Evolution and Revolution in Site Management

While virtual and decentralised trials continue to proliferate and evolve, challenges still remain for site-based trials. A novel approach to clinical site monitoring could redefine the future of medical research

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Prior to the global coronavirus pandemic, monitoring clinical research sites throughout the lifecycle of a study accounted for substantial allocations in a study's schedule and budget. Sponsors often allotted 25-30% of a study budget for site monitoring, and the process of qualifying and initiating sites often required six months or more. For the CRAs responsible for site monitoring and management throughout a study, most of their time involved travelling and conducting a wide array of tasks at the site. With exhaustive checklists of requirements for multiple concurrent studies, the CRA role was heavily burdensome, resulting in burnout and high turnover rates. At the same time, clinical trials have been growing in complexity, scale, and quantity. For example, ClinicalTrials.gov shows that the number of registered studies in the US nearly doubled between 2015 and 2020 (1).

Remote site management solutions developed over the past decade reduce the need for travel and on-site time for certain tasks, such as source data verifications and reviews. However, these solutions replace only some of the activities traditionally done in person at the site, and they can introduce new risks. In this context, and in parallel with a global public health crisis, a truly virtual site monitoring approach has emerged that can finally bridge the gap between traditional and remote site management. Using an innovative, wearable, live video streaming device along with a multifunctional telemedicine application, a CRA can access facilities, documentation, and site staff remotely from anywhere. When 80-100% of on-site activities can be completed virtually, sponsors can significantly reduce site monitoring budgets, prevent CRA burnout, and accelerate the study start up and drug development process.

Challenges in Traditional and Remote Site Monitoring

Beginning with pre-study qualification visits (PSQVs), the CRA plays a critical, if unheralded, role in the success of a clinical trial. The CRA must interview the principal investigator (PI) and study coordinator, assess the clinic facility and drug storage areas, evaluate security measures, review patient enrolment and informed consent procedures, train staff, as well as perform numerous additional tasks to determine whether the site has the resources and capabilities required for a particular study.

Site initiation visits (SIVs) and interim monitoring visits (IMVs) also require detailed inspections, multipoint interviews, and evaluations. Each visit is followed by visit reports, follow-up letters, questions, and/or recommendations – a process that limits CRAs to completing as little as two or three site visits per week.

Since 2013, the FDA has encouraged a shift toward remote monitoring, referred to in *Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring* as 'centralised monitoring', a method to replace activities that can be done as well, or better, remotely (2). Cited

Virtual site monitoring video streaming glasses

activities include informed consent form review, communication with sites, and source data verification. Subsequently, solution providers have developed remote site monitoring platforms that help CRAs perform some parts of a monitoring visit remotely, such as document management. However, these platforms do not fully augment all the required activities needed to monitor a site. In addition, remote monitoring solutions may introduce potential errors and compliance issues, such as site staff forgetting to redact identifying information, or losing track of who has access to sensitive data.

Closing the Gap

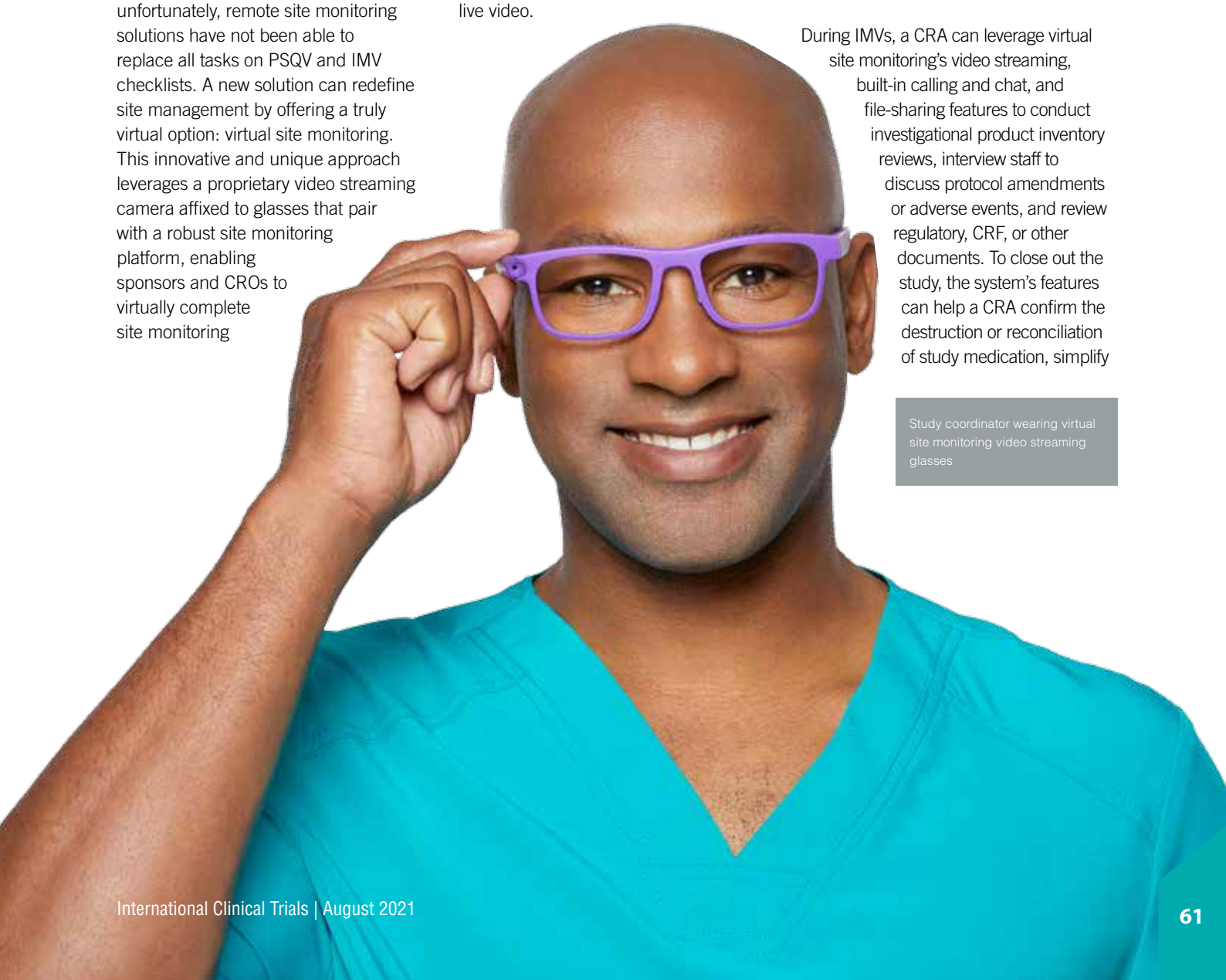
The traditional site monitoring process is inefficient and expensive, and, unfortunately, remote site monitoring solutions have not been able to replace all tasks on PSQV and IMV checklists. A new solution can redefine site management by offering a truly virtual option: virtual site monitoring. This innovative and unique approach leverages a proprietary video streaming camera affixed to glasses that pair with a robust site monitoring platform, enabling sponsors and CROs to virtually complete site monitoring activities that previously could only be completed on-site.

Virtual site monitoring video solution to attach to existing glasses

Throughout the pre-study qualification and SIVs, CRAs can virtually tour sites anywhere in the world. When a study monitor wears the custom glasses equipped with 1080p video streaming capability, the CRA can see exactly what the monitor sees in real time from a first-person point of view with high-resolution, live video.

CRAs can visually inspect the clinic facilities, equipment or drug storage areas, licenses, certifications, product labels, and any other physical spaces or items required by the sponsor and protocol. In addition to this video streaming functionality, embedded video calling links a study coordinator with a CRA and allows guests to be added to the call, such as a busy PI who may have trouble getting to the site, or other site staff, for interviewing.

During IMVs, a CRA can leverage virtual site monitoring's video streaming, built-in calling and chat, and file-sharing features to conduct investigational product inventory reviews, interview staff to discuss protocol amendments or adverse events, and review regulatory, CRF, or other documents. To close out the study, the system's features can help a CRA confirm the destruction or reconciliation of study medication, simplify



Study coordinator wearing virtual site monitoring video streaming glasses

final reviews of regulatory data, and facilitate PI oversight of study completion responsibilities.

Because it eliminates the need for constant travel and gives complete access to the facilities, people, and relevant files involved in a study setup, virtual site monitoring makes it possible for study teams to complete two to three virtual site visits and reports per day rather than per week, substantially reducing travel budgets and improving study start-up time.

Novel Applications for a Novel Solution

Although the virtual site monitoring approach is novel, and the life science industry is typically cautious when adopting new technology, the COVID-19 pandemic spurred rapid testing and acceptance of new, but proven, technologies. Sponsors and CROs who have participated in the development of, and utilised the virtual site monitoring solution have confirmed it alleviates the most common site monitoring challenges and makes many of the site monitoring visit checklist tasks easier. It can also be adapted for special applications beyond its intended clinical site monitoring capabilities, creating new possibilities for decentralised studies, wherein assessments take place in participants' homes.

In 2020, a CRO conducting a paediatric growth monitoring and safety study approached the company with its first fully decentralised trial (planned and designed prior to the COVID-19 pandemic). Since a home healthcare nurse would be measuring and evaluating infants in their homes, the CRO and the study sponsor needed a way to prove they had PI oversight as well as to verify the accuracy and consistency of measurements. While this would not be feasible with typical telemedicine solutions, the virtual site monitoring video glasses provided a hands-free method for the nurse to perform the measurements, and the CRA and PI to have a bird's eye view for oversight purposes. Using this approach, the study team was able to address not only the needs of the nurse performing the measurements, but also the FDA's regulatory concerns associated with transferring the study from the controlled clinic environment into a more patient-friendly, yet uncontrolled, home environment.

In this way, virtual site monitoring easily transitioned to a home healthcare telemedicine solution for a decentralised trial, a mode of trial administration in which the home commonly serves as the clinical site. While this application strayed from the intended clinical site monitoring uses, the collaborative relationship between the CRO, sponsor, and their solution partner proved that working together to solve challenges can reveal new ways of applying technology to address clinical operations challenges.

No Turning Back

The traditional site monitoring process has undergone transformative change in a short time, primarily in response to the COVID-19 pandemic, but the underpinnings of change were in place before that catalyst. Sponsors, CROs, and sites recognised that modern technology offered opportunities to accelerate the drug development process, while reducing burdensome site monitoring travel schedules and costs. Virtual site monitoring goes beyond enabling remote access to data for source verification. It reinvents the sponsor/CRO and site relationship entirely – study monitors can reproduce the site experience and engage with more sites – while adhering to good clinical practices and regulatory standards, and rebalance the work/life demands of their role. Virtual clinical research site monitoring also provides a helpful workaround for the travel restrictions and safety precautions associated with COVID-19 and future pandemics.

This new paradigm empowers sponsors and CROs to conduct traditional, hybrid, or fully decentralised trials anywhere in the world, with substantially reduced timelines and cost investment. With such drastic improvement to the patient and site experience, these are just a few of the many compelling reasons to pivot away from the traditional site management model for good.

References

1. *Visit: clinicaltrials.gov/ct2/resources/trends#RegisteredStudiesOverTime*
2. *Visit: www.fda.gov/regulatory-information/search-fda-guidance-documents/oversight-clinical-investigations-risk-based-approach-monitoring*

Emil Hoeck is a clinical research professional with wide-ranging experience. He began his career as Study Coordinator at a dedicated clinical research site and later transitioned into the CRO world, initially in a niche, full-service CRO focused on mechanistic and proof-of-concept pain trials. Emil assumed a key position with responsibility for client relations, contracting, quality assurance, and site staff training before moving to a large global CRO where he was integral in building the global strategic site relationship programme in a wide range of therapy areas including psychiatry, paediatrics, ophthalmology, oncology, and vaccines. Today, Emil serves as Senior Director, Virtual Trial Solutions at **Signant Health** and represents company interests outside the US.

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