## ORACLE

### Oracle Health Sciences. For life.

2019 Market Research Report: The Use of Virtual Components in Clinical Trials



RESEARCH REPORT

Oracle Health Sciences and CNS Summit are pleased to share the results of this research with our colleagues in the industry. We hope this report will provide the foundation for an industry-wide effort to define what constitutes a decentralized clinical trial, and in turn help remove barriers to the effective use of patient-facing technologies and digital endpoints in the future.

## Contents

Executive Summary	3
Overview	4
Findings	
Question 1- Definition	6
Question 2- Problems Solved	8
Question 3- Challenges	9
Question 4- The Future	10
Conclusion	12



## **Executive Summary**

Patient-facing digital technologies play an increasingly important role in the conduct of human clinical trials for new drugs and medical devices. Some say that the use of such technology will enable remote patients to participate in these 'virtual' or 'decentralized' trials, where they haven't been able to before.

As the industry looks forward to a time when this type of technology is core to every aspect of a trial, it's also confronted with a host of challenges. Beginning with a lack of clear agreement on what constitutes a decentralized trial, these challenges extend to technology design, implementation, data integration, data validity, regulatory acceptance, and – crucially – its effect on the patient experience.

To explore these challenges, Oracle Health Sciences, in partnership with CNS Summit, convened a series of focus groups and supplementary research with individuals representing key stakeholders in the clinical trial ecosystem. All of the participants had significant experience in both clinical trials and the use of patientfacing technologies. As far as the benefits of decentralized trials, participants described the value of technology to widen the pool of trial participants, increase retention, improve the quality of the data, and improve patient convenience.

Conversely, participants also reported on how challenges in incorporating technology have (in some ways) slowed the clinical trial process and failed to realize the full potential of "virtual components" in a trial. However, they believe that the solution lies in cross-industry efforts to standardize terminology and data models, as well as a gradual incorporation of digital endpoints and patient-facing technologies in Phase II and, later, Phase III trials. They also stressed the importance of defining areas where technology should remain only an adjunct to traditional human interaction with patients.

Oracle Health Sciences and CNS Summit are pleased to share the results of this research with our colleagues in the industry. We hope this report will provide the foundation for an industry-wide effort to redefine what constitutes a decentralized clinical trial, and in turn help remove barriers to the effective use of patient-facing technologies and digital endpoints in the future.

## Overview

The past few years have seen a marked increase in the use of patientfacing technology1 in the design and management of clinical trials. As more technology has become incorporated into each component of the trial process, both the conduct of the trials and the expectations of how clinical trials might be managed in the future have changed.

A variety of terms have been used to describe this new generation of technology-supported trials, most notably "virtual trial." That, along with other words, has been used in literature and throughout the industry, setting widely varying expectations as to the scale and scope of change that this technology will enable. This underscores the absence of a clear agreement across the industry (or even among individual stakeholders in the industry) as to the definition of these terms.

The lack of a common understanding has led to a disparity between what some believe technology might do and the reality of what it is accomplishing. There is a high degree of confusion throughout the industry as a result.

This affects how the technology itself is designed, along with expectations of how it will be applied in a given trial. In turn, it can lead to doubts about the validity of the data collected, which calls into question the ability of such studies to produce valid endpoints for presentation to regulatory authorities. Thus, the very technology that is supposed to be making trial design and operations more efficient, is instead creating chaos and slowing down the progress of clinical research.

To bring clarity to the discussion, Oracle Health Sciences and CNS Summit arranged a series of four focus groups in the summer and early fall of 2019. Each was comprised of up to 10 professionals representing different stakeholders in a clinical trial. This included representatives of large and small biotech firms, pharmaceutical companies, contract research organizations (CROs), sites, and providers of specialized technology, such as patient-worn sensors or apps. To the degree possible, each of the groups was composed of individuals with similar roles at similar organizations to enable us to compare and contrast the responses in terms of different stakeholder perspectives. The 28 focus group participants had industry experience that ranged from approximately 10 years to more than 40 years. All were selected because of their direct experience with using or providing patient-facing technology in actual Phase II or Phase III clinical trials. In total, the focus group participants reported involvement with nearly 1,100 such trials.

For purposes of this report, patient-facing technology includes devices, technology, or apps that a clinical trial participant interacts with directly for the purpose of data gathering (such as a tablet for keeping an e-diary or a body-worn sensor); to aid with study compliance (such as a smartphone app providing reminders for taking drugs); or to otherwise take the place of an in-person site visit (such as a telemedicine app). It also includes online methods for enrolling patients (such as electronic consent forms) where no face-to-face interaction takes place.

The 28 focus group participants had industry experience that ranged from approximately 10 years to more than 40 years. All were selected because of their direct experience with using or providing patient-facing technology in actual Phase II or Phase III clinical trials. In total, the focus group participants reported involvement with nearly 1,100 such trials.

"There is increasing interest in the concept of virtual end-to-end studies – both in the startup world and in biopharma." – Leslie Shinobu, MD, PhD, Portfolio Transformation Team, Biogen

Situations differed across organizations as to where talent resides, and opinions differed around whether there is a shortage of talent or not. As clinical research becomes more digital and data becomes more accessible, individuals with a deeper understanding of analytics are in high demand. While these skills were isolated to specific functions in the past, they are now more broadly in demand, and there is the expectation that people invest in obtaining these skills.

The focus groups consisted of a two-hour, facilitated discussion centered on four basic questions: <sup>2</sup>

"There is increasing interest in the concept of virtual end-to-end studies – both in the startup world and in biopharma."

LESLIE SHINOBU, MD, PhD, PORTFOLIO TRANSFORMATION TEAM, BIOGEN

Question 1	Question 2	Question 3	Question 4
How do you define the term "virtual clinical trial" for trials that involve a Principal Investigator (PI)?	When you have employed patient-facing technology in some aspect of a trial, what was the primary problem you sought to solve?	What are the challenges or obstacles you have identified in incorporating this type of technology into trials?	What do you believe needs to be done in order to effectively move forward in realizing the potential of patient-facing technology in clinical trials?

As an adjunct to this research to further round out the site perspective, Oracle Health Sciences also asked professionals attending the Global Site Solutions Summit in October 2019 to fill out a survey concerning their use of technology in clinical trials. Their responses are incorporated into this report.

This research included an attempt to capture the regulatory perspective through a focus group and online survey, as well as through 1:1 interviews. Unfortunately, the regulatory audience did not respond to these efforts. However, the facilitator was able to speak with one person familiar with the regulatory perspective, which is captured in this research.

Following is a summary of the discussions around each question, examining the major areas of consensus and differentiating, where relevant, the dissimilarities or disparities between the various groups based on their roles in the clinical trial process.



<sup>2</sup> While Oracle Health Sciences personnel conducted the focus groups, the discussions were product agnostic, and did not in any way touch on Oracle's technology or solicit input for future versions of those products.

# Findings

#### **Question 1**

How do you define the term "virtual clinical trial" for trials that involve a Principal Investigator (PI)?

>

A variety of terms have been used to describe clinical trials that incorporate at least some patient-facing technology, e.g., a tablet provided to patients for them to record basic data related to the study, a smartphone app to provide patients with guidance on protocol adherence, a wearable sensor that transmits data to the study team, etc. These terms include decentralized trials, remote trials, direct-to-patient trials, hybrid trials, patient-centric trials, and most commonly, virtual clinical trials.

None of these terms, however, have an accepted definition across the industry; rather, each of them has a number of disparate definitions attached by various groups or companies in the clinical trial space.

This is particularly the case for the term "virtual trial." There was little agreement among focus group participants when it came to defining the term. In fact, most acknowledged that this lack of a common definition is a source of confusion within the industry.

"There are so many different aspects that can be virtualized, so if you virtualize one, does it become a virtual trial? Or is it 50%, or 75%? At what point does it become a virtual trial?" – William Jacobson, Senior Director, Clinical Development, Harmony Biosciences Participants gave a variety of conditions they felt defined what constitutes a virtual clinical trial. Some felt that the use of almost any patient-facing technology constitutes a virtual trial (for example, where the sole "virtual" components are the use of tablets or apps to capture data about the patient). Others said that a virtual trial only describes those where every aspect of the trial after protocol design are entirely technology-based, from patient recruitment and consent, to data collection. By this definition, there would be no physical trial sites for patients to visit, and neither the PI nor anyone else involved in the study would ever have face-to-face interaction directly with the patient.

Some participants, particularly out of the biotech group, said that a virtual trial would mean no human-to-patient interaction at all, including telemedicine examinations or interviews. That would entail that all data collection and patient reporting would be automated (as well as the delivery of test drugs, compliance reporting, and even safety reporting). Many called this a "fully virtual" trial to distinguish it from one that was entirely technology-driven, except for home visits from a medical professional for purposes of taking physical samples (such as a blood draw).

"There are so many different aspects that can be virtualized, so if you virtualize one, does it become a virtual trial? Or is it 50%, or 75%? At what point does it become a virtual trial?"

#### WILLIAM JACOBSON,

SENIOR DIRECTOR, CLINICAL DEVELOPMENT, HARMONY BIOSCIENCES Except for mainly technology suppliers and biotechs, almost none of the participants said they had ever been involved with, or had any familiarity with, a "fully virtual" trial. For those few who had experience with a "fully virtual" trial, they clarified that those trials were not intended to produce data for regulatory approval. For Phase III trials involving an experimental drug, none of the focus group participants reported having been involved in trials that entirely separated the patient from direct contact with a provider of some kind.

"I've conducted clinical trials for 29 years. I've done probably 150 as a principal investigator and 40 may have had a virtual component... [But] no completely virtual trials as of yet." – Cherian Verghese, MD, Medical Director, Keystone Clinical Studies; Assistant Professor of Psychiatry, Temple University

Almost all participants considered the use of technology on a continuum from "traditional" to "fully virtual" trials.

The most commonly used term for a clinical trial in the middle of the continuum was "hybrid trial." This term was used to cover trials with a wide range of technology deployment, but still included direct-to-patient interaction by the PI or participating physicians (although not necessarily to the same degree as traditional trials).<sup>3</sup>

Most participants describe the current state of hybrid trials as involving technology for data gathering, data reporting, or patient/provider interaction, including the use of patient-worn sensors and smartphone apps to maintain patient participation and compliance. Such trials are becoming more commonplace, according to focus group participants; one, from a large pharma company, said that 70% of his trials in the past eight years have been hybrid.

From the site survey that was conducted at the Global Site Solution Summit (N=48), the majority of sites (N=38) who responded to the poll (79%) are involved in decentralized trials.<sup>4</sup> The three most common "virtual components" used in decentralized trials were mobile technology (92%), web-based patient diaries (84%) and wearable technology (82%). With regard to mobile technology and web-based diaries, sites tend to receive the patient data in real-time. With regard to wearable technology, sites tend to receive the patient data at defined intervals. "I've conducted clinical trials for 29 years. I've done probably 150 as a principal investigator and 40 may have had a virtual component... [But] no completely virtual trials as of yet."

#### CHERIAN VERGHESE, MD,

MEDICAL DIRECTOR, KEYSTONE CLINICAL STUDIES; ASSISTANT PROFESSOR OF PSYCHIATRY, TEMPLE UNIVERSITY

3 Some within the industry further refine this definition of a hybrid trial into two separate categories. In this nomenclature, a study where patients do not visit a study site and all data is collected remotely is considered a decentralized trial. Hybrid trials are those where the patient has some face-to-face contact with the PI, a research team member or a healthcare professional.

4 According to the Clinical Trials Transformation Initiative (CTTI), decentralized clinical trials are trials that are run through telemedicine and mobile health care providers.

#### **Question 2**

When you have employed patient-facing technology in some aspect of a trial, what was the primary problem you sought to solve?

>

The degree to which technology has been employed or integrated into a clinical trial has increased significantly over the past three to four years, as reported by the focus group participants. In some cases, the PI proposed that technologies should be incorporated into the protocols; in other cases, the technologies were pre-determined and sites were required to conform to their use, which included training personnel on the technology.

Participants reported several reasons behind the use of technology. Most commonly, they reported using technology to deliver a better experience for patients enrolled in the trials. Even if the initial choice of technology was meant for another purpose – streamlining data collection, for example – the way the technology was employed most often relieved some burden off of patients and made trials more patient-centric.

According to the focus group participants, the most frequent benefits realized by solving these problems were widening the pool of trial participants, increasing retention, improving the quality of the data, and improving patient convenience. In addition, by running the trial using this decentralized model, some critical problems actually solved were:

- Site staff inconvenience
- Not receiving primary endpoints at the time of occurrence
- Maintaining required patient safety monitoring
- Eliminating second-hand data sources
- Eliminate the need to run another trial to validate digital efficacy endpoints
- Improve screening and diagnostic methods and tools
- Ensure patient literacy regarding the trial study

For some focus group participants, making trials more patient-centric reflects the need or desire to improve patient recruitment and retention. That includes widening the potential pool of patients and improving the quality of patients who are enrolled for a given trial.

"The assumption from everyone is that it was going to make it easier [but] I think an important part of the motivation early on was access to patients that were really hard to get through the traditional channels." – Adam Butler, Independent Consultant Other participants noted that the ability of technology to generate regular patient interaction or actively provide reminders to them creates more patient engagement that can keep patients motivated to continue with the trial.

"The most important thing, the key, is retention of patients. It's not like legacy-type trials where you see the patient, then time goes by, you see them again, and more time goes by. We're keeping in constant contact [through triggers and reminders]." – Dr. Mylea Charvat, PhD, CEO, Savonix, Inc.

Another benefit cited by several participants is the potential for technology to improve the quality or reliability of data, e.g., by having electronic diaries with time and date stamping versus paper diaries that patients might not fill in until just before a site visit.

Some of the other problems cited as technology targets differed by group:

- Site participants noted that technology can streamline the trial process for sites by removing layers of management, and can also assist with increased site engagement by helping to provide them with a better quality patient population.
- The biotech and tech supplier participants noted that a hybrid trial using at-home data collection might enable the gathering of additional data and longitudinal information that would not be possible using a site-visit model.

>

#### **Question 3**

What are the challenges or obstacles you have identified in incorporating this type of technology into trials?

The focus group participants universally pointed to a range of challenges or obstacles related both to the current use of technology in hybrid trials, as well as the potential for moving farther along the continuum towards the "fully virtual" trial. Some participants indicated a strong belief that the fully virtual trial, as defined in the answers to Question 1, would be an impossibility for Phase III trials for many reasons. At least one participant – who represented sites – said she would never participate in a trial where there was no direct contact with patients. The primary challenges focus group participants identified were:

• A lack of data integration – too much data produced by too many technologies and devices can't be put together in ways that will allow for effective analysis, and still be able to pass regulatory review. Some participants felt that technology providers were overly focused on adding new functions to their products without considering issues of interoperability.

• Potentially compromised patient safety and Serious Adverse Events (SAE) reporting – if patients don't have direct personal contact with sites or study physicians, will there be sufficient recognition of SAEs and any assurance that patients will get the relevant care?

 Unclear regulatory acceptance – for Phase III trials, the larger regulatory agencies are not yet ready to accept digital endpoints.<sup>5</sup>

"We have a lot of platforms coming up and they're being developed in a very innovative manner. But they do not speak to each other. They do not have consistent data models. There is no way to easily integrate them." – Ted Finlan, Senior Vice President, Planning & Project Administration, Worldwide Clinical Trials

Another challenge cited by participants was that in some hybrid trials there can be dozens of different technologies required to conduct the trial, each having a separate portal and login credentials for sites. This actually slows down the clinical trial process, as site personnel need to be trained to use each technology and must contend with vastly different user experiences for the various portals. It also poses the potential for a high training burden on technology-averse patients, or for those who will be asked to use an app, but do not themselves possess a smartphone. Thus, both the technology itself and the training to use it raise the overall cost of the clinical trial.

#### **Question 4**

What are the challenges or obstacles you have identified in incorporating this type of technology into trials?

>

The focus group participants across all roles were generally positive about the ability of patient-facing technology to make clinical trials more efficient, cost effective, and patient-centric. They also believed that the trend of adding virtual components to trials would continue, and that these components would find themselves operating in all aspects of trials and in all trial phases. "We have a lot of platforms coming up and they're being developed in a very innovative manner. But they do not speak to each other. They do not have consistent data models. There is no way to easily integrate them."

#### TED FINLAN,

SENIOR VICE PRESIDENT, PLANNING & PROJECT ADMINISTRATION, WORLDWIDE CLINICAL TRIALS

The focus group facilitator subsequently interviewed an individual familiar with the thinking in current US regulatory policies. While there is general support by regulators for the use of virtual components in clinical trials, the level of support depends upon the particular trial and the specific experimental drug being tested. There is a general reluctance to consider trials labeled as "virtual" because one possible interpretation is that the trial could be conducted by analyzing pre-existing data only, rather than conducted with actual patients. The term decentralized is preferred.

However, for that to happen effectively, the efforts across the industry concerning how these trials are conducted, the standardization of terminology and data models, and the identification of areas where technology should remain only an adjunct to traditional human interaction with patients will be required.

One key recommendation was for industry consortia to make the development of standards for patient-facing technology and data a priority. This would address the concern about the lack of integration and data reliability, helping to ensure that as new technologies are developed and deployed, their use would not be disruptive to the trial process.

Participants also believed that the move from hybrid trials toward the type of "fully virtual" trials that are currently used in Phase I and IV investigations should be a gradual shift beginning with Phase II trials, and only move to Phase III after successful use in Phase II. The perception amongst the various groups was that regulators would most likely accept virtual components for recruitment in Phase III before moving toward more extensive use of patient-facing technologies. As noted previously, the regulators were not available to comment on this point directly.

Many of the participants, except for the small biotech and technology vendors, expressed concerns about technology entirely replacing the interpersonal relationships among PIs, site staff, and patients. While the participants who are deeply involved in technology believe that the patient experience could be significantly improved in "fully virtual" trials, most other participants feared that the loss of the personal touch would be detrimental to both patients and to the results of a trial.

Specifically, participants representing sites and CROs said it is vital to maintain personal interactions between patients and Pls. The commitment being asked of Pls is both significant and has legal ramifications, so the need to build trusting relationships is crucial; technology could interfere with that.

Representatives of sites also indicated that they believed face-to-face interaction with patients is the only way to obtain a truly accurate assessment of the patient. That's particularly the case where SAEs are concerned, which led one participant to call for the creation of backup safety plans where technology is the first line of reporting.

"My comfort level will increase as I know the safety for my patients increases. You can't throw it out there and on the patient." – Kyle Magner, RN, BSN, Director, Clinical Research, Community Clinical Research Network (CCRN) "My comfort level will increase as I know the safety for my patients increases. You can't throw it out there and on the patient."

#### KYLE MAGNER,

RN, BSN, DIRECTOR, CLINICAL RESEARCH, COMMUNITY CLINICAL RESEARCH NETWORK (CCRN)

## Conclusion

As a whole, the participants in these focus groups did find that the use of technology in decentralized trials delivers value, particularly when it came to data quality, increased patient retention, and increased patient enrollment. Technology is also helping make studies more convenient for patients. This is encouraging as the industry moves toward precision medicine – where a particular treatment may produce different outcomes for some patient groups – and for rare diseases where the global patient population is small and it is essential to access, attract, and retain patients in trials.

As clinical trials continue to add virtual components and patient-facing technology, the full potential of these digital enhancements may be difficult to realize. From inconsistent terminology to difficulties in integrating data and safety fears, focus group participants reported a range of concerns that have prevented patient-facing technology from becoming mainstream.

Challenges still remain, particularly in the realm of developing standards and in working closely with regulatory agencies on the application of these technologies in later-stage trials. There is also the issue of retaining the human element in trials, and, as one participant put it, ensuring that technology does not compromise the scientific or patient care principles that are the bedrock of clinical trial practice.

As virtual components become more central to the conduct of clinical trials, the best outcomes will be realized with a concerted effort by all stakeholders to better understand how individual virtual components can work together for the benefit of patients. Technology holds exciting promise for the future, and with the proper standards and collaboration by all stakeholders, the "virtual" trial may reduce both the time and the cost of clinical trials, bringing better treatments to patients sooner to improve their quality of life.

# Thank you to the focus group participants:

Cherilyn Boller, Premier Research Dr. Stephen Brannan, Pharma Industry Adam Butler, Independent Consultant Dr. Mylea Charvat, Savonix Ted Finlan, Worldwide Clinical Trials Shwen Gwee, Novartis Christina Hughes, Independent Consultant Dr. William Jacobson, Harmony Biosciences Bryce Kasuba, Syneos Health Dr. Annette Madrid, Independent Consultant Kyle Magner, Community Clinical Research Network Dr. Glenn Morrison, Zogenix Nelson Rutrick, Adams Clinical Kerensa Saljoogi, Independent Consultant Jan Samzelius, NeuraMetrix Dr. Leslie Shinobu, Biogen Omer Siddiqui, Alector Gurdish Singh, Vygen Dr. Todd Solomon, Avanir Pharmaceuticals Dr. Egilius L. H. Spierings, MedVadis Research Corporation Terry Stubbs, ActivMed Practices & Research Dr. Jane Tiller, BlackThorn Therapeutics Dr. Chelsea Trengrove, Empatica Dr. Cherian Verghese, Keystone Clinical Studies Ellis Wilson, PPD Richa Wilson, Genentech Charles Wolfus, Alector Susan Wong, Transparency Life Sciences

#### **About Oracle Health Sciences**

As a leader in Life Sciences cloud technology, Oracle Health Sciences' Clinical One and Safety One are trusted globally by professionals in both large and emerging companies engaged in clinical research and pharmacovigilance. With over 20 years' experience, Oracle Health Sciences is committed to supporting clinical development, delivering innovation to accelerate advancements, and empowering the Life Sciences industry to improve patient outcomes. *Oracle Health Sciences. For life.* 

#### Copyright ©2020, Oracle and/or its affiliates. All rights reserved.

The preceding is intended to outline our general product direction. It is intended for information purposes only, and may not be incorporated into any contract. It is not a commitment to deliver any material, code, or functionality, and should not be relied upon in making purchasing decisions. The development, release and timing of any features or functionality described for Oracle's products remains at the sole discretion of Oracle.

#### CONTACT

#### +18006330643

healthsciences\_ww\_grp@oracle.com

www.oracle.com/healthsciences

#### CONNECT

linkedin.com/showcase/oracle-health-sciences