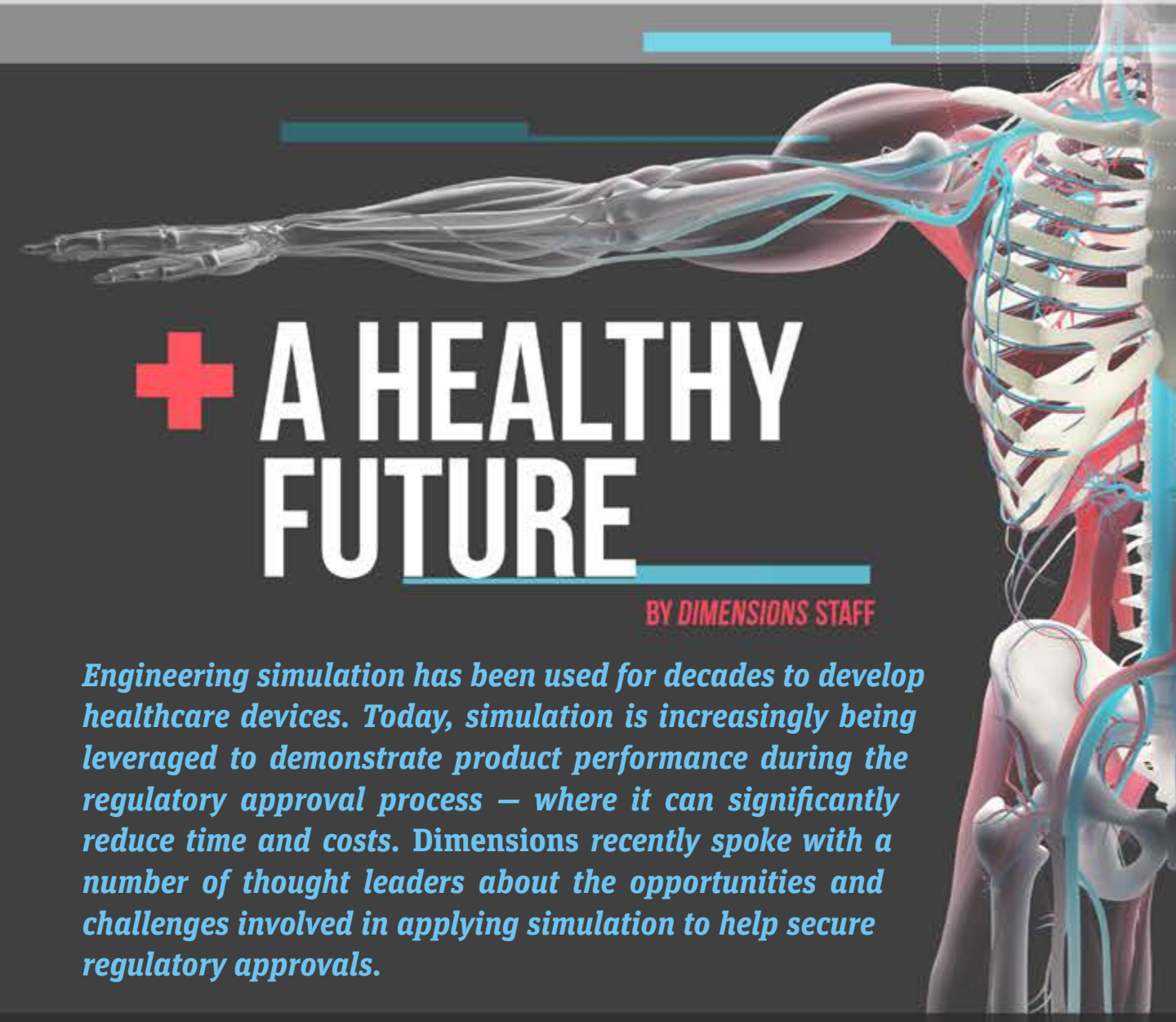


A HEALTHY FUTURE

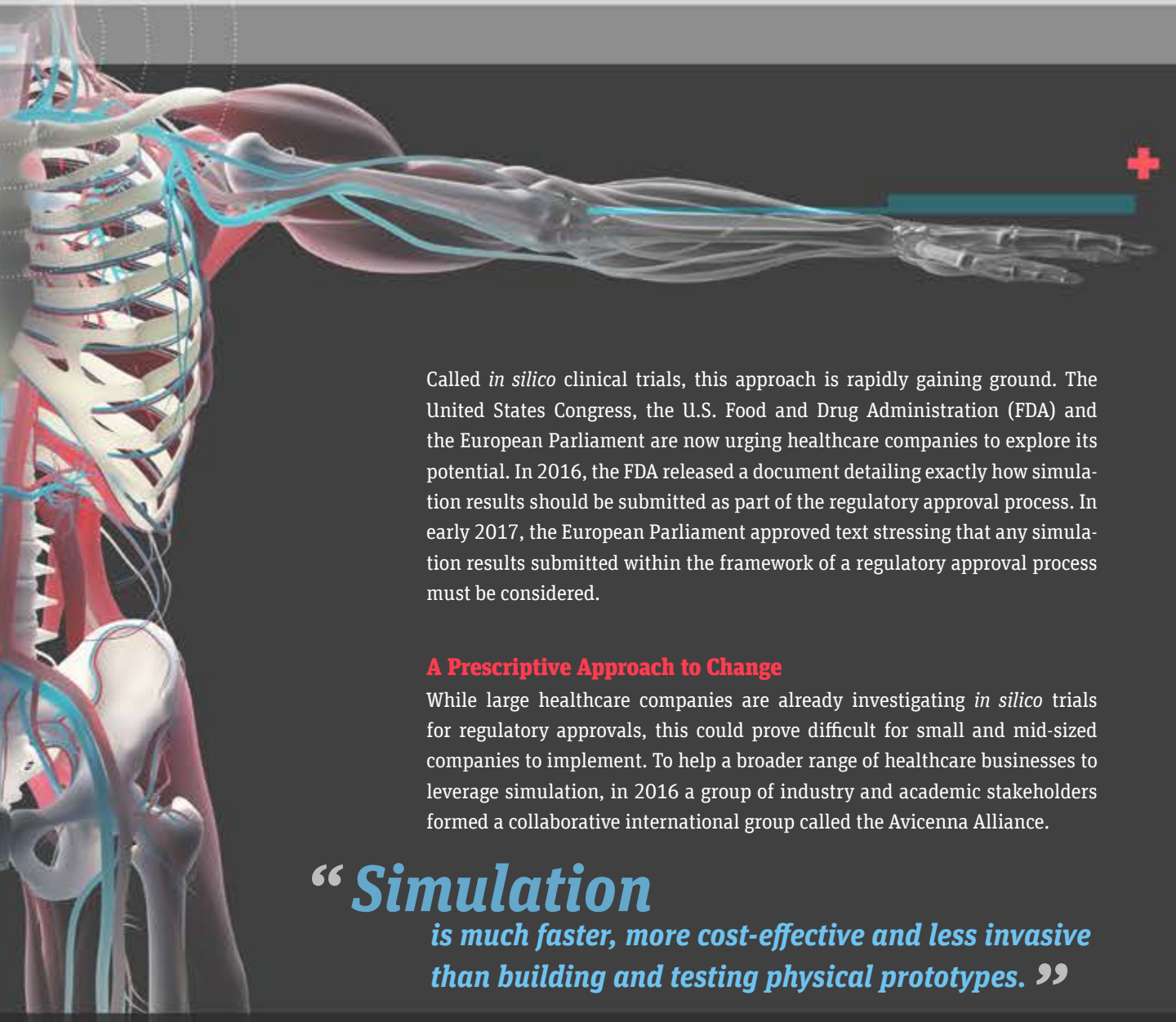
BY DIMENSIONS STAFF

Engineering simulation has been used for decades to develop healthcare devices. Today, simulation is increasingly being leveraged to demonstrate product performance during the regulatory approval process — where it can significantly reduce time and costs.* Dimensions *recently spoke with a number of thought leaders about the opportunities and challenges involved in applying simulation to help secure regulatory approvals.

While all product development processes are rigorous, time-consuming and resource-intensive, this is especially true in the healthcare industry — where devices have the potential to impact the well-being of millions of patients. For decades, engineering simulation has helped reduce the time, cost and risk involved in designing these devices. By engineering and testing patient solutions in a virtual design space, healthcare companies can propel products to the launch phase much faster, and with a higher degree of confidence that they will perform as expected in the real world.

By building 3D models of products and the human body in a virtual design environment, healthcare product developers can test and verify performance, using simulation and digital exploration to make modifications quickly and easily. Simulation is much faster, more cost-effective and less invasive than building and testing physical prototypes.

However, product development is only the first step in launching innovative healthcare devices — which must next undergo a lengthy process to secure regulatory approvals from government agencies. Historically, simulation has been largely ignored during this phase. However, healthcare companies and regulatory agencies alike are now recognizing that, because it can replicate and demonstrate the way devices will actually perform under real-world conditions, simulation is critical to support the regulatory approval process.



Called *in silico* clinical trials, this approach is rapidly gaining ground. The United States Congress, the U.S. Food and Drug Administration (FDA) and the European Parliament are now urging healthcare companies to explore its potential. In 2016, the FDA released a document detailing exactly how simulation results should be submitted as part of the regulatory approval process. In early 2017, the European Parliament approved text stressing that any simulation results submitted within the framework of a regulatory approval process must be considered.

A Prescriptive Approach to Change

While large healthcare companies are already investigating *in silico* trials for regulatory approvals, this could prove difficult for small and mid-sized companies to implement. To help a broader range of healthcare businesses to leverage simulation, in 2016 a group of industry and academic stakeholders formed a collaborative international group called the Avicenna Alliance.

> *"Simulation is much faster, more cost-effective and less invasive than building and testing physical prototypes."*

Named for the Persian philosopher and scientist who is often considered the founder of modern medicine, the Avicenna Alliance was created by four founding members: ANSYS, a developer of simulation software; medical device manufacturer Medtronic; consulting group Rohde Public Policy (RPP); and the Virtual Physiological Human (VPH) Institute, a European initiative that aims to enable collaborative investigation of the human body as a single complex system. Today the Alliance has incorporated other healthcare stakeholders, including private companies, lobbyists, consultants and medical experts who are committed to the use of simulation for regulatory approvals.

Adriano Henney, secretary general for the partnership, holds a Ph.D. in medicine and worked for years in pharmaceutical and biological research before helping to form the Avicenna Alliance. He first became passionate about modeling devices and the human body while working for AstraZeneca, establishing one of the first Systems Biology departments in the industry. He subsequently led a collaborative, government-funded study on liver

dysfunction. "Modeling a healthcare device inside the human body, and looking at interactions in a simulated environment, just makes sense," notes Henney. "It reduces costs, it saves time and it minimizes the impact on human patients. The potential benefits of using this process over traditional clinical trials are enormous."

"The only problem is that this idea is so new," Henney continues. "Private companies, researchers, government regulators — we're all working to understand how *in silico* trials can be implemented consistently on a global basis. That's why we formed the Avicenna Alliance, to create a bridge between all the stakeholders, inform policy decisions and begin to articulate a structure for leveraging simulation that everyone can agree will produce the highest-quality results."

A Prescriptive Approach to Change

One of the Avicenna Alliance's most critical activities is working with policymakers around the world to educate them about the benefits of *in silico* medicine, so they can make informed decisions as they draft new regulatory guidelines. James Kennedy is associate director with Rohde Public Policy Group, which serves as the secretariat of the Alliance and leads this effort.

"It's very unusual for a consultancy to invest heavily in a scientific topic," points out Kennedy. "But if we can take the same technology that Formula 1 carmakers use to develop fuel injection systems — and apply it to optimize blood flows inside the human body — why wouldn't we want to do that? Advanced modeling technology opens up so many doors and holds the potential to improve the health and well-being of millions of people."

Kennedy regularly meets with both government regulators and healthcare executives to promote the need for practical guidelines for the use of *in silico* clinical trials. "The policy structure we have today simply can't take the weight of all these new *in silico* approaches," states Kennedy. "Policy needs to evolve along with technology."

Henney notes that legislators and regulators are extremely enthusiastic about healthcare simulation, which supports the general trend toward patient-specific treatments and personalized medicine. "I think everyone realizes that customized treatment approaches represent the future of the healthcare industry," he says. "If we can use simulation and modeling to verify not just that a device works, but that it works for a specific individual, we are now taking product safety and confidence to a new level. We can design devices aimed at a specific patient. This represents a quantum leap in quality of care, which can reduce overall treatment and insurance costs significantly."

Diagnosing and Meeting Technology Needs

In addition to supporting the development of clear legislation and regulatory guidelines, the Avicenna Alliance is working to ensure that user-friendly simulation technology is available to a new group of healthcare customers. As a founding member of the Alliance and an industry leader in simulation software, ANSYS is spearheading this effort.

"Simulation is a standard practice in developing healthcare products," says Thierry Marchal, industry director for healthcare at ANSYS. "To begin employing simulation as part of the regulatory process, most businesses simply need to bring their simulation experts together with their regulatory experts — and investigate how their efforts can be combined."

In Silico Trials: Getting Started

To help small and mid-sized healthcare companies capitalize on the benefits of* in silico *trials, Adriano Henney and James Kennedy of the Avicenna Alliance offer these practical guidelines:

+ Identify the simulation experts within your company. "Chances are, someone in your product development organization is already using engineering simulation to model products," Henney says. "Find out who they are, and discuss integrating the existing results into your existing regulatory approval process."

+ Explore opportunities for collaboration beyond your own organization. "By partnering with companies who are further along in the *in silico* journey, you can make faster progress and benefit from the lessons they've learned," notes Henney.

+ Open a dialogue with local regulatory officials. "Many businesses view government agencies as adversaries, when in fact they can be valuable partners," Kennedy states. "Because simulation is still a relatively new topic for regulators, they are eager to learn — and to partner with healthcare companies to advance this practice."

ANSYS partners with technology startups like Promeditec to develop specialized apps and portals that help integrate simulation into accepted clinical trial workflows (see sidebar, "Promeditec: Facilitating *In Silico* Trials"). "By identifying and collaborating with innovative companies like Promeditec, ANSYS simulation software is placed into the hands of healthcare specialists who already require regulatory approvals," explains Marchal.

"We're not suggesting that *in silico* trials will completely replace traditional clinical trials in the short term," Marchal adds. "But, to remain competitive and begin to accelerate the approval process, healthcare companies must define new practices for sharing simulation data and establishing simulation expertise outside of the product development function."

While the Avicenna Alliance was founded in 2016, this collaborative effort is already making great strides in promoting the use of simulation for regulatory approvals. This could mean significantly reduced healthcare costs, more personalized medical treatment and improved well-being for patients worldwide.

Promeditec: Facilitating In Silico Trials

Based in Milan, Italy, Promeditec is a technology startup that supports healthcare companies in executing clinical trials — including the management of data, processes and workflows, and documentation for regulatory compliance. To add value, Promeditec has partnered with ANSYS, the industry leader in simulation software, to support its customers' use of *in silico* trials for regulatory compliance via an interactive website called inSilicoTrials.com.

"inSilicoTrials.com represents a new concept for the small and mid-sized companies we serve," explains Luca Emili, CEO of Promeditec. "Our goal in collaborating with ANSYS is to create an easy, cost-effective tool that enables them to capitalize on simulation technology and model their healthcare products in a low-cost, risk-free virtual environment."

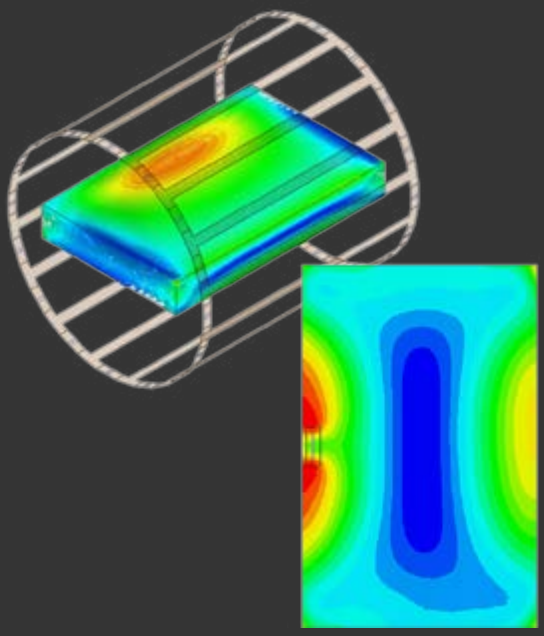
Promeditec hosts ANSYS software in the cloud, and has also devised an extremely user-friendly app that gives customers easy access to the power of simulation — while also offering compatibility with the company's apps for data management and other functions.

Already, Promeditec customers have begun realizing the benefits of *in silico* modeling to support their regulatory approval processes. For example, the first application publicly available on inSilicoTrials.com is a tool for magnetic resonance imaging (MRI) safety analysis for implanted metal stents. The simulation, developed by the U.S. Food and Drug Administration (FDA) as part of a joint five-year collaborative agreement with Promeditec, is accessible through a user-friendly web interface and runs in the cloud. This tool will provide users with a report that follows FDA guidelines and is suitable to be submitted for regulatory approval.

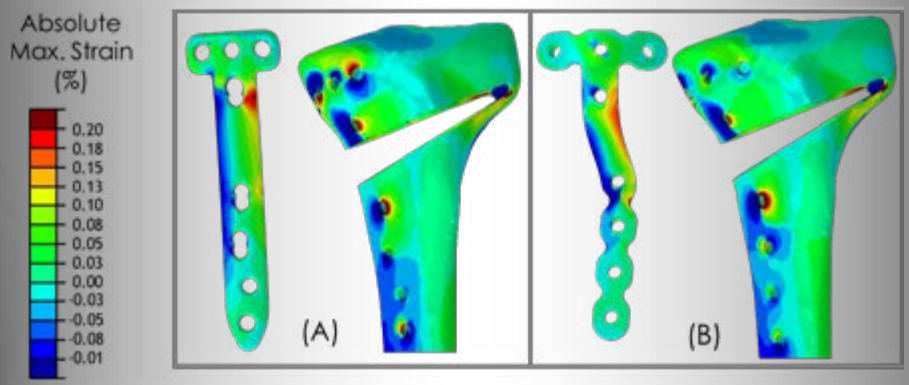
Another example is a specific web process developed for the simulation of a novel, patient-specific orthopedic device for treating early stage osteoarthritis of the knee. The aim of the *in silico* trial is to evaluate the safety equivalence between a well-established existing generic device and the novel patient-specific device, ToKa, which was designed by a collaboration between the University of Bath, the Royal Devon and Exeter Hospital, and 3D Metal Printing Ltd.

Based on the 3D anatomy of a cohort of 30 patients, a multi-objective robust design optimization and multi-criteria decision analysis was implemented, while the computational time required was reduced. The simulation report will be part of the regulatory submission package for the new medical device.

This could mean significantly reduced healthcare costs, more personalized medical treatment and improved well-being for patients worldwide.



MRI safety simulation for implanted metal stents



Simulation of the original device for treating osteoarthritis of the knee (A) and patient-specific device (B).