Successful wearable device selection for the evolving clinical trials landscape

An introduction to the emerging adoption of wearables in clinical trials

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The number of wearable, connected medical devices (wearable devices) available for use in healthcare and clinical research has increased significantly over the past few years, making it difficult for clinical trial sponsors to determine which devices to use in their clinical trials. For example, when looking at activity monitors only, there are a plethora of different devices available, ranging from commercially available actigraphy to specialized, and medically approved devices.

Wearable devices offer a wealth of opportunity to help patients, sites, and sponsors within clinical trials, such as:

- **Patient engagement:** Wearable devices provide convenient insights to the patient by providing near real-time feedback on their physiological signs and/or quality of life, where some devices can even provide patients with readings about their health improvement; information which they would only have been able to receive during site visits in the past.
- **Site engagement:** Sites will have access to patient results outside of the context of site visits where they can now review near real-time data that they did not have access to before the emergence of wearable devices, even allowing for review of the drug effect on the patient on a daily basis. As a result, the number of patient visits to the site can be reduced and the site has the power to book ad-hoc, targeted visits based on at-home data.
- **Sponsor engagement:** Sponsors have the potential ability to design applicable clinical trial endpoints based on near real-time, continuous, home-based data instead of the more traditional, infrequent, site visit-based data. Although regulatory bodies and guidelines may not fully embrace the use of wearable devices yet, it is only a matter of time before applicable endpoint assessments, such as the 6-minute-walk-test, are removed from trial protocols and replaced by activity monitor data collected via wearable devices. Such near real-time data collection may also allow sponsors to make early decisions on efficacy and safety endpoints, and hence should allow for more timely decision-making during the trial execution. Trial sponsors are encouraged to engage with regulatory bodies early on in the clinical trial protocol development process to confirm if the use of wearable devices will be satisfactory.

In order to realize the advantage wearable device data collection provides, sponsors must first select the most appropriate device for their purposes, which can be a daunting and difficult task.

Key considerations in device selection

What should sponsors consider when looking for the right wearable device for their clinical trial?

Clinical trial objectives, endpoints, and associated measurements and/or assessments

The selection of a wearable device should always be based on what the sponsor is expecting to demonstrate with the trial data. Collecting data without an objective in mind will never provide useful information.

Clinical trial sponsors should first determine the trial objectives, including endpoints, that will be used, based on the trial therapeutic being tested and intended patient population. Based on the expected outcome, possible measures and/or assessments will be defined. An example of an exploratory endpoint could be measuring a physiological sign (e.g., blood pressure, temperature) over time to determine if the frequency of dosage is adequate and helps maintain physiological values as expected or in some cases, if urgent intervention by the patient physician is required. With these possible results in mind, the sponsor can determine the frequency at which measurements have to be taken by the device and/or the patient and/or the frequency that the data needs to be reported and monitored by the site and trial sponsor. Thinking about such a parameter will provide information about which type of device to consider.

Once the appropriate device is selected, wearable devices will enable collection of more real-life data with higher frequency and accuracy. This will lead to high statistical power when testing the underlying hypothesis for the trial endpoints.

Data accuracy

Once the data points to be measured have been determined, as based on the trial endpoints, the sponsor should search for wearable devices that collect these specific data points and explore how the devices have been validated by the manufacturer. Device validation should focus on three aspects:

1. **Content validation:** Sponsor and/or designee should review the validation performed by the manufacturer to help ensure accurate, precise, and consistent measures to support endpoints are acquired. Such tests should include measures over a relevant period of time and verification that

data acquired over time is consistent. Additionally, the use of a small sample study to measure acceptability and scientific accuracy against gold standard with the desired patient population group is highly recommended, when appropriate, to ensure that the targeted patient population is capable of using the device in a consistent manner.

2. **Intra-device and inter-device validity:** Testing with multiple devices, including comparator devices, which would ideally be what is considered gold standard at the time of the test. If testing against a comparator device is not suitable, the measures should be validated against existing clinical tests and/or validated clinical instruments.

3. **Regulatory considerations:** It is of strategic importance to review the regulatory status of a wearable device across different countries/ geographical regions.

   Wearable devices must meet general safety, performance, and data security requirements for their intended use. These general requirements deviate across countries and geographical regions, but include product safety, human factors design/usability, and strict personal data protection precautions.

   Achieving medical device approval or clearance status for wearable devices varies across different countries and geographical regions. For example, the US may require an FDA 510K clearance, whereas in the EU, a CE-Mark approval status may be mandatory. However, this regulatory status does not automatically ensure the device may acquire reliable and meaningful physiological measurements for a specific patient population of interest. Hence, the validation of wearable device performance is a key success factor.

Beyond the wearable device validation itself, the full data acquisition chain has to be validated to make sure it records data accurately, acquires data in a format that is adequate to analyze, and generates alerts (if applicable) that are meaningful. The data acquisition chain should also include processes covering the storage and loss of data files and how they can be recovered, to ensure that the full dataset is retrievable for a single patient.

Finally, the data acquisition chain needs to provide the relevant levels of security to ensure patient data remains confidential and cannot be retrieved maliciously or tampered with.

Usability

Patient comfort and user-friendliness are key aspects to consider when selecting a wearable device for trial patients, as they can have a substantial impact on the amount of available data there is to analyze at the end of the trial. The trial team should consider the patient's comfort not only in regard to wearing the device, but also in regard to user effort (e.g., re-charging the device and any possible interaction needed with the device). A device that is complex to set up will directly and negatively impact patient compliance and may require support from the site staff in the set-up process. The battery life and recharge process are also key points to consider, as it is important to ensure the device offers sufficient battery life to cover what should be measured in a given time period and also that the battery life will be consistent in various environmental conditions (e.g., temperature, signal strength).

When considering usability, the sponsor should be aware of the tolerability and acceptability of wearable devices within the patient population they are targeting. Devices should be selected with the patient population group in mind, and when possible should be considered easy to use and non-invasive for the participant in order to minimize patient burden and increase compliance results. Some patient populations are already used to interacting with devices due to their condition (e.g., continuous glucose monitors and blood glucose monitors for diabetes), but others may not need to use devices and/or may not have an interest in wearing a device. For such a population, it is important to think about ways of emphasizing the importance of the data collected through the device, and the sponsor may need to apply strategies to increase patient compliance, such as the use of companion applications that could provide feedback on their compliance and would encourage them to wear the device.

Data transmission and interaction

The reason for using wearable devices within a clinical trial is to collect data required to directly or indirectly support certain trial endpoint(s). Therefore, it is critical to select a data transmission or direct viewing solution that provides the relevant data to the sponsor, either via direct data transfer or through a visualization module. With either method, data collection from the wearable device is transferred remotely, thus reducing the burden on the patient and increasing the accuracy and frequency of data captured to support the clinical trial.

It is recommended to view data regularly, as it is one of the greatest benefits of using wearable devices. As wearable device data is collected at more frequent intervals than during site visits, it should be reviewed at more frequent intervals. Regular data review should allow for identification and rectification of potential issues with poor patient compliance, as well as highlighting potential unforeseen irregularities which otherwise may have gone undetected.

Ideally, a data visualization module will provide data in a format that is meaningful for what is being demonstrated. If that is not the case, then in addition to the data visualization module, it is recommended to obtain an agreement for regular data transfers with the device provider, because even if a visualization module is suitable, trial teams may still want to consider regular data transfers to perform ongoing reconciliation and data analysis.

Lastly, the data analysis should obviously focus on endpoint realization, but additional predictive analysis on raw data may also be beneficial. Utilizing the wealth of acquired data and computational modelling can lead to additional insights, such as stratification of patient sub-populations or measures to characterize therapeutic options (e.g., drug dosages and/or courses).

Wearable device logistics

When selecting devices for clinical trial use, it is important to consider the physical logistics, device provisioning, country-specific requirements, and end-to-end support services available.

When identifying participating countries, it is important to ensure that the device(s) required in the trial are compatible for use in those countries. Working with a global logistics provider can overcome the hurdles presented with differing local/country pharmacy laws which affect import/export licenses and direct-to-patient shipments. Your logistics partner should also have a process defined for device storage, management of faulty devices, device replacements, and device returns, ensuring that shipments can easily and quickly be sent to and from patients.

It is also important to consider the physical practicalities of each participating country's infrastructure and data privacy laws which will determine what is and is not possible. For example, some country regions require local, in-country data processing and data storage and some countries/regions require different plug sockets for charging and voltage. Ensuring that your device provisioning partner has experience in the countries likely to participate and creates a risk log to ensure labeling, packaging, and local provisioning risks are identified early and mitigated against will help prevent these items impacting the critical project plan for delivery.

Conclusion

An important aspect to remember in the selection of devices is the selection of the right technology and CRO partner. Although data collection through wearable devices can be performed and managed by many device providers and CRO partners, not all provide the appropriate level of data security and regulatory guidance. As such, it is critical to ascertain that all the relevant regulations are respected to protect participants' privacy and the confidentially of the data.

The regulatory environment is constantly evolving, leaving room for further innovation. It can be daunting to be the first sponsor using a certain wearable device or a type of device in a clinical trial, but so long as the strategies outlined in this white paper are utilized and the sponsor gets the green light from applicable regulatory bodies early on in the process, the use of wearable devices, whether they be first of their kind or already proven, is more than possible.

There is no doubt that wearable devices will not only continue evolving, but will do so at a faster and faster pace, offering even more possibilities in just the next few years. There are already many device types and manufacturers available today and sponsors do not need to wait for future evolution and optimizations of such devices to use them in clinical trials.

References

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