



Transforming the Drug Development Process

How TIBCO Spotfire enterprise analytics can guide you down the critical path to greater efficiency

In today's drug development environment R&D spending is out-pacing productivity. The pharmaceutical industry is under pressure to stem attrition rates and alter business strategies to account for the fact that fewer blockbuster drugs are going to market. As a result companies will need to run more trials than ever before in order to achieve more drug launches. But the traditional phased approach to drug development does nothing to address time and cost inefficiencies that might offset this. The FDA's Critical Path Initiative was an acknowledgement of the need to commercialize drugs more quickly and economically. But how to do this without slowing down drug development or worse, rush unsafe drugs to market?

One aspect of the solution can be attained by bridging the technological disconnect between discovery and development. As the industry continues its shift toward the "Learn and Confirm" paradigm, it becomes essential to have the right IT tools to improve cycle times between research and development and achieve greater cost efficiency in the process.

This paper will explore the reasons for the need to transform the drug development process and moreover, provide a prescriptive approach to transforming your organization's traditional clinical development process.



Addressing the High Cost of Attrition

According to the Tufts Center for the Study of Drug Development, the average cost of developing a new drug is estimated at \$1.7 billion, up from \$1.1 billion just 5 years ago (factoring in the cost of drugs that fail in testing). Much has been written recently about the reasons for the ever increasing costs of drug development and the decreasing R&D productivity of the industry, as measured by new drug approvals. These reasons include increasing attrition rates and pursuit of new, yet-to-be validated drug targets.

For many companies the effort to improve R&D productivity is now focused squarely on improving attrition rates, because it is one of the biggest factors in the increasing cost of drug development. Finding failures earlier would have the benefit of saving hundreds of millions of dollars in late stage trials and enable the reallocation of that saved money to advance the next generation of more promising drug candidates. However companies are finding that the traditional phased approach to clinical development doesn't cut it in today's environment.

Let's look at what is required to improve attrition rates:

- Companies must take a different approach to development. Drug development can no longer be about sequentially moving a candidate forward. It must be about simultaneously and proactively looking for and mitigating the potential causes of safety risk.
- Informed project teams need to de-risk their candidate earlier in the process. Project teams need better tools to evaluate the risks and benefits of continuing with a candidate or promoting a different candidate molecule instead.
- Scientists must improve the therapeutic areas' understanding of disease biology. This can be done through the analysis of data from previous studies, by combining data from multiple studies, and by identifying, validating and incorporating biomarkers into their clinical research strategy.
- The industry is looking for more targeted drugs rather than a blockbuster, but needs to be able to determine whether or not to proceed with that strategy as early in development as possible.



Reforming Data Analysis and Review Processes

As the industry is confronted with this need for change, data analysis and review processes need to evolve in many different ways. An emphasis on trial subject safety has created a need for earlier access to study data - some companies are developing “real time” safety surveillance systems. Traditionally, drug development teams are used to a long lag time between data collection and data review, as paper records are encoded into database systems, data is reviewed, the database is locked down and the biostats groups generate tabulations and reports for the team. With the emergence of Electronic Data Capture (EDC) and Clinical Data Management (CDM) systems in clinical trials, there is a great opportunity to start reviewing and analyzing data in-stream during a trial – giving development teams an advance opportunity to uncover safety issues in their candidates. This type of safety review and assessment requires different tools and procedures than most pharmaceutical companies have in place today.

For this type of data review, physicians and monitors need to be guided through a series of standard views and reports, and allowed to interact with and explore those reports to generate hypotheses about the safety and efficacy of their drug candidates.

An enhanced need for cross-study analysis capabilities is also imperative. What did we learn in Phase 2 that we should have learned in Phase 1? Did we miss something? What can we learn about disease biology from such a broad perspective? At the same time, it's important to have broad access to trials data within the project team, to allow many people to ask questions and generate hypotheses; and facilitate team meetings where data and hypotheses can be viewed and analyzed collaboratively.

Finally, the concept of translational medicine - putting research data into the clinic, and ensuring that clinical data gets back to the researchers is instrumental in improving disease understanding and enabling better business decisions about drug development strategies, thereby creating a better pipeline of drugs.



Using New Technologies to Complete an e-Clinical Infrastructure

A bifurcated approach involving incremental and transformative changes is required to evolve data analysis and review processes. Incremental in terms of improving productivity in running clinical trials and obtaining better insight into trial data, i.e., how safe is a drug candidate, where are the risks (in the hope they can be mitigated). And transformative – using translational medicine as a way to improve cycle times between research and development.

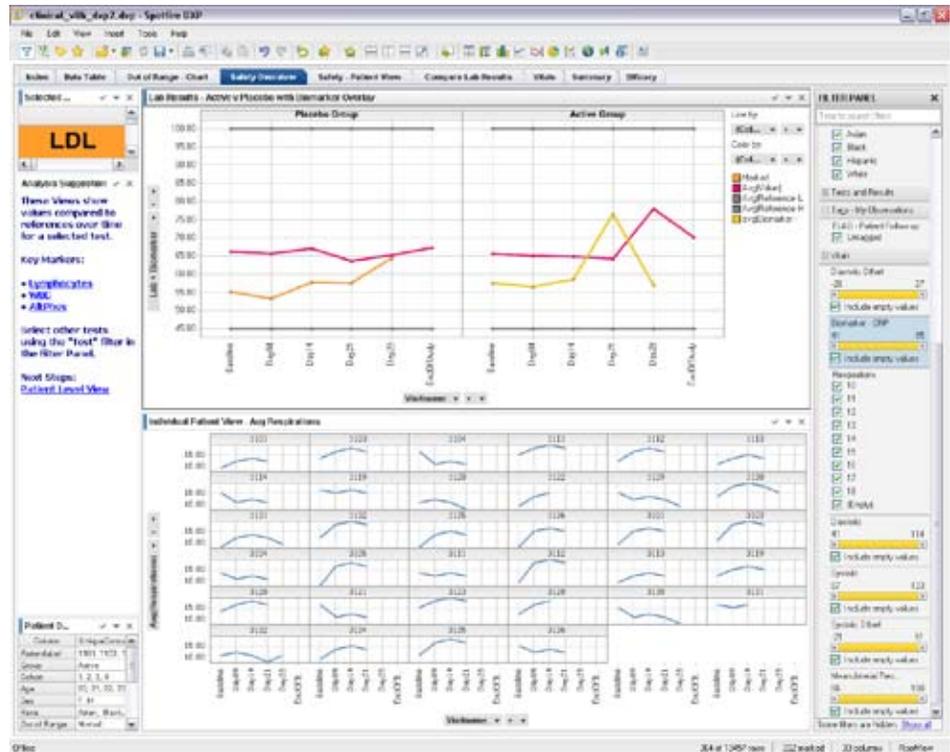
Pharmaceutical companies have been investing in e-clinical solutions at a rapid pace – “electronifying” to a much greater extent the information around clinical development. The industry has certainly evolved from the paper-based approach that until recently involved faxing data captured at the trial site back to the pharmaceutical company’s clinical trials group for analysis. But even with the advances that have been made, there are often delays in getting the reports into the hands of the scientists because of the time needed to prepare reports.

With TIBCO Spotfire enterprise analytics software as part of the e-clinical IT infrastructure there’s much more timeliness in terms of being able to look at and explore the kinds of data that scientists need. The software also provides the ability to look at data from multiple perspectives and see it more clearly. The software’s self-service data analysis model eliminates any barrier between a scientist and his data. A biologist that knows a lot about a disease area he is trying to treat can ask and answer his own questions and instantly see results that are meaningful, e.g., how a drug may be surprisingly impacting the cholesterol level of a particular group of patients or obtain quick reinforcement that certain anticipated side-effects are within the safe range.

Spotfire software enables the scientist to explore hypotheses himself without having to ask an IT person or statistical programmer to create reports or perform analyses. With other tools, the iteration cycle from scientist to IT person or statistician is costly in terms of time. With Spotfire enterprise analytics the scientist is likely to ask additional questions and explore more possibilities because he can interact directly with the tool.



Figure 1. Analysis of biomarker and clinical safety data, overlaying expression of C-Reactive Protein and LDL levels for patients in the active and placebo group and with detailed vital sign data for individual patients.



A Transformative Approach Takes Shape

As a result of the increase in costs of drug development and market pricing pressures, customers aren't just looking for incremental improvement; they're looking for transformative change in the way they determine if a drug can be brought to market.

For the first time in a long time, a lot of the technology needed for an organization to transformatively change its drug discovery process actually exists. EDC and CDM systems have certainly improved the way data from clinical trials is captured and structured. What is also needed is a better way of working with the data, which is where Spotfire enterprise analytics comes in.

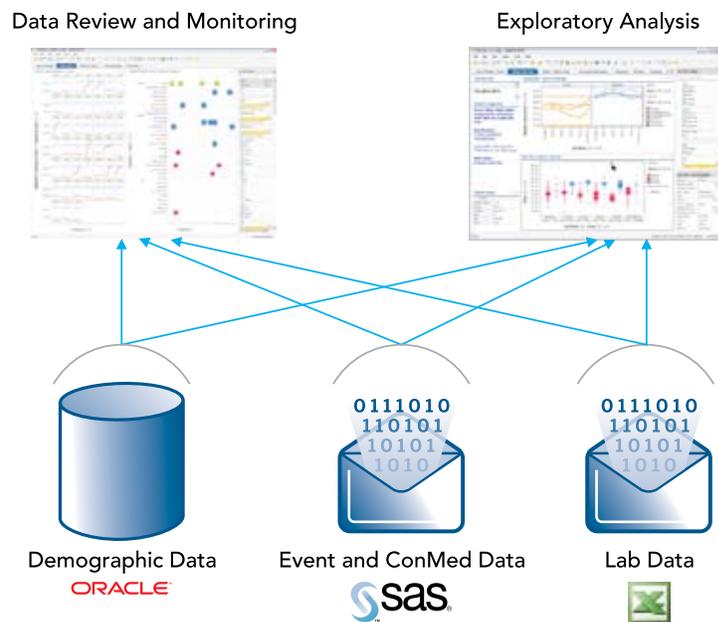
New workflows and business processes are required to move the data to the right people at the right time, thereby closing the loop created by these new technologies. Analytics becomes a key component of the workflow - looking at, exploring and analyzing data from different perspectives for different needs becomes central to asking and answering questions in early stage clinical trials. Questions such as is the drug safe, what is the



drug affecting or having an influence on, does the drug react differently in those of a particular race, gender or those with a particular biomarker. One of TIBCO's Spotfire Division customers talks about it being like a private investigator or detective - looking at something from different angles (data sources) to put together clues. Pharmaceutical companies need to learn a lot about the pharmacology of their candidates – it's necessary to look at all the data from the patients to figure out if a drug is working as they expected from a research perspective and to determine if it is safe from the perspective of everything that they know about other treatments of the disease.

The trend towards personalized medicine is also accelerating the need for transformation. The process of determining whether or not a niche drug prospect is the right strategy to pursue involves looking at an entirely different set of data. From a workflow perspective, the difference is that you need to start looking at the data earlier and more comprehensively because the strategy is different. Companies are using Spotfire enterprise analytics to accomplish this, looking at trends and patterns earlier, and saving much money and time in the clinical development process.

Figure 2. TIBCO Spotfire enterprise analytics sits on top of a range of databases and combines data from different sources, enabling analysts to perform regular data review consistently and accurately. It also allows scientists to do more exploratory analysis in search of patterns and trends in their data that might lead them to new insights and better decisions about their development strategy.





While EDC and CDM systems are increasingly common in customers' IT environments for data management, something they tended not to have was the analytics piece to deliver the right data to the right people, enabling them with the right workflow. TIBCO Spotfire Guided Analytics™ help them establish the proper workflow and ensure they are comprehensive in the way their data is reviewed and analyzed. Spotfire software doesn't require any change in an existing environment, so the investment in data systems is protected. Spotfire software takes the data (from any source) and uses it for these different work processes such as data monitoring, data review, clinical pharmacology, exploratory analysis, and pharmacovigilance.

Conclusion

The pressure to reform clinical research is not going away and the industry can't wait. Technology now exists to enable pharmaceutical companies to really transform the way they work. Spotfire software is enabling transformative change in its customers' drug development practices by helping to break down the boundaries between phases 1 and 2 and between 2 and 3, fulfilling the premise of Learn and Confirm. Analytics have become central to this; it is no longer just the domain of the statisticians.

As with many information businesses, the next decade of drug development will be about the enablement of scientists to make more informed decisions both individually and as a team, with unprecedented speed. The companies that are leading the way by embracing these new paradigms are enabling their people to explore more possibilities. In parallel they are automating routine workflows in order to free up cycles to explore the unexpected.

For the last 11 years Spotfire enterprise analytics has been at the forefront of enabling the pharmaceutical industry to gain insight from information from early stage research to sales and marketing. Looking forward, it is clear that the unique Spotfire software user experience and information insight will continue to enable pharmaceutical companies to adapt to and compete in an ever changing environment.



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