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The Golden Age of Clinical Research Innovation

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The golden age of pharmaceutical blockbusters is long gone. Instead, most "blockbusters" today take the form of enormous challenges, such as patent expirations. Not only does the average new drug generate less revenue than previously, but it is much more costly and time consuming to develop. Any industry dealing with declining revenue and increasing costs is facing the abyss.

Today, clinical research is a big part of the problem, so how do we make it into a big part of the solution? The recent CHI Summit for Clinical Ops Executives (SCOPE) conference in Miami gave more than 700 attendees from pharmas, biotechs, CROs and service providers the opportunity to discuss the prospects for turning around our part of the industry. Two conclusions became apparent: On one hand, today's challenges sound a lot like the issues we faced 20 years ago. On the other hand, a new age of clinical research innovation appears to be dawning. This is not to say that a bright future is assured, only that the time is right for hard work, smart investments, and some risk taking to achieve the high level of productivity we need to survive, prosper and save lives.

The industry can afford to invest in innovation. Profit margins for S&P 500 pharmaceutical and biotech companies averaged 19.3% in 2012.[1] Contract research organization (CRO) stock prices are at record highs.[2]

However, investments in innovation must generate better returns than other uses of resources. There are three ways to improve returns: Increase the payoff, accelerate the payoff, reduce the cost, or increase the chance of success. As it happens, recent trends in the industry support improvements in all four dimensions.

Risk-based monitoring (RBM) is reducing costs and improving quality (when some of the saved resources are applied to that purpose). The current system of 100% source data verification is absurdly expensive and trains research sites to rely on site monitors for quality control. Just as importantly, RBM drives instrumentation of clinical trials for near real-time control so deviations from plan can be identified and quickly addressed.

Electronic medical records facilitate patient screening and integration of data between clinic and clinical trial. With eSource (e.g., Clinical Ink), data flows instantly from the point of collection to the database, so missing data and other anomalies can be detected and remedied while someone actually knows what happened. Wearable devices and smartphone apps collect data much more efficiently, quickly, accurately, comprehensively and inexpensively than manual measurement and entry.

What appears to be lagging, however, is closed-loop feedback. For example, why do most studies still take longer than planned? Shouldn't our ability to forecast become more accurate over time? How many clinical research organizations have implemented the lessons-learned databases that have been common in the consulting and other industries for decades?

Just as important as new technology is new thinking. Historically, clinical research has employed an engineering paradigm that views clinical studies like construction projects, which can be managed like a giant machine. In theory, the protocol, standard operating procedures, and regulations precisely define each contributor's function — inputs go in and outputs go out. If each person exactly performs his or her defined function, everything goes

smoothly. If something does not go smoothly, that part of the machine must be repaired or replaced.

Most of the technologies discussed above streamline the machine's functions and improve the operator's (i.e., project manager's) control over the machine. That's all well and good, but clinical trials are not construction projects. Investigators, study coordinators, site monitors, subjects, etc., are not functional cogs but humans, with all their inherent strengths and frailties. Fortunately, we are in the process of reconceptualizing clinical trials as social networks, in which the people become more important than their functions. We always knew that people are people, but now we are starting to shape their activities around their humanity, rather than trying to shape them to fit into functional boxes.

This change in paradigm is evident in the emerging concept of patient-centricity. We have known for decades that study participants want to know their personal data and the results of their studies. However, we have thought of them as sources of data rather than recipients — once we have their data, they've served their purpose, so they should just go away. The problem, of course, is that they do go away, mystified by the researchers' change in attitude from keen interest to no interest at all. Every salesperson knows that the best potential customer is a current or past customer. Some research sites understand this, but, mostly, we just send study participants on their way and start recruiting for the next study from scratch. (If we were really serious about patient-centricity, we would help patients find the best study for them at any site, not just the one our site happens to be enrolling.)

Social media are inherently patient-centric. They are becoming a highly productive element of patient recruiting. However, we have yet to address a terrifying downside: Social media make it a lot easier for patients to corrode the scientific value of clinical trials. Online groups of study participants or patients with a particular disease are providing advice on how to answer the screening questions, how to break the blind, what adverse events to expect, and other questions that can bias results and endanger study participants. Potential remedies have uncertain value: educate study participants about the issue, monitor online discussions, urge caution on disclosing such information (without coming across like Big Brother), and create a secure discussion environment for the subjects in a study.

Study sponsors and CROs are starting to understand that clinical research sites are not commodities — the beginning of site-centricity. Some ask clinical researchers (and even patients), not just key opinion leaders, for their perspectives on new protocols. Some have created preferred site alliances to focus their efforts on the sites best able to perform. Some sponsors and CROs, along with service providers like Optum, BioPharm Clinical, ViS Research Institute, and DrugDev.org, are developing smarter databases for selecting sites. Both of these trends support site consolidation, which enables strong sites to become even stronger and participate in innovation. Multi-site organizations (site management organizations and networks) are growing again, but this time with more attention to reliable performance and quality. However, sponsors and CROs still do not embrace the concept that the easiest way to solve the site problem is to simply pay top dollar for top performance (and innovation).

RBM is inherently site-centric, since it adjusts the site's burden based on the quality of the site. (However, brute-force remote monitoring can be very burdensome on sites.) Study portals and related technologies both streamline the machine and make site-centricity more practical. (Why not encourage sites to talk among themselves to solve problems?)

To bring the full force of the industry to bear on innovation, CROs need to get more involved. CROs are service organizations. A few are true innovators and many are creative within the scope of a study, but most just do the best they can at what the sponsors pay them to do. Sponsor/CRO strategic partnerships make it worthwhile for CROs to invest in

innovation, provided the sponsors provide "encouragement." There are rumblings of trouble in strategic partnershipland, which should be no surprise, given their ambitions. While some sponsors are pulling certain functions back from their CROs, we know the center of gravity has shifted now that a principal investigator speaker at SCOPE has said that he generally prefers working with CROs rather than sponsors.

One of the most remarkable industry developments is the increase in collaboration, notably TransCelerate for pharmas and ACRES for sites. Five years ago, who would have guessed that big pharma would have classified so many "pre-competitive" projects suitable for collaboration? Effective collaborations enable sharing resources and creativity, support rapid adoption of innovations, and enable standardization.

Manufacturing industries learned the value of standardization when interchangeable parts became popular in the 19th century. Two-hundred years later, we are still handcrafting clinical trials. While human contributors provide flexibility, rapidly increasing study complexity simply cannot continue if the industry is to survive. A major contributor to complexity is variability — Study A does it one way, Study B another, and Study C yet another. With standardization, study personnel need learn only one way to do it. For example, MAGI makes over 70 standardized forms and other documents freely available. As a side benefit, if there is only one way to do something, complexity in that process is more practical to learn and handle.

Conclusion

Very poor industries cannot afford to innovate. Very rich industries see no need to innovate. If the pharmaceutical industry does not innovate, it is on the road from rich to poor. The good news is that the clinical research industry still has adequate resources to innovate, is realizing that innovation is essential, and can employ new concepts and technologies that make innovation highly rewarding. If we make the effort, the golden age of clinical research innovation is dawning.

References

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