 1572 form, so the hope is this guide will be useful to new sites, clinical research coordinators (CRCs), clinical research associates (CRAs), and other clinical research professionals.

This guide serves as a quick read in very simplistic and clear language that defines what a 1572 is, what a principal investigator (PI) is committing to when signing this document, how to fill it out, how to avoid common mistakes, and how to maintain it for the duration of the study. In addition, this guide offers a detailed look at each section of the document.

What is the Form FDA 1572 (Statement of Investigator)?

The Statement of Investigator (Form FDA 1572) is a form that is required to be filled for clinical trials involving investigational drugs or biologics. Through this form, the PI provides specific information to the sponsor, including his/her qualifications and information about the clinical site, in aim of assuring conduct of the clinical trial according to FDA regulations and guidelines.{1} By signing the 1572 form, the PI is making a legal commitment to adhere to FDA expectations by:

1. Agreeing to supervise or conduct the investigational trial according to the current study protocol. No changes are to be made to the study protocol without the sponsor's and institutional review board's (IRB's) acknowledgment and approval, unless it was mandatory for the purposes of protection and safety of the subjects.

2. Assuring his/her understanding of the study protocol and investigational brochure, including the potential side effects associated with the investigational product and his/her responsibility to ensure that all study personal involved in the conduct of the trial understand their responsibilities and duties.

3. Reporting all adverse events and serious adverse events to the sponsor that occur during the conduct of the trial in accordance with Title 21 CFR 312.68 in the *Code of Federal Regulations.*

4. Agreeing to obtain an informed consent form (ICF) from each participant by using the most up-to-date and IRB- and sponsor-approved ICF in accordance with Title 21 CFR part 50.

5. Agreeing to maintain adequate and accurate records and having them available for inspections in accordance with Title 21 CFR 312.62 and 312.68.

6. Agreeing to comply with all other requirements regarding the obligation of clinical investigations and all other pertinent requirements in accordance with title 21 CFR part 312.

7. Agreeing to oversight from an IRB that complies with all the requirements of title 21 CFR Part 56 and will be responsible for receiving and approving of the clinical investigation from beginning of the study until closeout. By this, he/she also agrees to report promptly any changes in the research activity, including any unanticipated problems involving risks to human subjects.{2}

When Must the Form FDA 1572 be Signed?

According to U.S. regulations, the Form FDA 1572 is required to be collected from all PIs for studies being conducted under an Investigational New Drug (IND) application, which would include clinical studies of an investigational product or biologic, excluding device-related clinical trials (which require a similar form called an "investigator agreement" to be filled out under an Investigational Device Exemption application.{1}

When Must the Form be Updated or a New One Completed?

- In cases when a new site is added or of replacement of an investigator at an existing site, a 1572 must be submitted to the FDA within a 30-day window of the site's/investigator's addition/replacement.
- Another case when a 1572 should be updated is when any site information is changed, such as the IRB or laboratory affiliated with that site.{3}
- Most sponsors require that if the PI listed in the current 1572 has his/her name changed for any reason (e.g., marital status), the document should be updated. If a sub-investigator has a name change, then in most cases sponsors ask for the form to be updated or a note to file provided explaining the name discrepancy from an audit and Good Clinical Practice (GCP) perspective.

Dissecting the Form FDA 1572 for Principal Investigators and Sub-Investigators

Sections 1 and 2

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **STATEMENT OF INVESTIGATOR** ***(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)*** (See instructions on reverse side.)	Form Approved: OMB No. 0910-0014 Expiration Date: March 31, 2022 *See OMB Statement on Reverse.* **NOTE:** No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR			
Name of Clinical Investigator			
Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED *(Select **one** of the following.)*

☐ Curriculum Vitae ☐ Other Statement of Qualifications

Important notes to keep in mind when filling Sections 1 and 2 include:

- Section 1: The name of the PI must match his/her legal name as it appears on legal documents, certificates, or qualifications (e.g., birth certificates, marriage certificate, medical licenses, or other titles). In cases when a co-investigator is assigned, then under 21 CFR 312.3 (b) the co-investigator must fill out and sign a separate 1572 form.
- The address to provide in Section 1 of the 1572 is for the PI's office, study site, or other business place where he/she can be reached by mail or in person.
- In any case when the PI is replaced with another investigator, Section 1 must be updated by filling out a new 1572 and supporting all required documentation listed in Section 2 in this form.{2}
- Section 2: Requires attachment of all investigators' *curricula vitae* (CVs) or "Other Statement of Qualifications" showing the education, training, and experience that qualifies the investigator as an expert in the conduct of the clinical trial of the drug/biologic under investigation.

Frequently Asked Questions for Sections 1 and 2

Q: What qualifications are needed to be assigned as a PI?

A: There are no specific requirements stated by the FDA in terms of the PI's qualifications. However, sponsors will always aim to select PIs who are qualified by training and experience to conduct the clinical trial, including their familiarity with human subject protection regulations (i.e., 21 CFR Parts 50 and 56) and GCP regulations (see 21 CFR Part 312).{2}

Q: Is it necessary that the assigned PI be a physician?

A: Again, the sponsor selects PIs who are qualified by training and experience to conduct the clinical trial, but there are no minimum requirements for the PI to be a physician. In cases when the sponsor selects a PI who is not a physician, a qualified sub- investigator (physician) must be listed on the 1572 for the trial to make all medical-related decisions.{4}

Sections 4 and 5

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY			CONTINUATION PAGE for Item 4
Name of Clinical Laboratory Facility			
Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code
5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES)			CONTINUATION PAGE for Item 5
Name of IRB			
Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

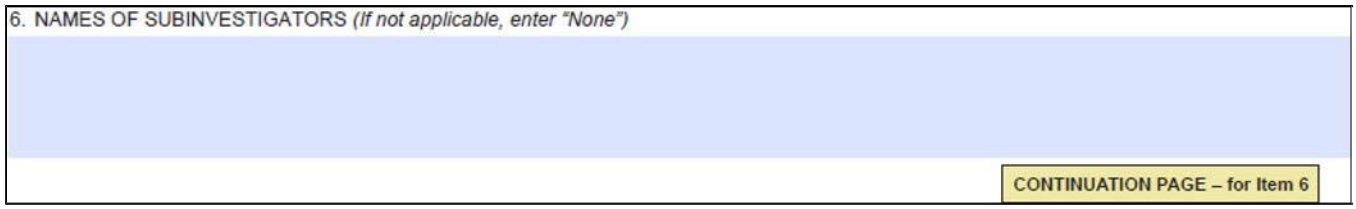
Frequently Asked Questions for Sections 4 and 5

Q: What types of laboratories should be listed in this section?

A: Note that it is vital to list all clinical laboratories or clinics that primarily conduct tests that are required or part of the clinical study. The listing of laboratories is not limited to laboratories conducting blood work, X-rays, etc.; it is very important to include any laboratories supporting pharmacokinetic and efficacy analyses for clinical trials listed under an IND application. In cases when the clinical laboratories or facilities are using another contract lab or satellite location, it is required that only the primary laboratory be listed, where it is used as a point of reference to trace samples to each of the contracted labs or satellites.{5}

Further, you should list all involved IRBs that will be reviewing and approving all related study materials.{2}

Section 6

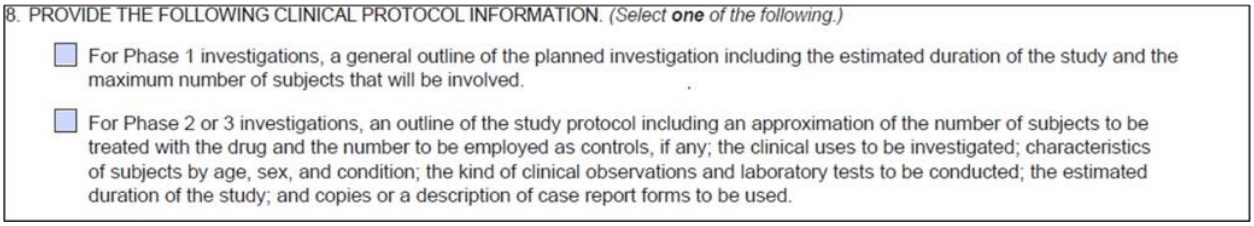


Section 6 is provided for delivering names of individuals listed as sub-investigators. According to 21 CFR 312.3(b), when an investigational study is conducted by a team, the PI is the sole lead of this formed team. All individuals who are assisting the PI and directly contributing to conduct of study procedures specified in the protocol and generation of data must be listed as sub-investigators on the Form FDA 1572.

It is the responsibility of the PI to supervise the team and delegate responsibilities and tasks appropriately, based on the team members' qualifications, education, and training. Any other office staff who provide any type of care or service that does not contribute to the overall generation of the trials clinical data do not need to be listed as a sub-investigator.{4}

Use the Continuation Page if additional space is needed.

Section 8



- Check only one box that is applicable to the type of clinical trial being conducted.
- For combined Phase I and II clinical studies, check only one box.
- Check the second box for Phase IV clinical investigations.

Section 10

10. DATE *(mm/dd/yyyy)*	11. SIGNATURE OF INVESTIGATOR Sign

Important notes to keep in mind when filling Section 10 include the following:

- The date must represent the date the form was signed by the PI.
- The signature must match the individual's name listed in Section 1.
- Sites never directly submit this form to the FDA; once completed, it is necessary for the site to provide all the other documents requested along with this form in Section 2 to the sponsor.{5}

Common Mistakes Identified in Audits

- Submission of incorrectly completed forms.
- Missing submission of requested documents in Section 2, especially when study personnel have been added to the 1572 or in cases when the original PI has been replaced.
- Failure to submit updated 1572 forms to both IRBs and sponsors.
- Site not having CVs for all study personnel listed on the 1572 form.
- Site lacking copies of current medical license for the PI.
- Upon collecting CVs that are not specific templates, it very important to be mindful of data privacy issues and make sure no sensitive information is listed on study personnel CVs, such as Social Security numbers, family members' information, etc.
- CVs provided are not current within the last two years.
- Missing documentation within the PI's CV of the his/her affiliation with the site conducting the clinical trial.

Form FDA 1572 Expiration Date

The most recent version of the Form FDA 1572 can be obtained from www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf.

In cases when a Form FDA 1572 is being collected shortly before a new version is released, sponsors can use the current version to obtain signed agreements from clinical investigators participating in their clinical studies. The expiration date given for using the form reflects the U.S. Office of Management and Budget's clearance of the form as meeting the requirements of the Paperwork Reduction Act. Despite the fact the form carries an expiration date, there is no need to provide a new form after the new version with the latest expiration date has been released.

Conclusion

For new clinical research professionals entering the field or in need of a refresher to their current knowledge, this paper was written as a guide to all study site staff, including CRCs, CRAs, PIs, and sub-investigators. It is very important to understand the many regulatory documents used in clinical trials—what they mean and how to fill out and maintain them properly. As there may be many more details readers have questions about that are not covered in this article, please visit the references and resource cited below for any extra information needed.

References

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2. U.S. Food and Drug Administration. Form FDA 1572 (Statement of Investigator) (OMB No. 0910-0014, expiration date February 28, 2019). https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

3. http://regardd.org/drugs/initial-ind-submission

4. U.S. Food and Drug Administration. Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs. Frequently Asked Questions—Statement of Investigator (Form FDA 1572). https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf

5. U.S. Food and Drug Administration. Form FDA 1572 Instructional Supplement. https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm223432.pdf

Resource

Sather S, Woodin K. 2016. *The CRC's Guide to Coordinating Clinical Research* (Third Edition). Pre-study: preparing for a study. Boston, Mass. https://store.centerwatch.com/p-293-the-crcs-guide-to-coordinating-clinical-research-third-edition.aspx

CLINICAL RESEARCHER—APRIL 2019 (Volume 33, Issue 4)

HOME STUDY

THE NUTS AND BOLTS OF CLINICAL TRIALS

An Overview of the Prospects for Using Wearables to Improve Clinical Trials

LEARNING OBJECTIVE

After reading this article, the participant should be able to describe the state of regulatory support for wearables technology, the challenges of its deployment, opportunities for its use in studies, and factors in choosing industry partners in this specialty.

DISCLOSURE

Geoffrey Gill, MS: *Employee of Shimmer Research, Inc.*

1. The article cites which of the following as a way wearables can improve how outcomes are measured?

A. They are inevitably cheaper to use in clinical trials than paid employees.
B. They are easier to employ than survey instruments across multinational studies.
C. They can provide continuous streams of objective data to the study team.
D. They are convenient to recycle for later use at the conclusion of a trial.

2. What is the current level of usage of wearables in clinical trials?

A. Less than 1%
B. Nearly 3%
C. Between 5% and 7%
D. More than 10%

3. Which of the following is true regarding the use of wearables in trials?

A. They must only be used by college-educated adults.
B. Their use requires approval by a Legally Authorized Representative.
C. Trial participants using wearables are very likely to steal them.
D. Their use does not require approval or clearance as medical devices.

4. According to the article, which of the following is a factor making use of data from wearables problematic?

A. The algorithms used by many have not been validated.
B. Users' recording of data is often affected by clumsy design.
C. Data may be intercepted and altered between user and sponsor.
D. Trial coordinators do not know how to interpret the data.

5. Which of the following is NOT cited as a reason for the low penetration of wearables in trials?

A. Risk of failure
B. Pain
C. Cost
D. Effort

6. The author cites the estimated total potential market for wearables in clinical trials at what annual level?

A. $250 million
B. $500 million
C. $1 billion
D. $2 billion

7. The article highlights which of the following examples of other fields from which the pharmaceutical industry can learn about using wearables?

A. Aviation and military science settings
B. Tourism and veterinary science settings
C. Meteorological and food agriscience settings
D. Academic and consumer neuroscience settings

8. The author writes that pharmaceutical companies collaborating on algorithms for wearables could agree on which of the following?

A. Costs of development to pass on to consumers.
B. Appropriate industry outcome measures.
C. Terminology to use in data reporting.
D. Intellectual property rights in non-U.S. settings.

9. Which of the following is NOT cited in the article as an attribute pharmaceutical companies should look for in a wearables partner?

A. Access to the raw sensor data.
B. Transparency of records on the company's investors.
C. Commitment to openness and industry collaboration.
D. Extendibility of the wearables platform.

10. Which of the following factors does the article cite as making it difficult for proprietary algorithms to be accepted as validated outcome measures?

A. They are too expensive for consumers to download for personal use.
B. They are prone to data-hacking complications from rival companies.
C. They cannot be extended into other uses by the wearables industry.
D. They cannot reliably be copied from one generation of the product to another.

Revisiting the Form FDA 1572

LEARNING OBJECTIVE

After reading this article, the participant will be able to articulate the importance of completing the Form FDA 1572 correctly and describe common areas of confusion in this regard.

DISCLOSURE

Anonymous: *Nothing to disclose*

11. What is the principal investigator (PI) doing by signing the 1572 form?

A. Complying with HIPAA regulations.
B. Notifying patients about a change of address for the trial site.
C. Informing the sponsor of his/her intent to participate in a trial.
D. Making a legal commitment to adhere to FDA expectations.

12. When can an investigator make changes to a protocol without sponsor/institutional review board (IRB) approval?

A. When it is mandatory for the purposes of protection and safety of the subjects.
B. The investigator cannot make changes to the protocol.
C. When it is in the review stage and not yet finalized.
D. When the trial site's host institution recommends the change.

13. What is the investigator's responsibility regarding study personnel?

A. To train staff on specific financial information to gathered from subjects.
B. The investigator does not have responsibilities regarding study staff.
C. To ensure that all study personnel understand their responsibilities and duties.
D. To ensure that each staff member completes a 1572 form prior to working on the study.

14. In accordance with which part of the *Code of Federal Regulations* should adverse events and serious adverse events be reported?

A. Title 21 CFR 11
B. Title 21 CFR 312.68
C. Title 21 CFR Parts 50 and 51
D. FDA guidance manual 7348811

15. What should the investigator ensure when obtaining consent from each participant?

A. That the consent form is printed and legible.
B. That the consent process is reported to the IRB.
C. That the most up-to-date IRB- and sponsor-approved consent form is used.
D. That the consent form is translated into the subject's first language.

16. What aspects of a clinical trial does Title 21 CFR 312.62 refer to?

A. Safety reporting
B. Subject protection
C. Investigational product accountability
D. Maintaining adequate and accurate records

17. Which requirement does the IRB have to comply with?

A. Title 21 CFR Part 56
B. Title 21 CFR Part 50
C. Title 21 CFR 312.68
D. Title 21 CFR 312.62

18. For which clinical trials is the Form FDA 1572 not required?

A. Investigational New Drug trials
B. Biological product studies
C. Device-related clinical trials
D. Post-marketing observational studies

19. Within what timeframe must a Form FDA 1572 be submitted if an investigator is replaced?

A. Within a 21-day window period of replacement of investigator.
B. Within a 30-day window period of replacement of investigator.
C. Within a 14-day window period of replacement of investigator.
D. There is no window period for submitting the Form FDA 1572.

20. What needs to be completed on the Form FDA 1572 if laboratories are using a contract lab?

A. No such laboratories are required to be listed.
B. The directors of the main lab and of all sub-labs must be listed.
C. Only the primary laboratory needs to be listed.
D. Only laboratories located in non-U.S. countries must be listed.