

Profile: Statistical and Graphical Analysis and Reporting Company

Insightful, Life Sciences Division Seattle, Wash.

An interview with Michael O'Connell, director of Life Science Solutions Group

What is Insightful's background?

Insightful is a maker of statistical software. Our flagship product is S-PLUS, which is widely used by statisticians and is the dominant software used in graduate school by people developing their own statistical methodology. We are complementary to SAS, which is a statistical analysis system with robust data management tools. We do some data management, while specializing in statistics, graphics and reporting. So, the technologies work well together.

We've been around for 20 years. Our first release of S-PLUS was 1986. The S language came out of Bell Labs in the early 1980s. Doug Martin, who founded our company, was a professor of statistics at the University of Washington, and he did a number of resident sabbaticals at Bell Labs, collaborating in the development of the language. Doug made a deal with Lucent to be the exclusive commercial outlet for the S language and we funded the statistics group at Bell Labs for a number of years to continue development of the language.

Insightful has had a couple of name changes over the years. We were originally called StatSci, or Statistical Sciences. Then we were acquired by MathSoft in the early 1990s. We spun back out of that company in 2001 and that's when our name changed to Insightful. We purchased the S language from Bell Labs in 2002. When we were licensing that technology from Bell Labs, it was difficult to build solutions on top of the language for various legal reasons. Once we acquired the technology, we've

been able to build freely on top of it and hence these new Life Science Solutions. It's the same crew at Insightful that was at the original Statistical Sciences company.

What solutions do you offer in clinical drug development?

In the life sciences area, our focus is on clinical drug development where we have solutions for clinical graphics, clinical review, clinical trial design, safety data analysis and clinical reporting in support of clinical study reports and registrational documents submitted to the FDA. It's a regulated environment and our software can be readily validated in the customer environment to support clinical development. We have some solution components that actually support that validation process as well. In late stage, we offer statistics and graphics for data analysis, clinical review and submission reporting. In the early stage, we offer modeling and simulation and PK/PD reporting. We offer trial design and safety analysis solutions across both early and late phases.

Our clinical review solution allows researchers to view data interactively, patient profiles and so on; but it also allows them to bring in quite sophisticated analytics for identifying safety signals earlier. We have some Bayesian modeling techniques and a number of other innovative machine learning methods. These are useful especially in the early phases when you don't have a lot of data and you're trying to get as much information out of it as possible.

Year founded: 1986

Employees: 112

Contact: Michael O'Connell/
Yonnie Tauschek

Telephone: (919) 740-1560/
(206) 802-2237

Email: moconnell@insightful.com/
taushek@insightful.com

Web site: www.insightful.com

Predictive modeling works well in that setting. We have tools supporting such modeling and reporting on both the safety side and the efficacy side. There's a lot of action right now in trying to make the most of data as it starts to come in on a trial—to detect dose response, get the right dose for use in later stages or to detect safety signals early in the process.

Our Life Science Solutions, in particular Insightful Clinical Graphics, which is the focus of our current release, integrates some new Web 2.0 concepts to create collaborative working environments. There's a lot of re-inventing of the wheel that goes on right now during clinical drug development: people are re-creating code as well as reports in different trials or even within the same trial. We're introducing concepts in our software so that user-generated content can be re-purposed, re-styled and re-used across the software end-user community. We have the tools, components and workflows for automating many manual processes around analysis and reporting. Insightful Clinical Graphics is a point-and-click graphics solution that simultaneously generates S-PLUS code that can be run in a 21CFR11-compliant environment to produce graphs that can go into clinical study reports, registrational submissions and so on.

page 5



**Cardiovascular
Clinical
Studies, Inc.**

Are you planning a heart failure trial?

Since 2000, CCS has worked on 21 clinical trials in acute decompensated and chronic heart failure, enrolling over 7,000 subjects at over 700 investigative sites in the U.S., Europe and South America. Contact CCS, a full service, academically oriented cardiovascular research organization at www.ccstrials.com

Profile (continued from page 4)

Data capture has been revolutionized over the last five or 10 years in the industry. There are more streamlined and standardized processes in place around data capture and management, but downstream of that the analysis and reporting lingers along a bit. We are introducing some modern software concepts into that world to enable rapid graphical analysis and reporting, and interactive graphical review.

Who uses your products?

We have folks who want to keep their hands on the data and interactively review the data as it comes in, looking for safety signals. We have medical monitors looking to clean up the data, looking for potential outliers and queries. We have statisticians and researchers using our interactive Clinical Review and the Clinical Graphics solutions to produce graphs for safety review, clinical study reports, registration submissions, scientific presentations, publications. Review graphics and report graphics are fundamentally different. Review graphics are interactive with not many rules around formatting. Report graphics have lots of formatting rules and publication requirements. The nice thing about our software is that all the graphics come out of the same code base, so the same S-PLUS code can be used to create an interactive graph as a publication report graph. Those graphs can be re-purposed in a variety of environments with minimal fuss.

Graphics is our beachhead and that's what a lot of folks use us for—graphical analysis, reporting, and interactive review. But we also are a full-blown statistical engine and in fact, historically and even currently, when a new statistical method surfaces, it typically surfaces in our software first. The S language enables a rapid and flexible scripting of modeling

and simulation methods. So, by virtue of that, most statistical methodology comes out first in S-PLUS or R, which is the open source dialect of S. These days, R and S-PLUS are used in the academic setting.

What challenges do you face?

One challenge we're facing right now is that the industry is on a hair trigger with regard to safety. It seems like these days an academic can write a paper and get it published somewhere and the FDA slaps a black box warning on the drug as a result of this. So, some of our big customers have been doing some re-structuring. The market itself is also a bit challenging, with thinner drug pipelines and generic pressures. But such a market does offer opportunity as well. If a customer has to respond to a situation like a potential black box warning, it is faster for them to pull up our software to look at their data and quickly generate some graphics and reports. Our safety solution, graphics and reporting, and our interactive clinical review are all tools that can help in the safety analysis, either in a preventive/proactive setting or in an emergency-response mode.

Describe Insightful Clinical Graphics.

Insightful Clinical Graphics' initial thrust is around clinical graphics for exploration, presentation, publication and submissions: all of the different functions where graphics are used in clinical development. In implementing this solution, we've put in place a framework for re-purposing so that different folks from different functional areas can create and share graphics, thus enabling end-users to benefit from all the talent in the social network of their organization, while minimizing multiple re-workings of similar graphical analyses. You can save your work to

include the user interface settings along with the S-PLUS script representation of the graph. You can tag these with searchable metadata when you save the graph, for example the study protocol and graph description, which enables re-purposing and mash-ups of the graphs by other users of the software. Someone else working on a different trial can come in and say, 'I want to draw a shift plot for these lab values. I want to see how these lab values are changing over time, let me search on shift plot.' They might then realize that someone else in another part of the company already has a graphic for that. They can then bring up this saved graphic with the user-friendly interface settings already included by the other person, and with S-PLUS script code that is ready to be run in a production-compliant environment. They can put their data into it and see what this graph looks like on their data. It's a very short operation and they have a graph for their clinical study report, scientific presentation, publication, and exploratory meeting with their team. We've introduced these Web 2.0 ideas of re-purposing and social data analysis with our Insightful Clinical Graphics solution. This re-use of graphs and software-generated S-PLUS scripts is going to be an underpinning for us as we bring our other solutions into this framework—interactive clinical review, trial design, safety analysis and so on.

What are your plans for growth?

Our plans for growth are to continue to evolve all of our solutions and bring them into this collaborative communication framework that we've introduced with Insightful Clinical Graphics. We see exciting times ahead for us as we consolidate and build our solutions in this new framework.



Emerging CRO's Increase Your VALUE!

Strategies for:

- Accelerating Sales
- Capital Accumulation
- Maximizing Enterprise Value
- Cost Effective IT Applications

Nichol Clinical Technologies Corporation
 F. Richard Nichol, Ph.D. • CRO Innovation Since 1975
949.760.5460 Email: frnjr@msn.com
www.nicholclinical.com