

seeing is BELIEVING

There is a growing pressure in today's climate for pharmaceutical companies to find tomorrow's wonder drugs and dominate the major market segments. Recently, they have also been under attack for poor research productivity, for failures in drug safety and for off-label marketing. The use of visual analysis could do much to improve their performance in research and across all areas of activity.

The pharmaceutical industry makes huge investments in time and resources to bring new drugs to market – a process that takes, as we know, an average of 15 years and can cost up to \$1 billion. As a result, pharmaceutical companies must look for more accurate ways to predict a new drug's chances for success, both during research and in development, in order to reduce time to market for the winners and minimise spending for the losers. Thus vigilance also needs to extend to the period after a drug is on the market – a time when adverse events might lead to the recall of the product, decrease in public confidence and large financial losses after heavy investment.

Advances in technology have promised better ways to evaluate drugs through the research process. High throughput and high density technologies have generated more data at all stages and yet the value of this data will be lost without the right tools and processes for analysis and decision making. Drug companies will continue to face tough competition and ongoing pressure from generics, expiring patents, compound attrition, and shrinking drug pipelines. Winning in such a highly competitive environment requires unlocking the hidden value of a pharmaceutical company's data and the power of its scientists to ask and answer the right questions.

Unfortunately, conventional data analysis is too rigid. The methods are often discipline-specific so that information cannot flow freely between such disparate groups as chemists, biologists, clinicians and statisticians. Too often, pharmaceutical companies rely on static reporting tools that reveal historical trends but restrict forward thinking.

To help companies respond more effectively to their data, analysis should be:

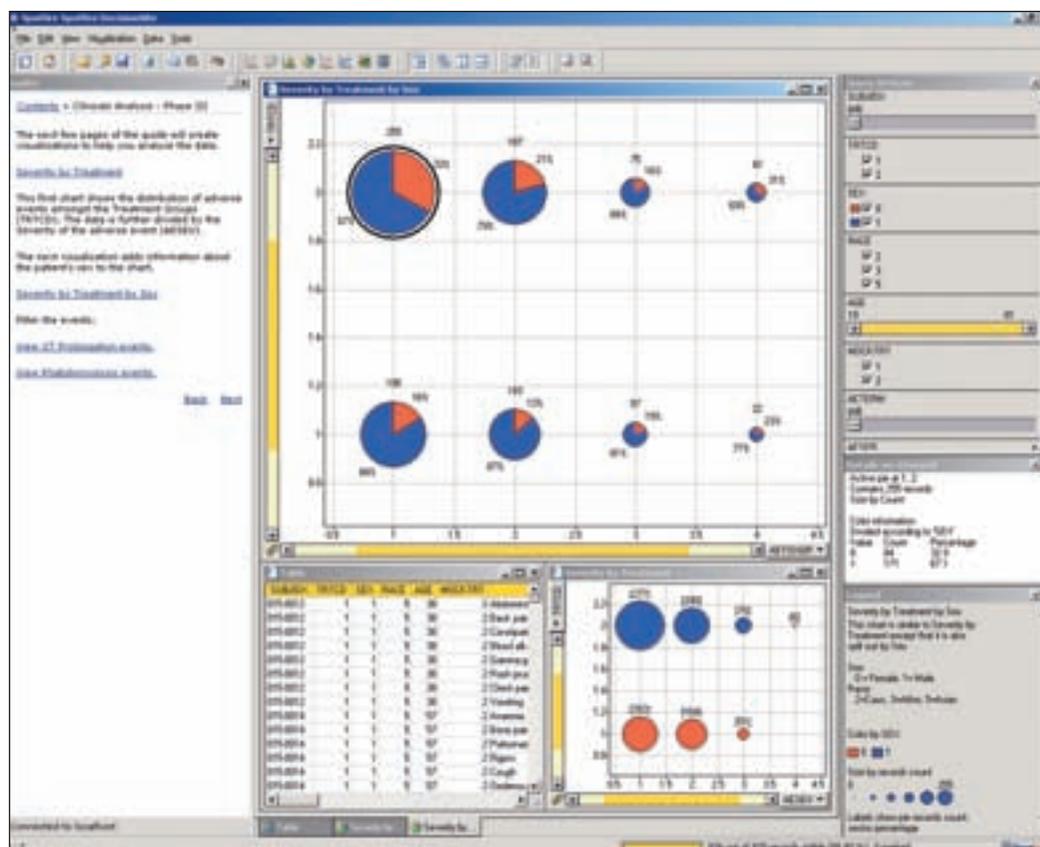
- Visual – so that results can be seen and understood and by all parties.
- Interactive – so that researchers ask the questions that lead to breakthroughs.
- Guided – so that all users can benefit from the expertise of their colleagues.

More and more pharmaceutical companies are therefore turning to interactive visual analysis, in which data can be displayed in an array of linked, interactive plots that dramatically increase insight and understanding of complex data. With this technology, important data trends jump off the screen so that problems, opportunities and factors that contributed to the final results can be identified quickly.

The best analytical tools allow any researcher to extract and merge up-to-date data from technical

By Dr Christopher
Ahlberg

Informatics



and corporate sources with a few clicks. They also have the ability to guide less familiar users through the process of conducting analysis. With such 'guided analytics' users can formulate various 'what if' scenarios and so make faster progress. Companies such as Spotfire, Oracle and Hyperion are all major players in this analytical marketplace.

Closing the gap

Pharmaceutical R&D organisations have shifted from loosely connected linear business processes to interdependent ones, critically reliant on information sharing. Therapeutic project teams need to incorporate and analyse data from chemists, biologists, clinicians and statisticians; and iterative cycles of compound library design involve a number of groups each with its own particular expertise. A critical gap exists between the requirements of forward-thinking organisations and the analysis tools available to them. Analytical tools for drug discovery are often hard to use and discipline-specific, making them difficult to re-purpose for new analytical challenges, and unsuitable for information and methodology sharing. Query and report business intelligence tools can be easy to use and deploy to large organisations, but they do not have

sufficient analytical power and cannot respond to change without time-consuming IT intervention.

Multi-disciplinary research and development teams that need to synthesise ideas and information across the diverse areas of target identification, screening, ADMET and drug safety, have not been able to turn to their traditional analysis tools for help. Until now, they have often trusted their most important decisions to the lowest common denominator technology by filling the analysis gap with spreadsheet-based applications, sacrificing best practices and scalability for simple convenience.

Visual analytics is the must-have technology that provides the tools for easier communication and better collaboration among the various disciplines that can see, interact and be guided along the way that can only lead to improved drug safety.

Improving drug safety

Visual analytics can also be applied for the earlier detection of potential safety problems, such as uncovering an association between an adverse event and a particular demographic subset of patients. The ability to browse and filter the data rapidly permits users to find answers to questions that may never have been asked in the past.

Beyond R&D

A great advantage of flexible visual analytics is that they can be applied across the range of business processes. Research and development may be the heart and soul of a pharmaceutical company but its analytics can be effectively applied to other business units, such as sales and marketing.

In sales and marketing units there is a need to understand and respond to changing circumstances, such as external market influences and competitive forces. With visual business analytics, these parts of the organisation can rapidly collate critical data without the intervention of an expert in information technology. Furthermore, with a finger on the pulse of an evolving market, the sales and marketing team can visually demonstrate trends and new market opportunities to the R&D team.

Similarly sales teams can use visual analytics to their advantage. In a highly competitive market, sales representatives need to be directed to the leading healthcare professionals in each particular therapeutic area. Just as R&D personnel can use visual analysis to make better use of research data, so their sales and marketing colleagues can use it to understand physician segmentation and targeting, sales force profiling and product line performance. Analytical applications easily fit into the sales and marketing process as well as incorporating the company's proprietary analysis tools, such as algorithms, and so give marketing analysts a powerful information advantage from existing data.

Visualising competitive advantage

Applying analytics in R&D is not a novel concept. However, the ability to use the same techniques across the range of an organisation's activities presents a new opportunity for pharmaceutical companies to gain not only an information advantage but also a competitive advantage. Ease-of-use and interactivity allow pharmaceutical companies to model an array of theoretical scenarios so that drugs can be brought on faster with improved safety. By broadening visual analytics beyond the R&D process, companies can gain valuable insight in other business units and so improve performance on all fronts.

Tularik is a biotechnology and drug discovery company based in San Francisco, California, and focuses on developing therapeutics for cancer, inflammatory and metabolic diseases. Like any drug development company, Tularik performs clinical pre-marketing risk analysis on drugs passing through clinical studies. The goal is to identify adverse events and changes in laboratory values,

physical findings and vital signs that might be related to the drug in question. It is essential to Tularik's bottom line that adverse events are identified early in the development process to avoid the cost of further development. Early detection enables analysts to design study protocols and assess risk/benefit status before the company has invested significant funds on a particular drug. With timely and accurate analysis, drugs with an unfavourable risk/benefit assessment can be discontinued as soon as possible. What is more, drugs with defined risks that still offer favourable efficacy can be more appropriately managed, for example by controlling drug dosage and method of administration while avoiding use in at-risk populations.

The challenge

Tularik's drug development efforts have progressed to the point where the company has a dozen or more clinical trials in progress. This trend has significantly increased the workload for clinical pre-marketing risk analysis. James Buchanan, the firm's lone analyst and director of drug safety and surveillance was finding it difficult to keep up. Because it was not yet feasible to hire another analyst, Tularik management agreed that a technological solution was in order.

Research into the options highlighted that many commercial packages were not appropriate for clinical safety data analysis and were expensive.

The application that Tularik eventually chose drew data from two main data sources; extracts from Tularik's clinical database, which were prepared as flat files and in the case of data for which extracts had not been developed, spreadsheets that Buchanan created himself.

The visual analytical tools that Tularik uses means that the application can be modified for different phases of clinical trials. In Phase I, for example, there is far more laboratory data than adverse event data, as Tularik looks for relationships between levels of drug exposure and adverse events of changes in laboratory values. Said Buchanan: "You may find that the people who have the highest drug concentration also have the highest level markers of liver damage. Although there are usually relatively few adverse events, you can start to examine the relationship between PK measure of exposure and various adverse events."

Visual analysis allows for multiple factors to be evaluated dynamically using colour-coded scatterplots and adjusting query device sliders on the fly. The tools allow you to explore pharmacodynamic relationships and let you interrogate the data.

Informatics

For Phase II trials, a slightly different set of visualisations and data sets are made available. Phase II trials include more subjects, more adverse events and more laboratory data, but PK measures do not play as large a role as they are generally available for only a subset of subjects. There are also data from multiple groups, either placebo or active drug, permitting comparisons of adverse events between two treatment groups. Here, Buchanan uses visual analysis to evaluate patterns of adverse event frequency subdivided by parameters such as severity, gender, age and duration on therapy.

In Phase III, there is not so much pharmacokinetic data and these trials are characterised by very large patient groups, providing a wealth of adverse event and laboratory data. PK measurements, if done at all, are performed on only a small subset of patients. Instead, the general approach is to do comparisons between treatment groups. In this case, Buchanan uses the application to evaluate data for time-dependent patterns, for example, whether adverse events cluster shortly after dosing or accumulate only after a prolonged duration of exposure.

Added Buchanan: "One of the greatest strengths of visual analytical tools is the ability to see three or more variables at once. One of the best visualisations we use is a 3D graphic of a lab value by a drug exposure parameter (such as Coax or AUC) by the time that lab value was recorded relative to day of dose, which allows you to simultaneously see clustering or patterns of the lab value by exposure and by time. It's quite powerful."

Results

Today, the tools have been helpful in developing adverse event profiles for drugs that support the safety information provided to regulatory authori-

ties, study investigators and study subjects. Being able to analyse the data in more detail makes it more accurate.

Because none of the Tularik drugs have yet reached market, it is difficult to judge return on investment. However, the company has already seen benefits in terms of time savings. Whereas these tools can lead to a boost in profits for pharmaceutical companies, its implementation in clinical data analysis is judged by how much it helps drug companies avoid financial loss. Its ROI will be determined by how many mistakes are avoided and how early they are avoided. Clinical trials cost millions of dollars, so drug companies don't want to have to terminate development of a drug only after conducting multiple trials and incurring that expense. It's an enormous cost in terms of dollars and time.

DDW

Dr Christopher Ahlberg is the CEO of Spotfire, Inc which he founded in 1996 based on his ground breaking research on information visualisation. Dr Ahlberg earned his doctorate from Chalmers University of Technology, has worked as a visiting researcher at the University of Maryland, and has lectured and consulted extensively for industry, academia and military – as well as published and lectured in computer science, psychology, linguistics, biology and chemistry. He has two granted software patents, and multiple patents pending. Dr Ahlberg was named among the World's Top Young Innovators by Technology Review, MIT's Magazine of Innovation in 2002.

ADVERTISEMENT INDEX

Akubio Ltd	73	CEM Corporation	58	Molecular Devices Corporation	37,49,87
BD Biosciences	33	CISBIO International SA	4	ProQinase GmbH	6
Beckman Coulter, Inc	18	CyBio AG	43	Society of Biomolecular Sciences	65
Bentham Science Publishers Ltd	88	ForteBio, Inc	79	SpinX SA	16
Biacore International AB	77	Gene Logic, Inc	IFC-3	Thermo Electron Corporation	34,OBC
BioDot, Inc	8	Genetix Ltd	67	TTP Labtech	21
Biotage AB	61	Hamamatsu Photonics KK	47	Upstate, Inc	40,91
Caliper Life Sciences, Inc	23	IBC USA	IBC		
Cambridge Healthtech Institute	93	Milestone Srl	64		