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The ARBM Ecosystem- Optimizing Process and Platform

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ABSTRACT

Powerful and sustainable analytic risk-based monitoring (ARBM) is accomplished when cross-functional risk analysis, mitigation and adaptability is approached at the study level not as an activity, but as an integrated ecosystem. This ecosystem is sustained by integrating a validated technology solution supported by clear processes and effectiveness checks. However, it thrives only when supported by strong teams and the organizational commitment to a methodology is well-articulated, auditable and connected through each phase of risk management: risk identification, mitigation, operationalization, issue detection, action and adaptation. This paper outlines the key characteristics required for an organized and integrated technology platform to support holistic and interactive risk-management through the lifecycle of a study. It critically evaluates the components of process and platforms necessary to support data-driven risk management. It also outlines possible "next steps" for a whole-study approach to risk management.

INTRODUCTION

Analytic risk based monitoring is often appropriately described using an ecosystem metaphor. A sustainable ecosystem is one that is able to thrive and continuously support itself by efficient use of resources, timely communication, and appropriate interpretation of signals and utilization of this information to adapt to change. Fundamentally, there is a necessary balance of the ecosystem elements: people, process and platform that enables teams to work effectively and comply with ICH E6 R2 guidelines (Wilson, 2014).

As champions of ARBM, we must ask ourselves:

What have we learned so far about this type of dynamic ecosystem?

What do we need to consider for a successful risk management process? And,

How do we assure our ecosystem is sustainable, can thrive and evolve?

Answering these questions requires the establishment of core concepts that form the ecosystem's framework.

Rather than risk management being considered as a series of activities primarily conducted at start-up, sustainable risk management requires a lifecycle approach. Once these sustainability concepts are understood, maximizing the effectiveness of such an environment relies on implementing processes supported by technology platforms and fully engaged teams to secure an ARBM ecosystem that can also thrive and evolve. The final component for evolution in the ARBM paradigm is establishing clear measures of success and managing iterative changes.

THE SUSTAINABLE ARBM ECOSYSTEM

At its core, analytic risk based monitoring (ARBM) is efficient risk management that is approached as an ecosystem rather than an activity. "Too much so-called "risk management" involves simply ticking boxes, going through the motions, attending risk workshops and review meetings and getting it over with as quickly as possible so we can return to the real job. Whatever this is, it is not managing risk." (Hilson, 2015)

The root cause of this "set it and forget it" attitude towards risk management and ARBM can be multifaceted; however, often this is symptomatic of one or more of the following:

- o An ill-defined process
- o Unclear expectations for the project team
- o Disengaged and disorganized project management
- o Insufficient change management and/or,
- o Lack of support from an organizational level

As each of these components is uniquely considered in the next section, a formula for sustainability is defined.

PROCESS

At the core of a well-balanced ARBM ecosystem is a simple and efficient cyclical process (Figure 1). This cyclical process articulates a clear framework for how risks and issues are governed throughout the life cycle of a project and demonstrates how each component is connected to the others. The activities supporting each element may be slightly different from one application to another, but by including effectiveness checks and process updates from feedback loops, the cycle is enduring. Embedding the risk assessment into a cyclical process in this way secures the connection to downstream activities and ensures the necessary focus on what is important to the overall vision while avoiding debates on whether a task needs to be done (TransCelerate, 2016). This in turn helps to ensure the team understands the interconnectivity of the process and how mid-stream changes to data review on or off-site has a compounding downstream effect that must be considered at each level.

Another critical element within the cycle is to have clearly defined measurements for success. Specifically, what we are measuring, how we are measuring each component and, how we are going to act on variances must be a part of the benchmarks during the “initial set-up” of the process.

Objectively quantifying benefits of your ARBM approach, both internally and externally, can be challenging and it is easy to move forward without consideration of effectiveness checks. However, establishing metrics supports a well-functioning feedback loop, which then enables the ARBM ecosystem to communicate issues and weak points within the process and generate recommendations for change and improvement.

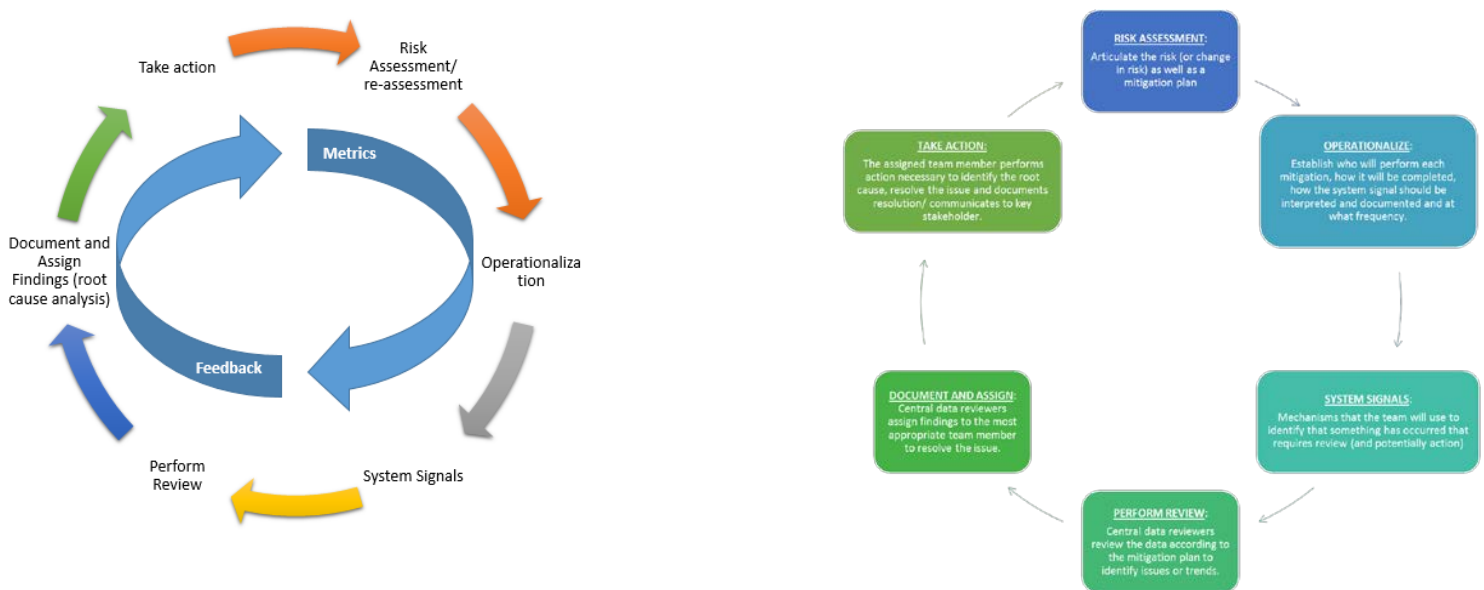


Figure 1: ARBM Ecosystem, Core Processes

To illustrate the importance of thoroughly evaluating the impact to each step of the core process and establishing effectiveness checks when a change or update is needed, consider the following scenario:

Scenario 1: Issue tracking shows a program-wide trend in under-reporting of Adverse Events. To manage this by off-site review on future studies the team decides to implement a visualization showing the connection between Adverse Events, Concomitant Medication and Medical History and highlighting unusual behavior at a site for follow-up.

Solution: In Figure 2, the impact of this change and important considerations for each element of the system are outlined. By asking and answering the questions noted, the change is easily implemented and ultimately improves the quality of the data.

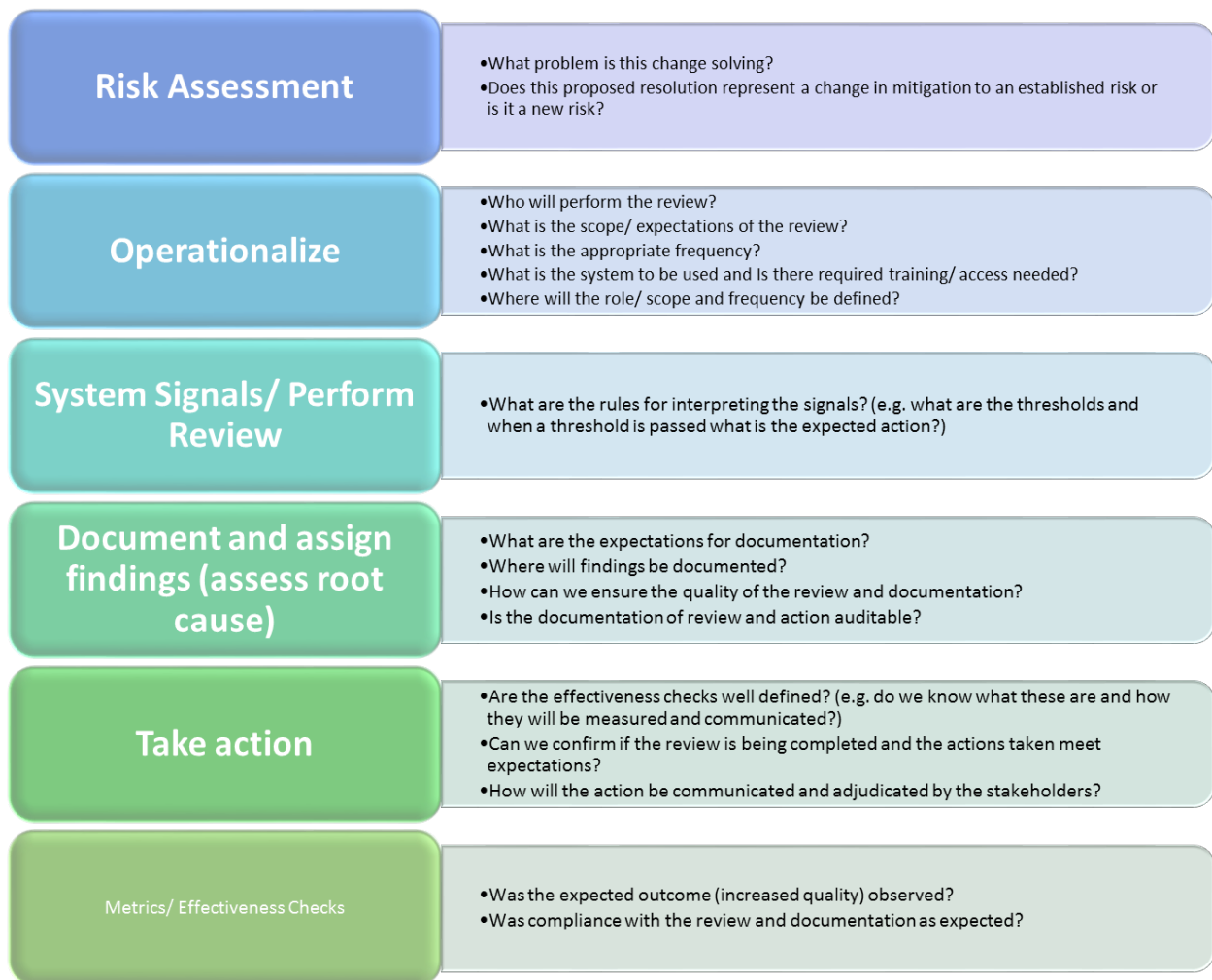


Figure 2: Considerations for adding details to the core process

PROJECT TEAM

Once the core process is established, communication of expectations to the team along with how success and compliance will be measured is the important next component. Expectations must be clear for the team that will engage in the process and comprehension checks are an effective way of establishing a baseline buy-in. The team is the energy source for an ARBM ecosystem and if they lack understanding or do not fully support the ARBM process the inevitable challenges will drain the system of energy. Measures need to be in place to identify, communicate and correct those issues.

During the risk assessment process loss of energy is often felt acutely. Identifying that a momentum lapse has occurred is often not an issue, but identifying why this has happened presents a challenge. Energy loss is often a result of several compounding factors. Issue management and “putting out fires” can be more exciting and have more immediate rewards than methodical, proactive mitigation and review of signals. Risk management takes a longer lensed view of activities, but it is not a passive activity. The process quickly loses value when team members fail to connect on continuous risk identification or when team members slip into routines/repetitive tasks rather than questioning what value a task adds or what risk management might mean for their project work for months to come. Combined with lack of focus on risk mitigation, team members often come with varieties of experience utilizing risk management and limited exposure to analytical risk based monitoring. This limited exposure can lead



to misconceptions about ARBM, specifically, that it is less important than immediate firefighting or even that it does not work. This perception can be inherently challenging to overcome. However, these energy depleting elements are effectively managed by factors both internal and external to the project. One key internal factor, is to establish a clear vision for the process supporting ARBM activities. Another internal factor is facilitation support for the team for both risk management and technology integration to promote team engagement and consistency. (Hillson, 2011).

Furthermore, the team interprets signals, exchanges information and converts energy into action and adaption, thus ensuring the sustainable feedback loop of the system. The Project Manager is essential to protecting this system. In the ARBM ecosystem, the Project Manager “breathes life into the vision” and serves as a compass by rigorously pursuing root cause, paying attention to the individual interests of the contributing team and external stakeholders and directing actions and decisions back to the shared interests of the process. (Turner, 2008). By effectively managing the cross-functional team in this engaged and supportive manner, identifying repetitive tasks and challenging the team to contribute their expert opinion to the findings that are being surfaced becomes part of the framework and sets the expectation for quality, consistency and adherence to process.

External to the project team, to both sustain and thrive, a successful ARBM ecosystem implements a comprehensive change management strategy. Whether or not teams embrace and adopt the process and platform will hinge on the comprehensive understanding of what is changing, why the change is being implemented and who is being asked to change. Addressing these core tenets of change management at each aspect of the ARBM process can help to identify the key areas where the team is struggling with maintaining desire to embrace the process and can help to identify where and how rewards for successfully engaging in proactive risk management can be implemented. Establishing an effective process to reward proactive risk management behavior must replace the destructive rewards realized by the constant excitement associated with issue management and an overall reactive approach to study management.

Finally, we must acknowledge the importance of organizational support for the process and vision for a sustainable ARBM solution. The ecosystem needs room and space to adapt to and accommodate change and allow space for “failing”. This is important as teams can be paralyzed by being afraid to adapt to anything that is not explicitly articulated in a current process design. To accomplish this, leadership must demonstrate a visible and consistent commitment to risk management as well as a robust approach to empowering study teams. This can be realized by being a champion of risk management, acknowledging successes and accepting that identification of issues and evolving the process is paramount to success. It is important for leadership to show that risk assessment and adaptive processes are aligned with the corporate objectives and to demonstrate that the teams are supported by relevant technologies to advance this unified vision.

THE THRIVING ARBM ECOSYSTEM

Along with organizational support, an integrated end to end technology platform is also essential to ensuring the connection of the process with the people performing the work.

“We are at the very beginning. Look at past achievements, agriculture being a good example. The plow, the combine and the tractor made us stronger. We could say that the human spirit was paired with the physical strength of the machine. The same applied later to cars and airplanes. Today we have come to the point where machines no longer simply supplement the muscle power or motor abilities we lack; they can take over almost all of our repetitive activities.” (Ammann & Brunner, 2016)

Once a clear vision is communicated, processes are identified and organizational support is demonstrated, the ARBM system is able to thrive by infusing automation in order to free up human potential to focus on more critical tasks. The support of an end to end platform, when well considered, can give the team “super powers” to quickly and meaningfully digest the data, communicate and enable the team to focus on what is important and use their unique expertise for the most value added tasks.

PLATFORM

Independently, technology is possible to support each element of the ARBM cyclical ecosystem. Some examples are an integrated risk assessment and risk tracking tool to support risk assessment/ re-assessment, an issue management tool to support issue assignment for action by the appropriate team member and workflow management, and a visualization tool to surface system signals from the data. Platform support needs to remain seamless with the core process flow and ensure its key capabilities and characteristics prioritize having the right team members looking at the relevant data available at the right time and in the most meaningful way.

The sequence followed to best apply platform support to the process is important. As previously stated, the core process elements are aligned with ICH GCP E6 R2 by design and how individuals must interact within the process to transfer information must be observed carefully to effectively establish the path forward. It is only once the interactions between the team members and process elements are identified and the interconnections are clear, that opportunities begin to present for how to manage the workflow, monitor process compliance, minimize touchpoints and allow for scalability by using automation and task centralization. It is inherently, and importantly, an iterative process. Thriving ARBM teams will streamline and simplify connections between functional groups and team members to the point where geographic location does not inhibit access to current data. Figure 3 illustrates how these opportunities for platform supported connections might begin to present themselves by interpreting observed connections within the core process.

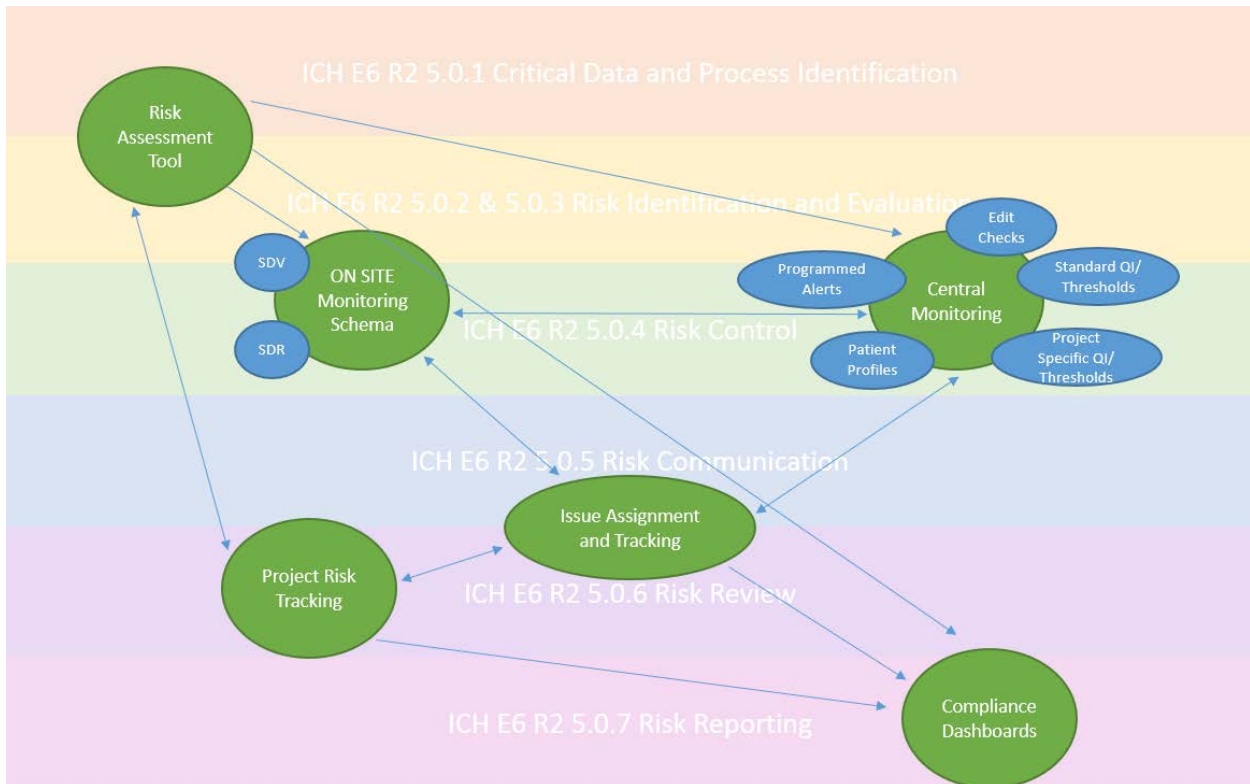


Figure 3: Platform support for the core process (automation pathways)

Once connections are identified, automation of activities within the system should promote consolidating tasks where possible to minimize transfers and site contacts and simplify the way team members exchange information. As the workflow evolves and simplifies, as outlined by Figure 4, trial team members become less defined by their roles and more defined by the value added tasks each individual performs.

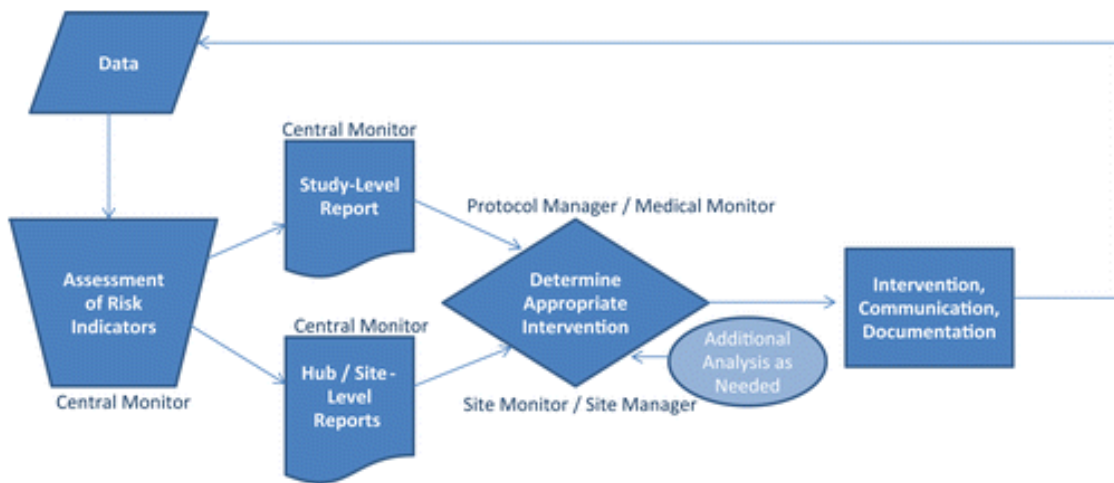


Figure 4: TransCelerate workflow example with central monitoring hub (Wilson, 2014)

Similar to the steps when making changes to the process, it is critical to highlight the importance of considering metric tracking and effectiveness checks as automation and centralization of workflow steps, integration of data and visualizations are built in to the system platform. The team must identify what problem is being solved by the change, what success of the change will look like and ensure that a mechanism to measure the quality and compliance of the updated platform to the core process is considered. While using the technology platforms and implementing ARBM processes, it is important to continually consider what metrics and feedback are relevant along with evaluating the need for process and metrics updates as new capabilities and project or regulatory needs are established.

Ideally, the platform is agnostic in that the connections and visualizations required to link the process steps can be surfaced regardless of the source of the input. Here, similar to the considerations for process and people for the platform support, we re-visit the importance of employing change management ideology for platform/ technology support for the ARBM process, and organizational support vis-à-vis investing in platform improvements. To provision this required connection and custom approach to platform and process synergy, there is substantial value in providing facilitation support for teams to align the overarching ARBM vision and problem solving for process pain points with the appropriate technology and data integration solutions.

This combination of a stubborn yet agile process vision, an observation before action approach to platform integration and a metered system change mechanism, which allows for feedback and facilitation support for both the change management and system agnostic integration of data, are the core elements to establish and maintain the required balance between process and platform.

Another key component in a balanced ARBM ecosystem is to be always looking ahead. The evolving ARBM ecosystem team asks: As the technology, regulations and priorities change are the process, platform and team situated to adapt?

THE EVOLVING ARBM ECOSYSTEM

Once established, the ARBM ecosystem is never stagnant. Process, platforms and people must evolve to survive and most importantly they must evolve together. As populations that are cut off from each other evolve independently, clarity of vision and quality of communication are paramount. It is essential to invest in the vision and ensure this is clearly defined, but also continuously seek new opportunities to achieve this vision. The vision must be unified by strong, seamless global communication across functional groups, as well as, internal and external stakeholders.



For the evolving ARBM ecosystem, change is crucial. As technology and access to data changes rapidly, traditional data review techniques (like SDV) are quickly becoming obsolete. Clinical data is becoming more prolific and the way we access this data is progressing, leading to increasing prevalence of eSource and possibilities for virtual trials. The environmental landscape is changing in patient populations and behaviors, compounding this change are the regulatory and ethical considerations. While considering the way data can be surfaced and utilized, teams must also navigate the regulatory framework that defines the way this data can be used and accessed, and this too is an evolving process. Specifically, concerns over data privacy and ensuring that the interests of those who contribute to data collection and/or are impacted by the data use are important to consider. Even when teams are able to access and use the data, there are questions over the reliability of the evidence based on observational data and whether there are enough standards established on how this data can be used for effective medical decision making (Fassbender, 2018).

As teams work quickly and aggressively to determine the rules of engagement for what constitutes reliable evidence, it is imperative we begin to consider how to operationalize scenarios where studies are run virtually with eSource (e.g. eCOA, direct EHR integrations and wearable technology for data collection). As these elements integrate into our clinical trial vocabulary and toolset along with additional disruptions such as predictive analytics and stronger machine learning capabilities, the life sciences community is challenged to think creatively about how to best apply these features to the way we do business in drug development with a critical patient-centric focus. In acknowledgement of the ongoing questions, it remains clear that the eClinical market is growing at an exceptional pace and demand for increased capabilities and functionalities is high, which presents a lot of opportunity; however, project life cycles continue to be long and ensuring a stable process and platform that meets current needs but remains agile enough to accommodate next stage needs is a challenge (Fassbender, 2018).

Teams must always consider scalability and durability of the process, they must acknowledge the advantages and limitations of the current state and invest in changes that intelligently deliberate how advancements in technology may be best incorporated into future state.

From a practical lens, to be able to connect the process, platform and people to the core vision, the team must be agile and adaptable. Project management approaches that more closely resemble the technology industry and employ agile project management methodology are more equipped to accommodate iterative change. Iterative change is necessary to ensure that system updates continue to represent the core vision and objectives of ARBM as the way we collect and interpret data and as the regulatory framework continues to evolve the supportive regulatory framework changes. "Above all other points, the ability for agile development requirements to emerge and evolve, and the ability to embrace change." (V2Soft, 2018) The focus is always on ensuring that the changes implemented continue to solve a problem that needs to be solved and the problem will evolve as the profile of ARBM changes. In short, to ensure an effective adaptive monitoring solution, the platform support itself must be adaptable.

CONCLUSION

As the traditional methods of accessing and reviewing data for clinical research continue to evolve and present ongoing challenges, organizations that adopt and support an ecosystem approach to ARBM will be among the leaders. Simply stated, by promoting an integrated process and platform that capitalizes on the strengths of the team and facilitates cross project and cross program communication and learning, an organization will be best situated for success in this disruptive environment.

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