Executive Summary
In the pharmaceutical industry, finding ways to improve core business processes is the only viable long-term business strategy. Faced with major changes in the business, biomedical, and regulatory environments, pharmaceutical companies have no choice but to embrace change. Downward pressure on prices, rising costs, and a more complicated global business environment make it imperative to shorten cycle times and reduce costs.

It is in this context that many pharmaceutical companies are scrutinizing their clinical trial data management processes, trying to find ways to move new compounds through the approval process faster and at lower cost. It’s a logical priority. Clinical trial data is the lifeblood of any pharmaceutical company. If the data doesn’t flow efficiently, the entire organization can be placed in jeopardy. For a new drug to contribute to profitability, it must move through the approval process and win approval expeditiously. The unfortunate truth is that at many pharmaceutical companies, clinical trial data doesn’t flow efficiently to whom it should, when it should. There are indications that this may soon change. Developments in technology give pharmaceutical companies new opportunities to transform their clinical trial data management processes in ways that produce significant new business value.

In this whitepaper, we discuss the convergence of business need with the emergence of new technologies and new business processes that make it possible to streamline and accelerate clinical trial processes. We provide an overview of how Liaison Technologies’ data management expertise and the technical capabilities of Liaison’s Contivo Vocabulary Management™ (Contivo VMS) solution can help companies overcome the clinical trial data management and analysis challenges that threaten their long-term success. We also will show how one industry leader, Merck & Co., Inc., has used the Contivo solution and Liaison expertise to begin transforming its clinical trial data management into a more agile and efficient process.

Transformative Trends Impacting Clinical Trial Processes
As a first step in determining how best to improve clinical trial processes, it’s helpful to understand the trends driving the current industry transformation. Some of the trends pose significant challenges. Others are creating opportunities for individual companies to outperform their competitors and achieve steady growth. For pharmaceutical companies, the intense focus on finding better ways to manage their business stems from the impacts of a number of industry-wide trends, including:

- **Revenues are Flat or Falling**: Because of the worldwide recession and other external factors, many pharmaceutical companies are struggling to achieve any level of growth. Some have even posted year-over-year revenue declines in the past few years. The revenue threat is aggravated at companies with profitable drugs whose patents have expired or soon will expire.

- **Research and Development Costs are Rising**: The average price tag to bring a compound from discovery and proof of concept to commercialization is now $1.3 Billion.¹ There are a couple of major factors driving the high cost of research and

development. For one, the easier biomedical challenges have been addressed by drugs already on the market. This makes it harder to identify new compounds, which in most instances need to be more sophisticated than their predecessors. Costs also are being driven up by trends in the clinical trial process itself. Trials are becoming more complicated because they involve more people, in more global markets, for longer time periods.

- **Regulatory Approval Processes are Becoming More Onerous:** Higher sensitivity to public safety has prompted regulators in many countries to make the approval process for a new drug more onerous and the penalties for infractions harsher. The situation is aggravated by the fact that established pharmaceutical companies are operating in more countries and, therefore, must contend with a greater number of differing requirements.

- **Industry is Consolidating:** With more than 700 mergers and acquisitions in the pharmaceutical industry in the second half of the last decade, there isn’t a major pharmaceutical company untouched by industry consolidation. The process has been driven, in large part, by a desire to accelerate the process to bring new drugs to market. The acquired company is often one that has made progress developing a new compound the acquiring company thinks will strengthen its portfolio and financial prospects. But integrating companies is never easy and, quite often, disruptive and costly. There usually are disparate technology platforms and business processes that can be difficult to integrate. After an acquisition or a series of acquisitions, the resulting company is larger, more complex and harder to manage.

- **More Companies are Outsourcing Core Activities:** While it’s true that pharmaceutical companies are trending larger, there also is a trend to keep fewer processes internal. Research functions and data collection functions are increasingly being outsourced to companies that specialize in those activities. Many organizations, whose core focus is research, are giving up direct management of clinical trials. Instead, they are looking to companies that specialize in managing clinical trials. As with mergers and acquisitions, the outsourcing trend is creating challenges for clinical trial data management due to the difficulties integrating information and systems from one company to the next.

It’s not all challenges and threats, fortunately. There also are a number of trends creating new opportunities to improve the clinical trial model. The positive trends stem from specific proactive actions on the part of the industry as a whole and by individual companies. Starting in the early ‘90s, the industry began seeing the operational problems inherent in having propriety information technology systems and outmoded business processes. Much of the response has been driven by consortia formed by industry leaders. The major positive industry trends include:

- **Adaptive Clinical Trial Processes Being Implemented:** New, more flexible approaches to conducting clinical trials are emerging. The adaptive clinical trial methodology is replacing the long-standing approach where no data is moved until all data collection is completed. Instead, pharmaceutical companies using an adaptive approach flow the data in the early stages of collection. By analyzing interim data, companies can spot issues with a trial early and respond. They can modify the trial to make it more effective, like changing a dosage. Or they can stop the trial if a major problem occurs, basically cutting their losses. Adaptive clinical trial processes are being made possible, in part, by advances in computing power.

- **Meta Data Simplifying Communications:** The Clinical Data Interchange Standards Consortium (CDISC) created the Shared Health and Clinical Research Electronic (SHARE) library to enhance communications within clinical trials. The SHARE library enables precise and standardized data element definitions that can be used within applications and across studies worldwide. The standardized metadata definitions in SHARE simplify communications within trials and within pharmaceutical companies and their supply chains.

- **Integration Simplifying Communications:** Communication between business partners and applications can be overwhelming due to the variety of methods and integration requirements. However, leveraging best practices and well-defined processes, can greatly simplify it and allow for uninterrupted, real-time communications.

- **Access to Healthcare Data Improving:** Another CDISC initiative, the Biomedical Research Integrated Domain Group (BRIDG) model, provides a logical data model that can be used in both healthcare and biomedical research. BRIDG creates a way for pharmaceutical companies to
leverage information collected by healthcare companies in clinical trials for new drugs. By using healthcare data, pharmaceutical companies can make more informed decisions about the structure of a clinical trial. BRIDG data also represents part of the data collection process for individual trials.

**Data Collection Formats Aligning with Submission Requirements:** The CDISC Clinical Data Acquisition Standards Harmonization (CDASH) creates 18 recommended data collection fields that align with the data submissions fields pharmaceutical companies must use in the drug-approval process. Pharmaceutical companies that use the CDASH fields can save considerable time and money by avoiding the need to reformat data just prior to the submission phase.

**Prevailing Clinical Trial Data Management Techniques Inadequate for Emerging Requirements**

Despite opportunities for improvement being facilitated by industry consortia like CDISC, pharmaceutical companies still have data management processes that aren’t robust and flexible enough to deal with emerging requirements. Several technology and business process characteristics make the prevailing approaches to clinical trials ill-suited for the current and future business environment. These include:

* Integration is Point-to-Point: In most pharmaceutical companies, the integration of technology and processes is ad hoc. Integration is typically database to database, which leads to throughput problems and the inability to adapt easily to change. Companies that have relied on multiple vendors for their technology infrastructure invariably face integration problems. Companies that have relied on a single vendor may experience fewer integration issues. However, these advantages are offset by higher costs and the fact that no single vendor can create the best technology for every requirement.

* Applications Support this Point-to-Point Approach: Several applications have been developed to address specific clinical trial requirements within the point-to-point integration framework. They can be a source of frustration for pharmaceutical companies because they lead to the presence of multiple data hubs, which in turn, lead to data integrity problems and the need to perform manual steps to share data.

Leading industry-specific applications include:

* **Electronic Data Capture (EDC):** A system for collecting clinical trial data in electronic format
* **Clinical Data Management Systems (CDMS):** Paper-based or electronics-based tools used to store and manage data for a clinical trial
* **Clinical Trial Management System (CTMS):** A software system for managing large amounts of data collected for a clinical trial
* **Clinical Data Repository (CDR):** A real-time database used to consolidate multiple data sources that comprise a clinical trial
* **Statistical Analysis System (SAS) Analytics:** Software products from the SAS Institute, Inc. that enable classification, analysis and interpretation of clinical trial data to reveal patterns, variables and relationships

* Extent of Collaboration Varies: Pharmaceutical companies currently follow one of three approaches to collaboration in their clinical trials. The extent to which a company collaborates internally and with other companies during a clinical trial is dictated by the decisions it makes about integration, architectures and applications. The three approaches—Traditional integration, Extended integration, and External integration—each offer advantages and disadvantages.

* **Traditional Integration:** Applications are managed, for the most part, within the company. It’s used typically for internally managed trials only, since the collaboration with other entities is limited. When there are interactions outside the company, the EDC and its variant RDC (remote data capture) can be hosted externally using a software-as-a-service (SaaS) platform.

* **Extended Integration:** Some pharmaceutical companies extend their internal EDC via the web or virtual private network (VPN) so they can partner with CROs (contract research organizations) and other entities. This approach is similar to traditional integration except that a firewall and other security measures are used in extending applications to partners. Extended integration reduces the challenges that can occur when outside data is integrated into the internal CDMS.
Benefits
- Supports internal integration and extension of applications within the company’s network
- Supports hosted and SaaS solutions
- Security is tightly controlled

Challenges
- External integration is a custom mapping and migration exercise
- Scalability of applications, especially involving global business units, can be difficult
- Internal hosting costs can be high and can be considered a non-core competency

Benefit of Extended Integration:
- Supports extension of applications to partners
- Maintains security of host partner
- Host maintains data control

Challenges with Extended Integration:
- Managing multiple partner connections, identity and access management
- Lab data is still an external integration issue
- Scalability can be difficult
**External Integration:** Pharmaceutical companies who adopt an external integration approach for conducting clinical trials receive incremental or final data sets from CROs, labs, and other entities. This is typical of a complete outsourcing business model or joint venture for clinical trials. The benefits of outsourcing can be offset by additional requirements for integration.

**Benefits**
- Supports integration of applications and data batch transfers from partners
- Some integration through an enterprise service bus (ESB) level can be successful, but there is a cost to the integration and technical capabilities must be in place at both parties

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Pharmaceutical Industry Positioned to Leverage Advances in Other Industries

It’s true, there is a business imperative for pharmaceutical companies to dramatically improve the efficiency of their clinical trial data management processes. It’s equally true that pharmaceutical companies are well-positioned to transform these processes. The growing momentum of current industry consortia is only the latest development in a long tradition of industry-wide collaboration and innovation. In addition to positive developments within the industry, there are numerous technologies and techniques emerging in other industries that can be applied to the current challenges.

When paper was still the dominant communications medium in business, the pharmaceutical industry led other industries in establishing a common terminology and standard ways to communicate within companies, from company to company and from region to region. The industry formed the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in 1990. The MedDRA (Medical Dictionary for Regulatory Activities) and Common Technical Document (CTD) were early developments that ushered in more efficient communication practices within and between companies in the pharmaceutical industry.

In the past decade, there have been numerous developments in other industries that are ripe for implementation in the pharmaceutical industry. Some examples of industries and the developments with potential to help pharmaceutical companies:

**Financial Services:** The use of canonicals and service-oriented architecture (SOA) is delivering significant benefit in Financial Services, another dynamic and consolidating industry. Banks and mortgage companies established canonicals to standardize the way data is described as a precursor to establishing networks that move massive amounts data within companies and from company to company instantaneously. In much the same way, pharmaceutical companies could leverage canonicals to map data so all data pieces are presented the same way. The potential applicability of canonicals for pharmaceutical companies is reinforced by the fact that mortgage companies move and manage data whose complexity is on par with clinical trial data.

**Consumer Packaged Goods and Retail:** Standardized messaging and supply chain collaboration in the consumer packaged goods and retail industries keep communications, as well as products, moving within and between a large number of companies.

**Criminal Justice:** Interpol, the international police organization, uses a shared infrastructure to manage data about crimes and criminals for its 188 member countries.

**Data Mapping Plus Canonicals:** The company has created innovative data transformation solutions that help companies implement a low-cost of entry mapping strategy that sets the stage for later implementing a more sophisticated data management strategy involving canonicals. The combination of mapping and canonicals sets the company apart from other technical providers working in the pharmaceutical industry.

Liaison Technologies has extensive experience using canonicals in financial services and other industries to deliver new process efficiency and business value.

**Meta Data:** Liaison Technologies has successfully leveraged collaborative data models like BRIDG and CSHARE in other industries, including paper and retail.

**Shared Infrastructures:** Liaison Technologies is a leader in establishing and managing shared infrastructures in the paper industry.

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Contivo Vocabulary Management Solution (VMS)
Liaison’s semantic integration technology provides a robust data transformation design and code-generation environment that helps pharmaceutical companies manage clinical trial data. A patented and customer-proven solution, Contivo VMS provides automation, leverage and repeatability for integration projects. Central to Contivo’s capabilities is a metadata repository that stores and maintains the vocabularies used to describe data and business documents. Key characteristics:

- **Simple, Flexible Architecture**: Enables fast, efficient movement of specific, small data sets to where they will be compiled, stored, and/or analyzed. Supports fast and efficient change within a trial and across multiple trials undertaken by a single pharmaceutical company. Supports easy integration of multiple solutions.
- **Fast, Efficient Implementation**: Implements in weeks, not months. Requires configuration; no coding
- **Reusable Data Structures**: Creates data structures that can be used from one trial to the next
- **Process Automation**: Automates and streamlines technical processes for clinical trials
- **Scalable**: Enables the clinical data management system to scale to support large individual mega trials and many trials being undertaken at once
- **Strategic Use Of Metadata**
- **User Friendly Graphical User Interface (Gui)**: Facilitates easy data entry and understanding of the data and processes
- **Streamlined Code Generation**: Helps analysts create deployable runtime code without using valuable development resources

Data Exchange Platform (DXP)
The Liaison DXP is a SOA-based integration platform that facilitates movement of data between parties. With a cloud-based integration, the DXP can be leveraged across multiple data sources to streamline clinical trial data
management. The Liaison Enterprise Navigation System (LENS) is a business activity monitoring tool that enables pharmaceutical companies to monitor messages and activity within the DXP.

Case Study: Merck & Co. Inc.
Liaison Technologies worked with leading pharmaceutical company, Merck & Co. Inc., to analyze and help correct problems the company was experiencing with data flow for a mega-trial and is engaged in helping them to gain more efficiencies for all clinical trial processes.

The Business Issue
A mega trial planned by Merck couldn’t be started because the legacy clinical trial data management system couldn’t support it. Merck had been experiencing recurring data flow problems in other trials, but it was the magnitude of the mega-trial that prohibited data flow. The data flow problems in the mega trial, which accounted for upwards of 70 percent of all clinical data to be collected by Merck in that fiscal year, was delaying the start and completion of other clinical trials and, as a result, was creating a drag on overall corporate performance.

Merck was using a single map for all data that had to be deposited in the clinical data repository. Because of the scope of the mega-trial, the map size was extraordinarily large. This meant that for every change in the study, no matter how minor, there would have to be a change to the single, comprehensive map. The inevitability of frequent changes meant there would be ongoing changes in the map, which would prevent movement of data.

Merck’s Objectives
In enlisting the help of Liaison Technologies, Merck established clear and specific project objectives:

• **Reduce Time:** Reduce the number of days required to deploy a clinical trial and reduce the time to complete the regulatory review for new drugs and bring them to market
• **Automate and Streamline Processes:** Implement process efficiencies that automated and streamlined key clinical trial data processes
• **Reduce Costs:** Reduce costs by accelerating and streamlining processes and by efficiently using offshore resources

• **Achieve Scalability:** Redesign the database that hosts trial data to make it more scalable and high-performing
• **Position for Cloud-Based Implementation:** Implement a solution that would not restrict Merck from taking advantage of cloud-based services in the future

The Liaison Solution
Liaison analyzed the data flow problems and developed a solution based on Liaison’s Contivo mapping platform. The recommended solution included:

• **New Architecture:** Replace Merck’s database-to-database transfers with message-based transfers
• **New Processes:** Design new map development, testing and deployment processes to streamline and optimize the map-development processes
• **More Scalability:** Design a hosted, scalable, run-time system capable of efficiently managing more than 200 clinical trials simultaneously
• **Library of Standard Forms:** Create a library of standard forms that could be used repeatedly, from one trial to another. Since approximately 60% of clinical trial forms used by Merck are generic and usable for virtually every trial, the library could dramatically reduce the time and money required to create forms for each new trial.
• **Training:** Train Merck and their offshore contract research organization (CRO), Accenture, in how to use the new Contivo VMS solution

The Implementation
Merck conducted a six-month pilot of the Contivo solution. Based on the success of the pilot, Merck selected Contivo as its technology for data modeling and interface mapping for all future clinical trials.

Merck now creates more flexible, simple clinical trial processes. Since implementing the Contivo solution, Merck has begun to see improvements in its clinical trial process and is working with Liaison to gain the following business efficiencies:

• **Accelerated Clinical Trial Processes:** Using the Contivo mapping solution, Merck now has the capability to create maps more efficiently, reducing the average map development process time. Another by-product of this is that offshore resources can be utilized more efficiently through the use of the standardized Contivo solution.
• **Greater Ability to Change**: Using Contivo, Merck now has more agile clinical trial processes, including the ability to more easily change maps.

• **Improved Problem Resolution**: Merck replaced what was essentially a sequential error identification and resolution process with a more dynamic process. Initial indications are that the overall reduction in trending errors is on track to meet business objectives.

• **Greater Capacity to Handle Multiple Trials**: Because Merck vastly improved its data flow capabilities, it is now able to simultaneously conduct trials of more drugs.

• **More Easily Assimilate New Businesses**: As Merck acquires new companies, it is better equipped to implement its more efficient CDMS.

**Conclusion**

For pharmaceutical companies, there is nothing more fundamental to their business success than the timely and successful completion of clinical trials. Clinical trials are incredibly complex data management undertakings and unless there are efficient processes and modern technology in place, numerous problems can occur. Without the right processes and supporting technology, pharmaceutical companies can pursue a flawed trial or flawed compound for too long and fail to cut their losses. Even if the trial design is good and the compound is promising, the inability to collect, manage, analyze and package the clinical data can produce long delays that cause costs to soar and keep the drug from the marketplace.

In recent years, there has been significant progress in the sophistication and raw power of information technology, which present opportunities for pharmaceutical companies to streamline and accelerate their clinical trials. Liaison Technologies has invested heavily in developing a new generation of integration and data management capabilities that can transform the clinical trial data management process from a business problem to a strategic advantage. These solutions are currently delivering significant business value to pharmaceutical companies and companies in other industries like financial services that have comparable integration and data management challenges.