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The Most Powerful Name in Corporate News

Efficient Clinical Research for Biopharma and Medical Device Companies

Michael Rosenberg, MD, MPH - *CEO*

About Health Decisions, Inc.
Health Decisions is the CRO of choice for forward-looking biopharma and medical device companies and a driving force in the modernization of clinical development. Health Decisions uses data-driven insight and agility to deliver clinical development success, reduce timelines and risk and increase quality and returns for biopharma and medical device companies worldwide. For 25 years and in more than 300 clinical trials involving tens of thousands of patients in many therapeutic areas, Health Decisions has improved the efficiency of clinical development through innovative methodology, processes and technology. Health Decisions' clinical-development services have enabled biopharma and device companies to bring new products to market faster and at lower cost, thus providing the public with earlier access to improved treatments and diagnostics at more affordable prices. Health Decisions won the prestigious 2013 CIO 100 Award for delivering true business value through its innovative Agile Risk-Based Monitoring+ technology. Health Decisions is headquartered in Durham, NC and operates on five continents.

Interview conducted by: Lynn Fosse, Senior Editor, CEOCFO Magazine

CEOCFO: *Dr. Rosenberg, what is Health Decisions?*
Dr. Rosenberg: Health Decisions is a Clinical Research Organization. We conduct clinical trials and provide strategic consulting for biopharma and medical device companies that are developing new products. We focus on providing immediacy of information and enabling continuous decision-making to reduce risk and development timelines—in short, a more efficient development model than is the norm today. While many companies perform clinical research (both pharmaceutical companies and clinical research organizations) as part of developing drugs and medical devices, our mandate is to do so more efficiently than others.

CEOCFO: *Would you give us a couple of examples of how that works on a day to day basis or on a project by project basis? What are you able to facilitate?*
Dr. Rosenberg: Most fundamentally, we facilitate the decision making process. If you think about the complexity of developing drugs, much of this has to do with collecting information, making sure the information is accurate, timely and a suitable basis for decision making.

Historically, pharmaceutical development occurs in steps, or phases. Each phase involves one or more clinical studies, each designed and executed as a unit and assessed after completion. That means we start a study but do not have many answers about the new product's safety and efficacy until the study is completed. It is usually not until the end of the study that data get cleaned and we have validated, reliable data on which to base decisions. By then, it is too late to make decisions to improve execution of the study.

In contrast to the approach that views each study as a unit, with most information not available until after the study, Health Decisions' model is continuously adding to what is already known based on immediately cleaned timely data. Knowledge increases a bit every day. We can also use sophisticated modeling tools to predict where a study and program will end up. The most challenging aspect of this approach involves assuring availability of clean, immediate data about patient response and continuous performance metrics about where there may be operational issues in the field. The latter aspect is particularly important, because speed of enrollment has a great effect on the duration and cost of a clinical trial. Only about 15% of studies enroll on time and that slows development of new medical products and increases costs and ultimately prices. Our approach involves continuous adjustment of factors that affect enrollment. We enroll more than 80% of our studies on or ahead of time.

Similarly, continuous assessment of a product's performance, how much it is helping patients, is critical. Rather than wait until the end of a study before realizing there is a problem, we can quickly identify and respond to an issue. Earlier understanding of patient response opens a whole new field – adaptive design. The study design can actually shift during the study in response to data collected during the study. I should mention blinding constraints that sometimes limit who can know about patient response and require special arrangements for decision-making.

When something happens in the field, whether it is a clinical outcome measured as part of the study or operational metrics that indicate how we can improve field operations, our objective is to collect, clean, and immediately make available information for decisions. A further refinement is presenting information specific to each role and alerting individuals when something in their area of responsibility may be subpar, either now or in the future.

CEOCFO: ***It sounds so sensible when you say it. Why has it not been implemented in the past? How did the approach develop at Health Decisions?***
Dr. Rosenberg: That is a great question. I think there are a number of reasons, but mostly it is inertia. The pharmaceutical industry is very large and successful and has had the luxury of setting its own prices. When you are in a quasi-monopoly structure like that, there is not the same imperative to improve as when your existence depends on doing things better. You see this reflected, for example, in the cost of developing a new molecule. According to *Forbes*, the cost of developing each new drug approved for marketing is now more than $8 billion for big pharma—and the worst of the big companies actually spent twelve billion dollars to get a single drug to market. The biggest component of that is not the cost of developing the successful drug itself but the cost of many drugs that fail in development.

One inspiring book that I have read is a history of how the Japanese entered a staid, complacent automobile market and completely changed it. I believe that that kind of change is coming in the pharmaceutical industry. There are a number of analogies between the way the American automobile industry used to be and the way the American pharmaceutical industry is now. For example, current processes in pharma are fundamentally unchanged over the past 30 years—computers enable faster execution of old, inefficient processes but have not been used to enable new, more efficient processes.

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Japanese management realized that technology provides them inventory management and decision-making capability on a minute-to-minute, day-by-day basis rather than week by week and month by month. That allowed a big shift and ultimately the Japanese forced the US car industry to change. Few, including CEOs of big pharma companies, would disagree that these companies are by any definition ponderous and inefficient. However, there has not been competitive pressure to force change. That is why little change has occurred and is occurring.

I think the answer to improved efficiency is fairly straightforward. If you take a lesson from other industries, notably manufacturing, the basic principle is having timely, actionable information at your fingertips as a basis for decision-making. This capability completely changes the game. Health Decisions provides timely, actionable information that improves management of clinical trials by enabling earlier, better decisions.

CEOCFO: ***Are clients seeking you out because they know your approach or are the pleasantly surprised or maybe even a little bit unnerved by it?***
Dr. Rosenberg: It is a combination of all three of those things. Different segments in the pharma industry tend to react differently. Lean, hungry biotechs are anxious to do things in a better way and tend to seek us out. We have had some extraordinary successes for groups like these. For us, it works well if we have a partnership where we can bring something to a smaller company such as industry-leading operational capabilities that would otherwise not be available to them.

Midsized and big pharmaceutical companies tend to have entrenched infrastructure and they are looking for solutions that they can bolt on. Unfortunately, you cannot bolt a really new approach onto infrastructure designed to do things in a different way at a slower pace with less information available and less decision-making. If we can get discussions at the most senior strategic level, then we do have some very good success stories about work we have done with big companies. We usually approach the issue with big companies based on doing a "clean sheet of paper" demonstration project, after which they can decide which aspects are best suited for their companies and feasible within their infrastructure.

CEOCFO: ***Would you tell us about your book?***
Dr. Rosenberg: My book lays out a plan by which the industry can become more efficient. This involves three components, best thought of as a pyramid where each component depends on others. The most fundamental platform piece is the technology that streams information from the field. That includes not only clinical data, but also the performance metrics that allow us to work with the field and improve things like rate of enrollment.

The second piece in this pyramid is what I call Operational Adaptations, and the biggest elements of that are an adaptive approach to enrollment and monitoring. It is interesting that our industry enrolls only a small proportion, maybe fifteen percent of studies, on time. Traditional monitoring involves sending people out to the field to look at data that we are collecting to make sure that it has been entered correctly. If you are able to stream relevant information from the field, you can improve both enrollment and monitoring dramatically. As an example, against the industry's disappointing enrollment figures, Health Decisions' on-time or early enrollment is, as previously noted, more than eighty percent. We achieve that by being able to look every day at what is working and what is not working and making changes accordingly. Those changes might include where we advertise, messaging, frequency of advertising, and other factors. There are many internet advertising and social media opportunities such as Facebook, Craig's List, and others that are appropriate for certain studies, but not for others. The most basic issue is that we always try to make sure that we have a very flexible system that allows us to quickly ascertain what works and what does not. Again, I do not think there is anything remarkable about that approach, except that you need to have that information streaming and you need to have processes that translate raw data stream into a manageable amount of information tailored to each role in the study.

The third component is Adaptive Designs. That means how a study itself is configured in basic terms such as how many and what kind of patients must be enrolled to determine whether a new product works. We take this same approach of streaming information from the field, except for these design parameters, we focus on patient outcomes and surrogate measures such as biomarkers. In the same manner that we evaluate operational measures, we continually reevaluate certain design factors and we can make changes. For example, one of the most common reasons why studies fail is because did not enroll enough patients to determine whether the new products works – in biostatistics, the ability to determine whether a drug works depends on the size of the treatment effect, how a big a benefit the drug provides to a patient. A pharma company may go into a study and think that their drug works very well and so they decide how many patients to enroll based on that. If it turns out that the drug does not work quite as well as estimated, there may not be enough patients to provide a basis for conclusions and the study fails. With our approach, we have the option of looking at patient data during a study and saying, "This drug is not working quite as well as we expected but it does appear to be working in a way that is clinically meaningful. But to demonstrate that, we need to enroll more patients." We can utilize an adaptive design technique to adjust sample size, the number of patients enrolled, during the course of the study. We can not only increase sample size if the treatment benefit is less than expected but also sometimes decrease sample size if the treatment benefit is greater than expected. We can adapt based on the benefit observed during the study. That is why this approach is called adaptive—it allows changes in response to data and metrics as they become available during a trial.

CEOCFO: ***Do you find that most of your clients do follow your suggestions? Do they appreciate the attention you pay to a potential problem?***
Dr. Rosenberg: In the end, it is all about teamwork. It is not that we are right and they are wrong or the reverse is true. I think our job is to take care of the day-to-day tasks and to the extent that we have control of those things, most clients are very pleasantly surprised with the extent of the control that we can exercise. The benefit of this type of system is that it gives you choices, decision-making power, that often otherwise does not exist. For example, there are times that we can identify issues such as inclusion criteria – criteria required for a patient to enroll in the clinical study – that impede enrollment but are not necessarily required to identify patients that can benefit from the new treatment. A sponsor then has an option, subject to regulatory approval, to change an inclusion criterion that is needlessly excluding patients and slowing enrollment. There may be reasons why they do not want to do so, but at least they can weigh the two options. Most often, such choices do not otherwise exist. Our job is to help sponsors of clinical trials to be successful within the constraints that they set. There is a big difference between having information and making a conscious decision to do or not do something and not even knowing that there is an issue until it is too late to do anything about it. We enable earlier, better decisions that reduce timelines, cost and risk.

CEOCFO: ***Would you tell us about your global approach?***
Dr. Rosenberg: Our global approach is, again, quite different from what the industry is used to. By and large, pharma continues to rely on manual processes for a couple of reasons. First, many processes started in the 1970s and 1980s, when the kind of technology that we have available today was simply not available. So there is a lot of inertia. Second, the CRO industry evolved as a fee-for- service industry and CROs have little incentive to change the number of hours that they bill for a project when that's how they make their money.

In contrast, our approach is to leverage technology and take a much more strategic perspective. One example is a more than $50 million study that we are just finishing. We did this project at a fixed price. It is the only such example that I know of. If this big study had run longer than planned, we would have paid to complete it out of our own pocket. If we were able to do it more quickly, we save money and, most importantly, we create value for the sponsor by getting the product to market earlier. We prefer a business model in which we share in value that we create rather than one where we profit based on spending more time and increasing what we can bill to the sponsor. In this particular study, we hit our bonus marker fourteen months early. The bonus reflected the extra value created by enabling the sponsor to market the drug sooner and for fourteen months under patent protection that otherwise would have been lost to slow development. One of

our most successful studies ever got a major oncology agent to market a year ahead of schedule. That created between three hundred and five hundred million dollars of value in the estimation of one industry analyst.

CEOCFO: *That is substantial – completing a project a year ahead of schedule!*
Dr. Rosenberg: The interesting thing for me is that when we tell people about this work, many people think we are exaggerating. The most remarkable thing for me is the fact that this can be done, and that sets an entirely new bar for the industry as a whole, no question about it.

I returned from a conference yesterday where I presented a paper on how to save money on field monitoring while improving the quality of data. As I mentioned, our approach is, whenever possible, to develop technology that reflects what is happening in the field rather than frequently putting somebody on a plane to go out and assess the situation. Our approach provides immediate, actionable information, and the proof of the pudding is in being able to save a substantial amount of money—in the fixed-price study, nearly $10 million on monitoring—while improving quality, in this case by tenfold over usual industry standards. This really gets back to one of the most basic lessons about technology—it is not to simply make existing processes go faster, but to redefine processes to achieve the trifecta: faster, cheaper, *and* better.

While I am disappointed that our industry continues to struggle with these concepts and operational issues, the good news is that it can be done and represents real hope for the industry to improve efficiency.

CEOCFO: *Is that because it was not subject to a person's take on the data?*
Dr. Rosenberg: In part, and there is benefit in having a monitoring team with an in-house monitor and a field monitor responsible for each site. However, it is mostly due to the lack of timely, meaningful information on the types of errors that are occurring in the field and the ability to correct them quickly. The study that I used as an example of more efficient monitoring involving less travel was fairly complex—3400 patients, five countries. Those circumstances present a challenging management problem, and if you do not know what is going on you cannot effectively manage such a study. We provide streaming information that enables us to know where the management problems are and how to address them immediately. Most often we can pick up the phone and call a site in Russia and say something like, "I have noticed that you have had consistent problems with question 22 and 23. Let us take a few minutes to go over how you administer those questions." It is that kind of thing. What we do boils down to knowing exactly what is going on through streaming information and, based on that information, providing immediate feedback to the investigative sites, the medical offices that are seeing patients in the study. Our sites make the same errors that everyone else does, but we not only ensure rapid error correction, but also prevent recurrences. Our focus is on prevention of all types of errors and inefficiencies rather than remediating problems after the fact. The industry tends to focus on repeated remediation. I always tell my people that it is okay to make errors once, but only once.

CEOCFO: *Would you tell us a little bit about the corporate culture?*
Dr. Rosenberg: We try to have a thoughtful and flexible culture and at the same time one that is challenging and fun. Much of our work involves meticulous detail. As employees, you might imagine that we have many people who are pretty precise in what they do because they have to manage what happens in the field. You might assume that you need a formal culture for meticulous management, but we find that an informal atmosphere works best. We try to have an environment that is nice, warm, informal and friendly. For example, my dog is sitting in my office as I am sitting here.

CEOCFO: *How is business these days?*
Dr. Rosenberg: It is actually pretty good and getting better! I think more money is going back into the industry and the industry is increasingly searching for ways to improve efficiency, especially in terms of getting products to market faster.

CEOCFO: *What should people take away when they read about Health Decisions?*
Dr. Rosenberg: The basic message is that there is a far more efficient and less risky way of developing drugs than the way in which most people do it today.

BIO: Dr. Rosenberg has been involved with design and execution of pharmaceutical development programs for more than 25 years. He currently focuses on utilizing new technology and processes to improve efficiency and quality in clinical research. Under Dr. Rosenberg's leadership, Health Decisions has won numerous awards for innovation and growth. Such honors include the 2014 Award for Innovation in Clinical Research from the leading professional organization in the field, the Association of Clinical Research Professionals. Health Decisions also won the 2013 CIO 100 Award from leading technology publication *CIO* for utilizing technology to create true business value through Health Decisions' innovative Agile Risk-Based Monitoring+. In addition, Dr. Rosenberg was named a 2013 Health Care Hero Innovator/Researcher by the *Triangle Business Journal* in recognition of his quest to improve the efficiency of clinical research. Earlier awards include the Cisco Growing with Technology Award for "technology that promises to change the way a major industry works."

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