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FDA'S DIGITAL TRANSFORMATION JOURNEY

A Roadmap to the Agency's Modernization Action Plans

An Axendia Insight Brief Presented by Certara

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Introduction

Over the last decade, the FDA and the industries it regulates have recognized the need for a modern, well-integrated, reliable, efficient, technology and data infrastructure to support FDA administrative, regulatory, and business operations.

As Life-Science manufacturers embrace new technologies to speed time to market and products become more complex, FDA is developing systems to be more efficient and effective in the review, approval, and regulation of human drugs, biological products, and medical devices.

To achieve this transformational goal, FDA has embarked on a series of organizational and information technology activities. These activities are aimed at advancing ongoing electronic communications inside the Agency, with the public, and between the FDA and the companies it regulates.

"In September 2019, when we announced the U.S. Food and Drug Administration's Technology Modernization Action Plan (TMAP) we spoke about the ways that the FDA is modernizing our approach to the use of technology for the Agency's regulatory mission," commented Janet Woodcock, M.D., Acting Commissioner of Food and Drugs, and Amy Abernethy, M.D., Ph.D., former Principal Deputy Commissioner & Acting Chief Information Officer. "Data modernization is the next step in the Agency's overhaul of its approach to technology and data," they added.[1]

The Agency's modernization efforts are not simply focused on technology. The FDA is undergoing true Digital Transformation establishing Data Governance and modernizing and streamlining processes to make them more efficient and effective.

To achieve its goals, FDA is doubling down on cloud technologies and the use of shared inter-operable data and structured information. This approach enables longitudinal evaluation and modern capabilities like artificial intelligence (AI) for prediction and blockchain for track & trace. It also expedites the adoption of computerized modeling & simulation to inform clinical trial design, predict clinical outcomes, demonstrate safety and effectiveness, identify relevant patient populations, and support regulatory submissions.

This Industry Insight Brief delves into FDA's Digital Transformation initiative and its impact on the Life-Science industries.

[1]Source: FDA's Data Modernization Action Plan: Putting Data to Work for Public Health

The Future is Now

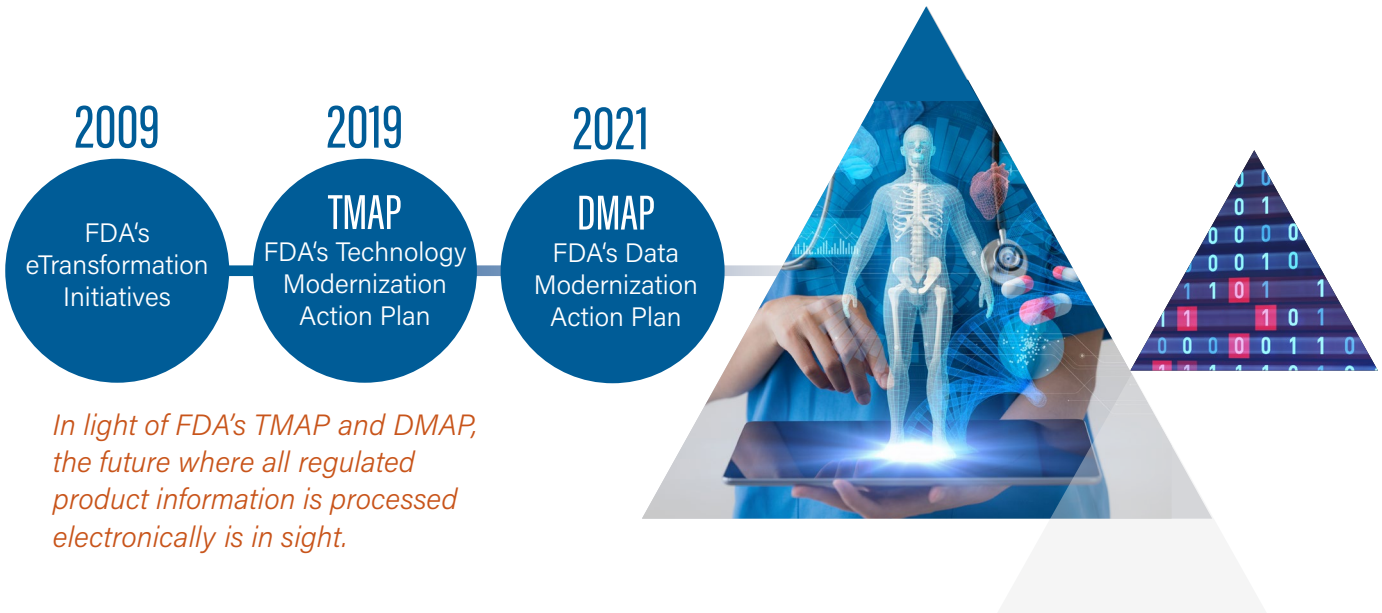
FDA recognized the need for modernization and digital transformation over a decade ago.

In 2009, Axendia interviewed several FDA officials regarding the need to modernize the FDA's electronic information infrastructure to support a research study on FDA's eTransformation initiatives. See: The Future of the FDA: Operating in an "Electronic World"

Dr. Armando Oliva, then FDA Deputy Director for Bioinformatics, FDA made a futuristic statement at that time, that is fast becoming a reality:

"It's fair to say the FDA is actively moving toward an electronic world where all regulated product information comes in electronically. I couldn't tell you when that is going to happen, but certainly there are active discussions underway to move to an 'all electronic submission environment' for all FDA regulated product information, whether it be product quality, manufacturing, pre-market, or post market data."

10 years later, FDA rolled out their Technology Modernization Action Plan (TMAP) to support its digital transformation journey, and in 2021 the Agency rolled out the next phase of their Digital Transformation journey, with the Data Modernization Action Plan (DMAP).



In light of FDA's TMAP and DMAP, the future where all regulated product information is processed electronically is in sight.

FDA's Modernization

Scientific and biomedical advances over the last decade have brought significant improvements in patient outcomes. In addition, product innovations continue to test the boundaries between product types and the historical lines separating FDA product centers.

However, the technology used by FDA to review, approve, and regulate these products has not kept up.

"The FDA legacy architecture is designed around internal data centers and a hard perimeter to keep outside threats out," admitted Vid Desai Acting Chief Information Officer (CIO) & Chief Technology Officer (CTO) at FDA. "This is similar to what many organizations have. However, the new emerging healthcare environment challenges this."[2]

As a result, the Agency is investing in a technical infrastructure as part of TMAP. This plan provides a solid foundation to address and close the current gap and supports ongoing technology modernization to help FDA scale its capacity to meet increased complexity and workload while reducing regulatory review times.

The use of a modern infrastructure and data schemes that can accept, evaluate, and analyze novel data sources (e.g., real-world data) and apply that data to support regulatory decision making will also allow FDA to deploy its resources more effectively and efficiently.

According to Dasai, "The new technology environment has to assume a very distributed and collaborative, but secure internal and external environment. The new environment has to be agile, with workloads that can be easily moved from on-prem to the various cloud environments and also to integrate and collaborate with data and people anywhere in a secure and trusted manner. The new environment we're building is going to be built around software defined networks and zero trust security concepts."

TMAP provides a robust technological foundation for the management, security, quality control, analysis, and real-time use of data—that will expedite the path to better therapeutic and diagnostic options for patients and clinical care providers, and better tools to enhance and promote public health.

[2]Source: FDA, Modernizing FDA Data Strategy

Digital Paper is not Digital Transformation

"We're not talking about PDFs and digital paper", affirmed Dr. Abernethy, "We're talking about digital transformation, use of cloud technologies, use of shared inter-operable data, digitized information," she added.[3]

Desai added "Modernization efforts at the FDA are not just about technology. Processes must also be modernized, making them more efficient and effective."

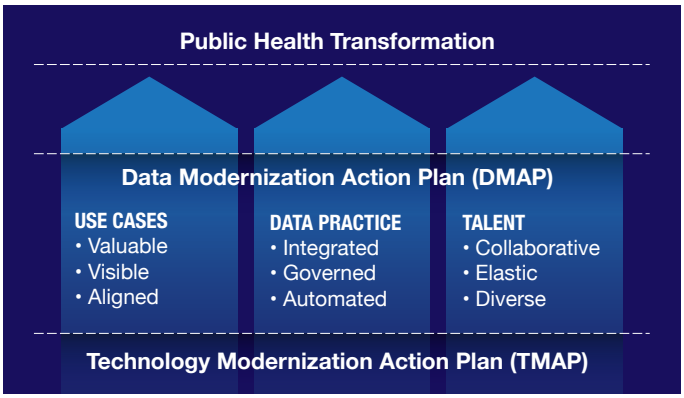
To support FDA's Digital Transformation journey the Agency is undergoing an enterprise-wide modernization of its technology infrastructure that includes these areas of focus:

- Cloud strategy and continued adoption of "as-a-service" models
- Streamlined software development capabilities for business-specific needs
- Data stewardship, data management and data exchange including application programming interfaces (APIs), standards, and other exchange mechanisms and tools
- Data clean-up and migration to cloud environments
- Ongoing dedication to cybersecurity excellence
- Integration of scientific computing into enterprise IT planning
- Organizational alignment within the enterprise-level technical organization across FDA
- Operational excellence and multi-year technical planning
- Cost containment and elimination of redundancy
- Enterprise IT governance
- Retiring legacy systems and software applications where appropriate

[3]Source: FDA, Modernizing FDA Data Strategy

Data are the Foundation for Good Regulatory Science

Data have always formed the basis of science-based decision-making. As technology becomes more sophisticated and our world becomes more connected, data from many new sources can help us understand how medical products are performing, pinpoint the source of foodborne illness, or understand emerging public health threats, shared Woodcock and Abernethy.[4]



Data is a critical component of FDA's approach to regulatory science. Today, most interactions and processes are digital and instrumented, creating an abundance of data. However, much of the information submitted to FDA is not in true digital form. As a result, most FDA data systems are still largely geared to a non-digital, document-based information standard.

"Although FDA's legacy technology and data systems allow the Agency to meet its regulatory responsibilities, FDA urgently needs new, robust, and flexible capabilities to avoid losing future opportunities to benefit patients and improve public health" according to Dasai.

The Agency is fully committed to Data Modernization as part of its Digital Transformation. "The creation of the first ever Chief Data Officer role at the Agency in itself is a manifestation and implementation of that strategy," noted Iyer Ram, FDA's Chief Data Officer. "Now we are embarking on modernizing our data strategy."[5]

To this end, FDA is deploying new data systems allowing it to manage and analyze data that previous generations of researchers, physicians, and FDA reviewers could have only imagined. The Agency's projects-based implementation approach is focused on demonstrating near-term value in specific areas while enhancing key data practices. However, a modern data strategy also requires proactive investments in foundational capabilities.

For example, reviewers currently spend 50% to 75% of the total review cycle identifying and analyzing data for a given submission. Modernizing data management and analysis strategies will greatly reduce reviewer cycle time and improve utilization of analysis resources.

Establishing of data governance and management practices will achieve the following goals:

- Enable better data quality and governance
- Simplify data acquisition and reduce cycle time
- Accelerate model development and use
- Provide security and scalability for enterprise use of data

[4]Source: FDA's Data Modernization Action Plan: Putting Data to Work for Public Health
[5]Source: FDA, Modernizing FDA Data Strategy

According to the FDA, data practices are based on 4 pillars:

 Identification	Building effective solutions using data requires the ability to identify the right data with the appropriate quality and completeness. Example capabilities are: ▪ Data catalog to search and review available data assets and relevant metadata. ▪ Workflow process to request and approve access.
 Data Curation	The organization and integration of data collected from various sources for effective utilization in data-driven decisions. Curation increases confidence in use of data and reduces cycle time without compromising the analytic rigor. Key activities and capabilities for data curation are: ▪ Characterization of data on attributes such as latency, completeness, security/privacy and quality. ▪ Classification of users based on proficiency and analyses based on impact of decisions. ▪ Development of "Fit for Purpose" services to match the curation with analytic needs using an agile and scalable model.
 Governance	In the DMAP context, governance spans the entire lifecycle of data and appropriate upstream and downstream activities. The objective of Governance is to reduce waste and friction in using data for decisions. The Governance program should be expanded to include appropriate use of models and AI-based algorithms, including: ▪ Technology, tools, data policies, analytic techniques, information disclosure and security processes. ▪ Reproducibility of results used for research. ▪ Architecture of transaction systems to reduce the need for curation.
 Automation	To meet the exponential growth of data and its pervasive use across the Agency, many data capabilities should be automated to assure reliability, predictability, and timeliness of data driven decisions. The Agency will: ▪ Learn from automation of application and security processes at the Agency in developing data operations. ▪ Place special focus on changes, prevent the introduction of potential bias and assumptions in data that drive models and algorithms.

AI is What's Next:

"FDA is sitting on a treasure trove of data, and we need a plan for how we're going to use it including how to leverage the right capabilities like AI," said Abernethy.

The Agency also intends to deploy artificial intelligence to increase the effectiveness of FDA reviewers and field investigators while ensuring analytical rigor and avoiding bias.

AI will be utilized to support a diverse set of regulatory needs such as detecting adverse events in different data sets, including postmarket data. Machine Learning (ML) will also be used to study the effects of synthesized data sets for training and testing in both pre-market testing and the FDA-regulated product lifecycle.

AI will be employed to inform the Agency's abbreviated new drug applications (ANDA) workload and prioritize research by predicting the time to first submissions for ANDAs referencing new chemical entities.

The Agency will deploy natural language processing (NLP) and human workflows to code adverse events (AE) in the International Conference for Harmonisation Medical Dictionary for Regulatory Activities (MedDRA).

The FDA will also leverage AI to support and accelerate the review process in areas such as:

- Improving the efficiency of reviewing regulatory submissions. Assessing the complexity of a submission upon receipt will enable FDA to allocate the correct number of resources early in the review cycle.
- Combining diverse data so clinical trial results can be analyzed in a more comprehensive and expeditious way.
- Developing and applying ML algorithms and natural language processing to retrieve and synthesize drug-related adverse events information from various data sources.
- Exploring how AI can be used in pharmacometrics, to aid efficient drug development, and/or regulatory decisions.
- Developing standardized metadata ontologies to leverage whole genome sequencing data to predict source tracking.

In fact, the Agency has already issued Good Machine Learning Practices (GMLP) as well as proposed regulatory framework for AI and ML[6] to support these initiatives. GMLP, describes a set of AI/ML best practices (e.g., data management, feature extraction, training, interpretability, evaluation, and documentation) that are akin to good software engineering practices or quality system practices.

[6]Source: FDA AI/ML-SaMD-Action-Plan

In Brief

FDA's influence is considerable – decisions made at the Agency will have a ripple effect not only across health regulators globally, but also throughout the industries it regulates.

To enable it to review, approve, and regulate the increasing complexity and variety of products and data that is growing exponentially, FDA needs to put data to use and create and encourage innovative partnerships to achieve this goal.

The Agency's modernization efforts are not simply focused on technology modernization. The FDA is undergoing true Digital Transformation establishing Data Governance with modernizing and streamlining processes to make them more efficient and effective.

To achieve its goals, FDA is doubling down on cloud technologies, and the use of artificial intelligence to analyze shared inter-operable data and structured information that enables longitudinal evaluation and modern capabilities.

FDA's Data Strategy will focus on the management, security, quality, control, analysis, and real-time use of data to accelerate the path to better therapeutic and diagnostic products that improve patient outcomes.

The future where all regulated product information is processed electronically is in sight, considering FDA's Digital Transformation journey.

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