MasterControl™

# 2020 Trends in Quality Data Management and Integrity for the Life Sciences

Data is rapidly becoming an organization's most valuable asset. It's readily available in high volumes, is more robust and reusable than ever before and is the catalyst for nearly unlimited possibilities to create business value. Still, the pervasiveness of data can make it overwhelming and difficult to control. Just like any other aspect of a business, data needs to be handled correctly and nurtured to ensure it sustains the level of quality and integrity necessary to provide value to the organization.

The following trends reveal how data is taking on a more active and influential role in the life sciences industry, and they illustrate how companies should adapt to the new trends in order to fully capitalize on next-generation data management practices.

1

# Regulators Are Elevating Oversight of Data Integrity

Compliance with regulatory data integrity requirements is not new to the life sciences industry. Regulatory agencies have been drafting guidances and other documents outlining and clarifying the requirements for ensuring data integrity for many years. Despite this, the number of warning letters for data integrity violations is steadily increasing. Recent statistics show that data integrity violations account for over 70% of the warning letters issued globally.[1]

Common scenarios that lead to receiving a data integrity-related warning letter involve at least one of the following:

- Laboratory operations do not include complete data derived from all tests, and procedures are not documented at the time of performance.
- Data is first recorded in an unofficial spreadsheet and later transcribed to an official form.
- Deviations are not thoroughly investigated, accurately documented and corrected in accordance with regulatory guidelines.
- Test result data is concealed, or tests are performed repetitively until desired results are achieved.

**The Changing Dynamic of Data Integrity Compliance**

Recent cases involving high-profile companies attempting to pass off altered, fabricated or incomplete data in submissions have prompted the U.S. Food and Drug Administration (FDA) to heighten its oversight of the data management practices of regulated companies:[2]

- Switzerland-based health care product company Novartis received a firm warning from the FDA in August 2019 when evidence revealed that the company submitted manipulated data from certain preclinical testing of its breakthrough gene therapy Zolgensma.
- Chinese over-the-counter (OTC) drug manufacturer Ningbo Huize Commodity Co. received a warning letter in August 2019 following a plant inspection where investigators discovered that documents provided by staffers were falsified.
- Prescription pharmaceutical company Akorn Inc. was issued a warning letter in June 2019, calling out the accuracy and integrity of its data.
- Mumbai, India-based Indoco Remedies LTD was issued a warning letter in July 2019, citing various GMP and data integrity violations in batch production and control records for products intended for the United States.

> **“We’ve focused comprehensive new efforts on these risks, both through our global inspections program as well as providing updated guidance, and to train our staff on identifying concerns related to data integrity.”**
>
> –Ned Sharpless,
> *Former Acting FDA Commissioner* [3]

**Data Quality and Integrity Guideposts**

The FDA's updated guidance on data integrity includes the addition of a series of threshold questions companies can use as a baseline for assessing their compliance with regulatory data integrity requirements:[4]

- Are controls in place to ensure that data is complete?
- Are activities documented at the time of performance?
- Are activities attributable to a specific individual?
- Can only authorized individuals make changes to records?
- Is there a complete record of all changes to data?
- Are all records reviewed for accuracy, completeness and compliance with established standards in a timely manner?
- Is data maintained securely from creation through disposition after the record's retention period?

Situations where data can be deleted or altered without including the proper justification documents often point to an ineffective or nonexistent audit trail system. For decades, regulatory agencies have stressed the necessity of audit trails for ensuring the capture and proper maintenance of complete and quality data. Audit trails are the "who," "what," "when" and "why" of records.

**A Peek at the Future of Data Integrity Regulation**

To comply with data integrity guidelines, companies are required to provide complete, up-to-date and unaltered data through accurate and verifiable audit trails. Expect to see more in-depth scrutiny of:

- All original raw data.
- All metadata.
- The data's history.
- User authentication and data security procedures.
- Audit trails.

The FDA is determined to ensure that consumers have confidence in the quality, safety and effectiveness of health care products, and the agency will take strong compliance enforcement actions when issues are discovered.

To stay in compliance with the updated and tighter regulatory data management guidelines, companies are urged to implement digitized technologies designed to automatically prevent omission, incorrect entry, unauthorized alteration, etc. of data. MasterControl Audit™ automates all audit-related tasks. It includes the secure, time-stamped audit trail that records and tracks users who create, modify and delete records — all of which is needed to meet the requirements for data integrity compliance.

# 2.

# Quality Shifts From Document-Centricity to Data-Centricity

Companies have long generated vast amounts of data as a byproduct of their processes, information management systems, equipment, personnel, products, communications and much more. To digitize and house this data, many purpose-built enterprise software systems have been developed over the past several decades that now comprise the tech ecosystem:

- Enterprise Resource Planning (ERP)
- Manufacturing Execution System (MES)
- Materials Requirements Planning (MRP)
- Customer Relationship Management (CRM)
- Quality Management System (QMS)
- And others

While these are powerful, precision tools for their respective areas, many do not connect with other solutions, nor do they surface the data they produce for meaningful human analysis and application. The result is fragmented, inconclusive and delayed business insights. And perhaps worst of all, they necessitate a continued reliance on paper-based and standalone systems as well as risky workarounds to fill digital gaps in the existing tech stack.

**Gaining the Most Value from Data**

Quality is one area of the business that is particularly dependent on data. In fact, more product-related data passes through quality than virtually any other department in an organization. But it is also one of the business areas most impacted by disconnected systems. When manufacturing and quality data is housed in paper records, standalone spreadsheets, or siloed systems, quality becomes document-centric — forced to focus less on the data itself and more on the accuracy, completeness and compliance of the documentation.

Although the data exists, it's most often packed away in banker's boxes or filing cabinets[5]. These data storage practices obscure effective analysis and valuable insights companies need to capitalize on opportunities to bolster their position as industry leaders in a competitive marketplace.

Document-centric quality checks the boxes of industry requirements and helps keep companies in compliance. However, it fosters more of a reactive rather than proactive approach to quality, reducing the discipline to an obligatory post-production enforcement of quality rather than a full-scale process and product improvement effort.

By surfacing data, ensuring its integrity and making it readily accessible to the teams that need it, digitization is enabling the transition from document-centric to data-centric product quality.

Not surprisingly, regulatory bodies also recognize the importance of this shift to data-centricity as a key part of 21st century quality management.

### Incentive to Modernize Operations

The FDA is currently considering a formal program of rewarding companies that invest in and practice "mature" quality management. According to agency officials, this program centers around data and the advanced technology needed to properly leverage it.

The current lack of transparency in the prescription medication industry is largely to blame for issues like drug shortages and pricing disputes, according to Janet Woodcock, director of the FDA's Center for Drug Evaluation and Research (CDER).

> **"Manufacturers with very high reliability usually have what is called a mature quality management system," Woodcock explained. "However, purchasers currently are not able to readily identify those manufacturers. The lack of information about which companies have mature quality management systems means that buyers of pharmaceuticals are unable to reward drug manufacturers that have these extra, and valuable capabilities."**

Though all drug manufacturers must adhere to the FDA's Current Good Manufacturing Practices (CGMP) to ensure adequate quality, this does not guarantee drugs are produced as quickly as or in the quantity needed.

> **"Unfortunately, incentives today are not high enough for many manufacturers to establish mature quality management capabilities. As a result, drug manufacturers are more likely to keep costs down by minimizing investments in manufacturing quality, leading to quality issues that can trigger supply disruptions and shortages of needed medications."**
>
> –Woodcock[6]

The program, which is currently under exploration by the FDA's Drug Shortages Task Force, will entail a rating system based on key quality metrics gathered from each company — in other words, data. The program is designed to incentivize companies to update their quality management and manufacturing technologies and practices, thereby making them more productive and profitable. It will also help rectify the perennial issues facing the pharma industry.

### Expanding Data's Ecosystem

In 2020, look for a new class of additive solutions and tools that will help companies more readily connect, surface and visualize quality and manufacturing data. Core enterprise and management execution solutions will continue to play a critical role in the organization. However, the trending "smart manufacturing applications" will be lightweight, mobile, context-aware and incorporate transformative digital technologies such as:

- Artificial intelligence (AI)
- Machine learning (ML)
- Industrial internet of things (IIoT)
- Augmented reality (AR)
- Smart assistance
- Predictive analytics

Because of their ease of implementation, low cost, and the game-changing insights they deliver, these technologies will allow companies of all sizes and industries to extend the capabilities of their technology and data ecosystem to the cutting edge of operations excellence.

# 3. Regulatory Expectations Going Beyond CGMP

The regulatory requirements for ensuring the quality, safety and efficacy of health care products remain unchanged. Despite the presence of these long-standing guidelines, afterthought, haphazard and patchwork approaches to quality still prevail in life sciences product development:

- Collecting data in various repositories in multiple formats and cleaning it up later for its intended purpose.
- Pulling together incomplete and error-prone data sets from disparate, paper-based sources for submission reports.
- Resolving procedure and product deviations, but failing to investigate root causes and activating prevention strategies.
- Performing quality management tasks as an add-on process after production is complete using a checklist to meet the minimum requirements for compliance.

**The Current State of Public Health Products**

The life sciences industry is still experiencing widespread product recalls, shortages and growing numbers of compliance violations. Meanwhile, significant scientific advancements in areas such as cell and gene therapies are endeavoring to evolve health care capabilities and patient options. The FDA is fully supporting these efforts and has been busily drafting guidances to help innovators advance the field of gene therapy, answer critical questions and make decisions as they move forward with their research and design of products.

> **"The growth of innovative research and product development in the field of gene therapy is exciting to us as physicians, scientists and regulators."**
>
> – FDA Commissioner Stephen M. Hahn, M.D.

"We understand and appreciate the tremendous impact that gene therapies can have on patients by potentially reversing the debilitating trajectory of diseases. These therapies, once only conceptual, are rapidly becoming a therapeutic reality for an increasing number of patients with a wide range of diseases, including rare genetic disorders and autoimmune diseases.[7]"

In addition to providing recommendations to innovators, the guidances are also designed to help shape the structure of the development of gene therapies while ensuring all products fit into the regulatory realm of safety and efficacy. The development and regulatory review of scientific gene therapies includes the need for:

- Obtaining and evaluating highly complex information on product manufacturing and quality.
- Addressing unprecedented and more challenging questions than those posed during reviews of more conventional products — many of which can't be fully answered during premarket processes.
- Effective tools for reliable postmarket follow-up (i.e., postmarket clinical trials).
- The ability to collect, process and analyze enormous amounts of data from a variety of sources and researchers.

The agency has also extended an invitation for developers to make use of expedited programs designed to address unmet medical needs in the treatment of serious or life-threatening medical conditions.

**A New Paradigm in Life Sciences Product Development**

New scientific innovations, along with the FDA's pledge to help accelerate product approvals are evidence that simply meeting CGMP requirements is no longer sufficient. The life sciences industry is trending toward a more modernized structure of quality and compliance.

Going forward, data management and product manufacturing will require all-hands risk intelligence, predictive analytics and more forward-looking insights that infuse the modernization mandate into the organization's culture as well as daily operations.[8]

Companies can boost the efficiency of their compliance framework by transitioning away from paper-based or hybrid systems to a digitized and connected environment:

- Obtain abundantly more industry and market data from internal and external sources to gain a deeper understanding of complex business issues and practices.
- Leverage data-rich insight to expand visibility and identify previously unseen variables and obstructions up and down the supply chain.
- Use predictive analytics to resolve current issues, foresee potential risks and make decisions based on accurate and relevant data.
- Automate quality to ensure compliance-readiness at every phase of a product's pre- and postmarket life cycle.

Digitized manufacturing solutions, such as MasterControl Manufacturing Excellence™, centralize data repositories, allowing you to gather, analyze and distribute data in real time, making it more useful for decision-making and strategic planning. It also digitizes all production processes, which helps eliminate the possibility of human errors and other production bottlenecks.

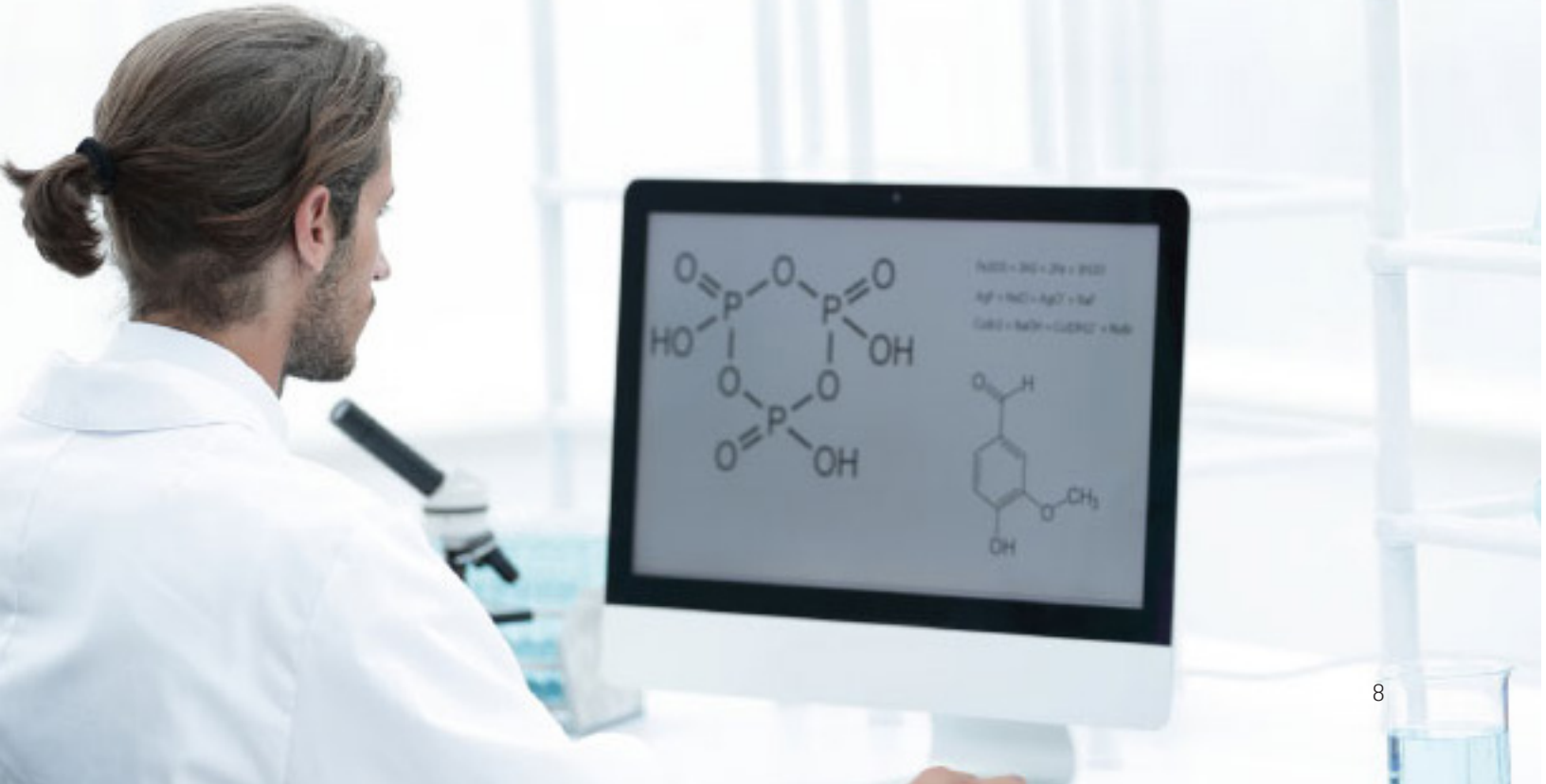
4.

# AI Technology Becoming Integral in Long-Term Business Strategies

Today's regulatory environment is experiencing significant and unpredictable change. At the core of this transformation is technology, which is creating new avenues for companies to reimagine their current business models, pursue new innovations and expand their business value. Breakthrough technologies such as AI, ML and natural language processing (NLP) are redefining the parameters of what is possible in life sciences innovation.

**Examples of AI Technology Currently in the Health Care Value Chain**

- **Icobrain ep solution** – AI tool that detects subtle abnormalities in the outer layer of the cerebrum in epileptic patients that may go unseen by traditional means. The product developer, icometrix, received 510(k) clearance for the solution in February 2020.[9]
- **Caption Guidance medical imaging** – Technology startup Caption Health received 510(k) clearance through the FDA's de novo pathway in Febuary 2020 for its AI solution that allows medical professionals to take ultrasound pictures of the heart.[10]
- **SubtleMR** – AI solution that uses denoising and resolution enhancement functionality to improve the quality of magnetic resonance imaging (MRI) images. Subtle Medical received 510(k) clearance for the technology in October 2019.[11]
- **QuantX** – AI-based, computer-aided breast cancer diagnosis system. During the latter part of 2019, QuantX became the first ever AI breast cancer screening tool to be cleared by the FDA for use in radiology.[12]



**New Solutions to an Old Problem**

Health care product innovators have abundant amounts of data is at their disposal. Because data comes from a variety of sources in a variety of formats, the perennial issue is the inability to use all the available data to its full potential. Unstructured data is particularly challenging because it's usually in the form of text that comes from word processing or spreadsheet programs, emails, transcripts, online forms, etc. It's more complex and is often stored in multiple locations. Much of this data goes unused because it's not standardized. Manually converting it to a usable format is laborious and prone to errors.

Unstructured data is too valuable to be ignored; companies risk missing crucial information. AI technology is helping companies resolve this issue. The NLP process leverages AI to compile unstructured data from multiple sources and convert it to structured data that can be interpreted by analytics systems.

**Why AI Is a Strategic Imperative for Life Sciences Companies**

One thing we've learned from Industry 4.0 is that the ability to gather, process, analyze, and use enormous amounts of data in real time can be a revenue-generator for companies in the highly competitive life sciences industry. The amount of available, focus-area-specific data is increasing, and AI is enabling companies to derive exponentially more value from the data in less time than ever before.

Unless a company feels confident pursuing operational strategies based on limited data and educated guesses, AI is the next logical step in the business ecosystem. Effective decision-making comes from data-driven insights not available without the use of AI:

- Obtain comprehensive and accurate insights about emerging trends.
- Connect relevant internal and external data for highly accurate predictive analytics.
- Utilize data compiled in a format that cannot be analyzed using traditional methods.
- Augment product design processes using algorithms that analyze all production parameters and restrictions and offer insight on the best design approach.

We welcome technology that gives us more time and the ability to develop and deliver what brings value to people. Turning over repetitive, time-consuming and arduous tasks to automated technology allows people to be creative and put more effort into innovation and problem-solving.

With the updates and changes in the regulatory landscape, the life sciences industry faces a challenging future, primarily involving compliance with more and stricter rules. Sustaining a competitive edge will require:

- **Better internal efficiency** – Less fragmented and more transparent and holistic organizational structures.
- **Modernization** – IT infrastructure capable of utilizing the technologies (integration, automation, data analytics, etc.) available for optimizing quality and compliance efforts.
- **Compliance competency** – A compliance-ready company culture.

Out of necessity, companies in all industries are modernizing their operations. At the same time, the workforce is transforming. The emerging employee population has more of an inherent aptitude for creativity, innovation and functioning in technology-driven environments where humans work in concert with AI-based technology. Companies will need to account for this type of organizational ecosystem when creating their business models.

## How MasterControl Provides an Advantage in a Competitive Life Sciences Industry

MasterControl's business excellence solutions serve as the foundation of quality and compliance for hundreds of life sciences companies worldwide. Providing much more than enterprise quality management system (EQMS) automation, MasterControl allows companies to efficiently manage the entire life cycle of a product from design, development and clinical trials all the way through to postmarket surveillance.

**MasterControl software solutions include:**


Quality

### Quality Excellence™

MasterControl Quality Excellence™ is an integrated, digital quality management system (QMS) that allows companies to track and monitor production quality and compliance and generate data-driven intelligence across the entire product life cycle.


Clinical

### Clinical Excellence™

MasterControl Clinical Excellence™ allows companies to automate clinical and quality management tasks throughout the clinical life cycle, from pre-clinical through phase IV trials and beyond — all on a single platform.


Regulatory

### Regulatory Excellence™

MasterControl Regulatory Excellence™ integrates content management with registration and submission capabilities to harmonize regulatory and quality processes, simplify global submissions, and accelerate time to market.


Manufacturing

### Manufacturing Excellence™

MasterControl Manufacturing Excellence™ automates a company's production records using a digital production records system with full connectivity to other systems. Manufacturing Excellence reduces human errors, ensures data is complete and accurate, and improves operational efficiency.


Development

### Product Development Excellence™

MasterControl Product Development Excellence™ aligns resources and expedites new product introductions, so companies can create, organize and manage new product development content, and efficiently manage content processes.


Supplier

### Supplier Excellence™

MasterControl Supplier Excellence™ ensures quality and visibility across the supply chain. The unsurpassed collaboration functionality seamlessly connects and integrates all internal and external supplier quality management processes.


Postmarket

### Postmarket Excellence™

MasterControl Postmarket Excellence™ facilitates coordinated regulatory reporting, optimizes customer complaints gathering and surveillance, and enhances an organization's capacity to analyze and route data to the appropriate points of use.

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