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White Paper:

How Effective Document Management Helps Pharmaceutical Companies Accelerate Time to Market

Introduction

This white paper will discuss common challenges pertaining to document control encountered by most drug companies from the preclinical stage through the post-market phase, and how the MasterControl™ GxP process and document management software solution addresses such challenges to accelerate time to market and improve product quality.

Preclinical Phase

One could say that the years spent by chemists, biologists, pharmacologists, toxicologists, and other scientists "discovering" the right combination of chemical and biological substances that could be used for a drug are geared toward the submission an investigational new drug (IND) application. FDA approval of the IND is necessary to conduct clinical trials and to proceed with product development.

Discovery research scientists typically start with thousands of possible compounds. Through continuous testing, screening, and refining that could take several years, they would whittle down the thousands of compounds to hundreds, and then dozens, and then three to five drug "candidates." This rigorous phase includes laboratory and animal studies that cover chemistry tests, biological tests, manufacturing tests, and pharmaceutical development studies. The overarching goal during this phase is to determine the safety of the candidates before they are tested in people.

The preclinical phase could easily generate thousands of documents. The IND submission alone requires the compilation of everything known about the new drug being developed: its chemical structure; how it might work in the human body; how it works in animals; any side effects in animals; and how the compound is manufactured. The IND also must include detailed information on how the company plans to test the drug on humans during clinical trials.

Pharmaceutical and biotech companies and the CROs that serve them need effective document control during this phase for two major reasons that directly affect time to market:

- **Efficiency:** Thousands of documents generated over a period of one to three or more years necessitate a formal document control process to ensure that documents are not lost, and that they can be tracked, retrieved, revised, and approved easily. Without an efficient system for managing documents, thousands of man-hours will be spent in even the simplest tasks.

- **Compliance:** FDA regulations such as 21 CFR Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies) and 21 CFR Part 312 (Investigational New Drug Application) require effective documentation. 21 CFR 58 has specific document control requirements pertaining to SOPs for animal care, lab tests, data handling, and equipment maintenance and calibration; protocols; and handling of records, reports, and raw data documentation. 21 CFR 312 has its own set of requirements pertaining to recordkeeping, record retention, and investigator reports. Management of IND documentation is particularly crucial because it serves as the basis for other information that will be submitted to the FDA later.

Clinical Phase
While preclinical work is directed toward the IND submission, the clinical phase is geared toward the submission of an equally important regulatory filing: the new drug application (NDA).

During this stage, doctors (called clinical investigators) carry out studies to find out if the drug is safe in people and whether it is effective in treating the targeted disease. There are three phases in every clinical trial: Phase I (the drug is tested in 20 to 100 healthy volunteers), Phase II (involving 100 to 500 volunteers who have the disease that the new drug is meant to treat), and Phase III (involving 1,000 to 5,000 volunteer patients).

Clinical trials could take up to 10 years, during which the sponsor will conduct parallel research on toxicity, dosage forms, and methods for full-scale manufacturing and packaging of the drug. Everything about the clinical phase is geared toward the NDA submission, which essentially summarizes 10 or more years of development work. The NDA dossier is complex and voluminous — anywhere from 100,000 to 600,000 pages of text that are meant to persuade the FDA to approve the new drug.

As in the preclinical phase the clinical stage requires effective document control to help achieve:

- **Efficiency:** Managing hundreds of thousands of documents generated by cross-functional teams during a period of 10 years or more is a daunting challenge. Bottlenecks abound during this phase because there are more people involved in the process and the data from clinical investigators grow exponentially from Phase I through Phase III.

- **Compliance:** In addition to GLP and GCP requirements that various teams must comply with, the sponsor also must manufacture the investigational new drug used for clinical trials in accordance with Current Good Manufacturing Practice (CGMP) requirements under 21 CFR Parts 210-211. GCP also includes guidances that call for effective documentation. Moreover, the sponsor must comply with 21 CFR Part 314 (Applications for FDA Approval to Market a New Drug) for its NDA submission.

Commercialization, Product Launch, and Post-Market Phase
While a sponsor is waiting for FDA approval, it is likely to be gearing up for mass production, or perhaps it is already manufacturing the drug. FDA approval takes 18 months on the average, according to PhRMA. As soon as the FDA approves the NDA, the company will be able to start selling the new drug. But even after the product is brought to the market, the company will continue to submit reports to the FDA, such as adverse reaction reports and quality-control records. In some cases, the FDA may require a sponsor to conduct Phase IV clinical trials to evaluate the drug's long-term effects.

With the clock ticking in terms of market exclusivity, the company that has just launched a new drug needs effective document management to help achieve:

- **Efficiency:** Document control needs after FDA approval are especially great in the areas of quality control, manufacturing, marketing, and sales. Voluminous documents will be generated by quality-related processes that will handle corrective and preventive action (CAPA), electronic batch records (EBR), consumer complaints and adverse event reports, quality audit, deviations, and nonconformances, among others.

- **Compliance:** Document control is a CGMP requirement. In addition, the pharmaceutical or biotech company with a newly approved NDA must address post-market requirements found in 21 CFR Part 314, including the reporting of adverse drug experiences and the submission of NDA field alert report, annual report, distribution data, labeling, report on CMC changes, etc.

The MasterControl Solution

The MasterControl™ GxP process and document management software provides a solid foundation for effective document control throughout the pharmaceutical product development lifecycle by accelerating overall time to market and by simplifying workflows, promoting efficiency, and making compliance easier. Below are some of the benefits of using MasterControl throughout the pre and post drug development process.

- **Virtual Workspace Makes Collaboration Easier** - Document collaboration at any time of the drug development process is possible regardless of location through a virtual workspace for cross-functional review and approval of documents. The system automates tasks pertaining to collaborative projects, including routing, follow-up, escalation, and approval.

- **FDA Submission Templates** - MasterControl provides appropriate templates (i.e., NDA, BLA, CTD, IND) to streamline document formatting to improve the dossier-creation process.

- **Authoring and Review of Submissions Documents** - MasterControl's document management and submissions tools help to create and publish submissions-ready documents early in the pre-clinical and clinical study phases. Early document publishing helps speed up the submission assembly process thereby improving time to market.

- **Integration Helps Optimize E-Submission Process** - MasterControl provides a single repository for all regulatory submissions, as well as a virtual workspace where different teams can easily and quickly revise the dossier.

- **Automated PDF File Generation** - To make an electronic submission to the FDA, the agency requires that electronic files of regulatory information be submitted in PDF format. MasterControl offers automated PDF conversion of documents, streamlining the process by not having to manually generate PDF files. The unalterable PDF format also provides added security and control.

- **Electronic Sign-offs** - With MasterControl, documents can be signed and approved electronically. Signature manifestations with name, date, time, and meaning of electronic signature can be appended automatically to each document as required by 21 CFR Part 11.

- **Increased Efficiency Through Automation** - MasterControl reduces the overall document cycle time and simplifies document management by automating routing, notification, escalation, and approval. Its robust tracking feature identifies bottlenecks by showing when a document was sent and to whom. It shows the document's history, including who has approved it and when. A document that has been rejected will automatically go back to the sender, so tasks don't languish. MasterControl can handle all types of documents, regardless of the software used to create them.

- **Centralized Repository Makes Search and Retrieval Easier** - You can store all records and documents from the discovery stage through the post-market phase in a centralized electronic repository, making it easier to update, and to search and retrieve them. Documents reside in secure virtual vaults that can be accessed only by authorized users. Access is limited by the extent of a user's system rights. Although the system is centralized, every department can compile documents separately using the Organizer, a MasterControl tool similar to Windows Explorer, which helps users find documents quickly.

- **Web-Based Platform Provides Easy Access** - A Web-based system will give employees in different locations and time zones easy access. Even CROs, suppliers, consultants, and other authorized users outside of the company can have system access based on the extent of their roles in any document-based process.

- **Automatic Revision Control Reduces User Mistakes** - With a paper-based document control process, there is no mechanism that would stop a user from inadvertently using obsolete or unapproved documents. With MasterControl, revision control is automatic, so only approved documents are released. Any outdated documents are automatically archived, and documents in the process of revision are locked. The system provides a time-stamped audit trail of all changes made to a document.

- **Integration Helps Leverage Existing Systems** - You can leverage your existing Laboratory Information Management System (LIMS), eSubmission, and Enterprise Resource Planning (ERP) solutions by integrating them with robust MasterControl applications without expensive custom coding.

- **Risk-Based Software Validation Offerings Help Reduce Compliance Burden** - MasterControl products and services designed to dramatically reduce the time, pain, and cost involved in software validation. Companies may choose the appropriate products and services based on their own risk assessment.

Conclusion

Time is a precious commodity for everyone, but especially for people involved in drug development. You can maximize development time starting with the way you control document-based processes. As this white paper has shown, a delay in time to market due to poor document management is largely preventable with the help of the right solution.

About MasterControl

MasterControl Inc. is a global provider of GxP process, quality audit, and document management software solutions for life science companies. MasterControl™ products are easy to use, easy to deploy, easy to validate, and easy to maintain. They incorporate industry best practices for automating and connecting every stage of the product development cycle, while facilitating regulatory compliance. By combining an integrated platform with a continuum of risk-based software validation products and services, MasterControl drives down the total cost of ownership and enables customers to extend their investment across the enterprise. Hundreds of companies, including 50 percent of the top 20 pharmaceutical enterprises, currently use MasterControl solutions for easier compliance, faster validation, and better process management. For more information about MasterControl, visit www.mastercontrol.com, or call 800-825-9117 (U.S.) or +44 118 9812838 (Europe).

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