

February 17, 2009

EDC, CTMS, IVR

i3Cube: Trial Swiss Army Knife

“Give us the tools and we will finish the job,” Winston Churchill wrote to a friend. The year: 1941. World War II was just getting started.

In 2009, thousands of web-based programs are sweeping over the entertainment, financial, and publishing industries. Do today’s clinical trial professionals have the tools to finish the job? Do they like the tools they possess?

Contract research organization (CRO) i3, it’s fair to say, has used the major tools for clinical trials. And the firm feels the equipment in the industry’s eclinical toolbox is not yet perfect. So it started from scratch. After spending two years to develop a web application, i3 has begun showing the technology to customers and the media. i3Cube, as it’s called, is something new under the clinical sun. It’s a major investment in software by a services organization.

If sponsors warm to i3Cube—a large if—it will be a paradigm-breaking approach. The system is now in the final stages of testing. “This looks at the process holistically,” says Joe Tetzlaff, i3’s chief technology officer. “It is genuinely novel and without precedent.”

Single Sign-on

For sponsors, i3Cube gives sponsors unusually comprehensive, end-to-end views of a study. It could eliminate the need to ask a CRO for a quick update on a minor aspect of the trial. Sponsors will be able to see what’s going on for themselves. With the right privileges, it’s possible to drill into data from any trial, site, patient or see roll-up reports that some CROs would struggle to assemble from 3-4 major systems that are inside i3Cube. There’s just one password needed.

The company says i3Cube can handle most of the data and process-related work in any clinical trial. There are systems for email, contracting, patient and site recruitment, clinical data management, electronic data capture (EDC), document management, project management, trial management, site payments and (later

this year) randomization. It’s an unusually broad eclinical suite. i3Cube has been added to the ClinPage list (which you can review in web and PDF formats), which includes 20 offerings from technology specialists and CROs.

Demonstrating the web app for a reporter, Tetzlaff shows attractive popup dialogue boxes and HTML email notices that would be sent even before an investigator is officially signed up for a trial. i3’s clinical trial experts (people like Cynthia Verst, whom we interviewed last year) were closely involved with the design and refinement of i3Cube. “We followed a very disciplined development process to meet Cindy’s vision,” Tetzlaff says. “We’ve tied our expertise in clinical trial execution into the web experience of the application.”

Part of the end user’s day-to-day experience with industry software, especially clinical trial management systems (CTMS), has been the opposite of most web apps: exasperation. i3 is aware that some people in the clinical trial trenches have given up on an employer’s CTMS. Instead, they harbor secret Excel spreadsheets with crucial, frequently-accessed data. For its part, i3 says it tried to design an application that would be easy enough to use that the secret-spreadsheet problem would begin to disappear. “We want to retire the spreadsheet and the isolated silos of information,” says Tetzlaff.

No Charge

He then displays different views of a trial by role. None would require squinting or training. Says Tetzlaff: “It’s designed to support their work activity. It is not a technology [for some other industry] that was modified to support what they do.” If the same person has multiple roles at different times, i3Cube can accommodate that.

The i3 technology is free. Or, to say it another way, the cost will be included in the trial budget. Naturally, i3

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personnel and sponsor personnel will be using the system. What about additional CROs? “We would examine on a case by case basis who the sponsor needs to participate,” Tetzlaff says. He says there is no technical reason that another CRO or functional service provider could not be given access to one part of the system.

i3Cube constitutes a rethinking of the prevailing approach today, in which drug and biotechnology companies agonize over selecting the best supplier for System A, and then connect it to the best provider of System B, and (if time and money allow) tie that to something else. The euphemism describing the linkages between such systems is “integration.” That was required by the sponsor community’s desire to pick the best possible software for every trial. The success of i3Cube will depend on a certain number of sponsors reassessing the merits of the “best of breed” philosophy, which works well for many companies today.

For other firms, the problem is that trials are getting more complex. Combining more than two eclinical systems, even from the same technology supplier, can be a risky and costly undertaking. Integration is generally only suitable for the largest, most sophisticated organizations.

No Integration

The i3Cube system, in contrast, is post-integrationist. It’s an electronic environment that also manages faxed and paper case report forms. But it is fundamentally different in that all data from a variety of subsystems are in a single database, at a single URL. i3Cube stores information from more of the clinical trial life cycle, from multiple versions of the protocol, to the investigator’s contact information, to the final submission to regulatory authorities. The i3 vision is akin to that pioneered by eTrials or DataTrak, in that it offers a unified system with multiple components.

But the new offering encompasses more functionality and a cleaner cosmetic look than competitors. For starters, i3Cube can draw upon data from its corporate parent, UnitedHealth Group, which insures 26 million Americans. That will allow the feasibility of clinical trial protocols to be assessed and patient and investigator recruitment to be managed within the i3Cube system.

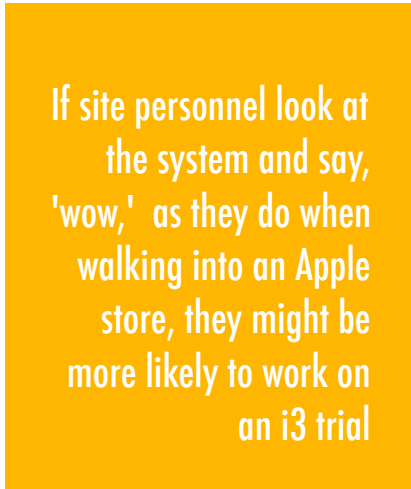
Then there’s the program’s sleek, modern interface. The merits of the i3Cube interface will be proven in the marketplace. But it’s easy to look at. In the consumer sector, it is risky to understate the importance of a clear, intuitive interface. The Apple franchise is built on one. The absence of an elegant interface has come to doom certain portable music players and smart phones.

Sleek Typography

In a world in which investigators are weary and discouraged by (among other things) remembering how to operate several eclinical systems at once, the i3Cube interface could be a competitive advantage. If site personnel inspect it and say “wow,” just as people do when walking into an Apple store, they might be more likely to work on an i3 trial. The company says it tried to sweat the details for two groups of users: those who use the system intensively, all day long, and those who log in sporadically, every few months, and just want to enter or retrieve a bit of data.

By appearances, to a refreshing degree, i3Cube is a true Web 2.0 application, the first of a new

generation of eclinical tools. There are sleek lines and subdued gray colors. The text is stylish, attaining a higher level of sophistication than is typically found in HTML-based eclinical applications pioneered in the late 1990s. i3Cube’s fonts could be especially refreshing to those required to use Microsoft Windows Internet Explorer. The world’s most popular browser has lately improved, but is still packed with bad fonts, violations of web standards and undocumented display-related gotchas that make it impossible to render the same content consistently across different brands of computers or operating systems.

A yellow rectangular callout box containing white text.

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i3 took a different approach. It used Adobe Flex, which makes browser nuances a distant memory. Flex is a platform for creating interactive web applications. (Without knowing it, you're probably already using the fruits of Flex on highly interactive sites.) Web apps built in

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Flex display identically on every web browser. In i3Cube, Flex helps the clinical and project reports look more professional than what emerges from most websites or even a few desktop programs.

The new system was conceived, from the outset, to support a regulated industry.

Documents and other data can be exported into formats for Documentum, trial master files, SAS, and the Clinical Data Interchange Standards Consortium (CDISC). Documentum is a key part of how the i3 data are stored behind the scenes but i3 customers will not need to purchase it themselves. By relying on industry standards, and understanding the importance of documents, i3 may have been inspired by the products and services of Octagon Research.

A Different Experience

Tetzlaff insists that the large number of things that i3Cube is doing will not impair the performance for end users. Screens will refresh quickly, he says. "We have done significant load testing on i3Cube," he says. "We're aware of the performance issues of other applications as we use them ourselves. The i3Cube experience is dramatically different."

Indeed, i3's goal is to make life easier for every major category of worker bee who may touch a clinical study. The company is familiar with the process of trials and created software to reflect the industry's workflow. The idea is to be able to start with a protocol, build the necessary case report forms, find the sites, resolve the queries, pay the sites, generate needed reports and, if necessary, publish the regulatory documents or burn DVDs for archiving purposes. All in i3Cube. No single

element of what i3Cube can do is unique. But in combination, its linked elements could spare a sponsor significant investments in multiple systems that are now built from scratch one trial at a time.

Tetzlaff doesn't telegraph the timing, or even the existence of a so-called "mobile" version of i3Cube, which would run only on a cellular phone. But that is clearly something the company is considering. "We're anticipating that a mobile device will be in the future of a clinical research associate going to a site," he says. "It will be very natural for them to have questionnaires on a mobile device."

Impressive as the i3Cube system is, there are missing elements. The randomization engine is still being refined, and slated to be added later in 2009. There is no visibility across multiple trials. There is only the ability to manage the communications around adverse events, not the time-critical submission of safety data or Medwatch forms. And sponsors inclined to use electronic patient-reported outcomes will have to acquire such systems separately. i3 views the system as a work in progress, and likely to be continuously enhanced over time.

So the degree to which sponsors warm to i3Cube will be fascinating to observe. i3's ability to win trials from competitors could inspire other CROs to invest in Web 2.0 programs in a bid to leapfrog over well-established vendors offering single technologies. Such CROs might attempt to bypass the first generation of clinical trial software in the same way that automobile manufacturers eventually moved beyond carburetors. After being invented by a gentleman named Benz in 1885, carburetors had a good run, until 1994 or so. Then they were done. Things on the web are moving a bit faster. —by **Mark D. Uehling**

For more information on i3Cube or i3 Global, visit:

<http://www.i3global.com>