Journal of GXP® Compliance

Volume 11 Number 4 July 2007

NUTRACEUTICALS AND THE GMP • PRODUCT TAMPERING PROCEDURE

RISK MANAGEMENT USING 14971 • DESIGN PHASE OF THE ADDIE MODE

Published by:
IVT
INSTITUTE OF VALIDATION TECHNOLOGY®

AN ADVANSTAR PUBLICATION

Process Transformation for Better IT Service Delivery in the Pharmaceutical Industry

By ***Kamal Biswas***

ABSTRACT

Soaring drug development costs, patent expiration, and reduction in the number of blockbuster drugs are driving pharma companies to look seriously at Information Technology (IT) enabled productivity. The pharma IT strategy must be strengthened to better support business needs. The traditional approach of "working for business" is evolving into a "working with business" model. Pharma IT processes must support this transformation and also manage mandatory regulatory requirements including the Food and Drug Administration's (FDA) Code of Federal Regulations (CFR) 21 Part 11 and the Computer System Validation (CSV) providing a high degree of assurance of a system's consistent performance. And IT process transformation must be able to deliver the right products, meeting all internal and external stakeholder needs including regulatory requirements.

A change management process helps users adopt the system and be part of the system development initiative, not just its recipient. No project can be successful if its users are not a part of the execution team.

INTRODUCTION

The traditional method of working in silos is not helping pharmaceutical companies combat the steep increases in the costs of drug development and sales and marketing nor does it enhance the productivity of workhorse manufacturing. In fact, it is posing a threat to double-digit growth. Pharmaceutical organizations are, therefore, considering IT as a facilitator to create a global collaborative work environment and to rein in the rising costs of drug development.

As IT is infused into all operations across the pharma value chain, regulatory compliance needs in IT-related activities are becoming significant. The traditional industry approach of not imposing Good Manufacturing, Clinical, and Laboratory Practice (GXP) requirements in IT areas has changed significantly in recent years. IT divisions are playing a more notable role in improving business productivity and are becoming the core component of every business function under regulatory authority's scrutiny. Thus, computer systems come under the purview of regulatory authority to bring more focus to IT processes, Standard Operating Procedures (SOPs), Change Management, Risk Management, Corrective And Preventive Action (CAPA), and revalidation. Compli-

ant IT processes now require considerably more rigor in documentation, review, and verification than previously accepted. This increases the overall cost of a project in comparison with traditional IT development project costs. The need for computer system validation further adds to costs.

Thus, on the one hand, the pharmaceutical industry is trying to leverage technology-driven productivity to drive down costs across the value chain, and on the other hand, it faces the inherent investment demands of IT projects. The magnitude of the challenge is compounded as pharma companies outsource IT services to drive down IT costs. To achieve an efficient balance between these conflicting requirements, there is a need to transform IT processes within industry. Service providers must use robust processes inline with regulatory necessity and deliver products with desired outputs to help achieve cost-saving goals. This requires additional internal validation efforts by companies. All these issues point to the need for the transformation of IT processes to ensure IT productivity, regulatory compliance, and cost reduction.

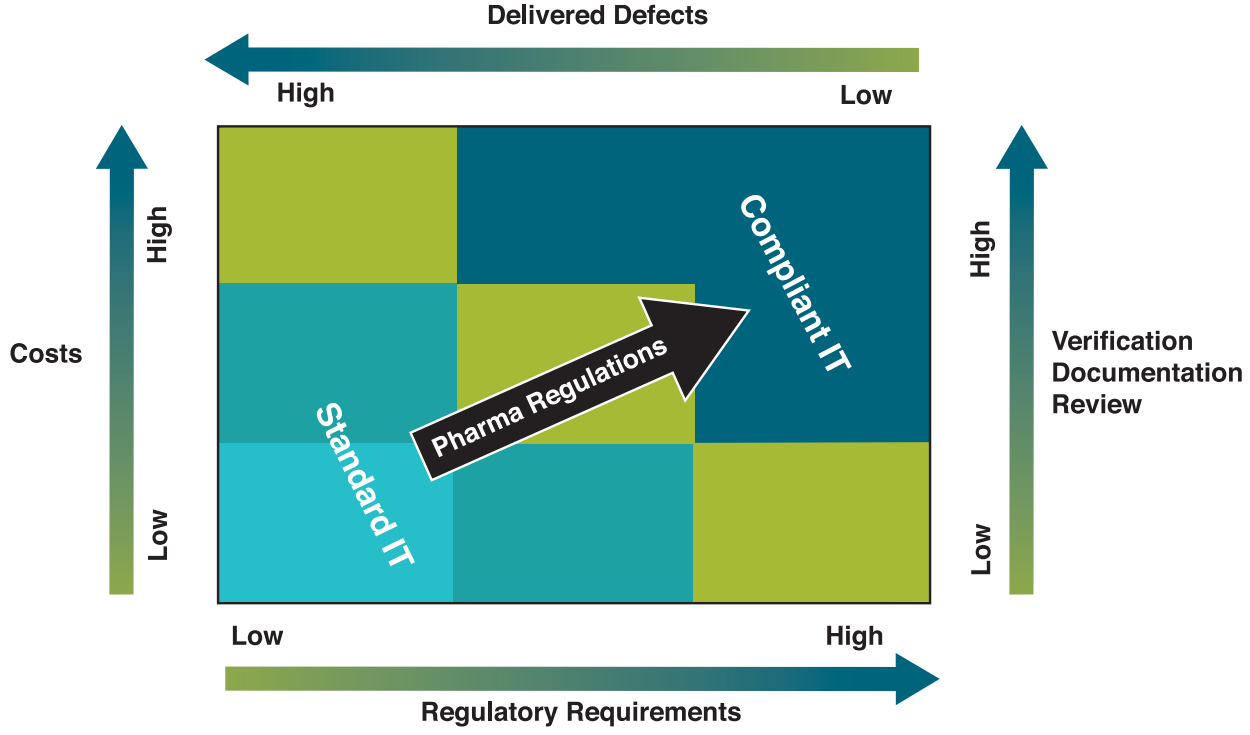
"Compliant IT" is different, and therefore, IT's planning and delivery is different.

IT in the pharmaceutical industry is different from IT in other industries. The single largest differentiator is regulatory complexity – systems must be formally qualified for use. As the predicate rule goes beyond the system under inspection, many more IT systems become subject to the compliance threat. This can be handled if regulated systems can be clearly segregated from non-regulated ones. Pharma companies are facing challenges in segregating regulated and non-regulated systems. Regulated systems must comply with regulations including FDA predicate rules, computer system validation, SoX, HIPPA and 21 CFR Part 11.

Ensuring compliance with these regulations places a high burden on IT processes across

Figure 1

Regulatory Defects within Requirements Delivered



planning, design, deployment, and management. Since pharma IT systems are liable to periodic regulatory audits, the rigor required is not limited to initial development, but must extend to the entire system lifecycle. In addition, every change – small or big - must undergo thorough change control activities, unlike in other industries where change is considered relatively routine. However, non-regulated systems that can take smarter excecutions using a risk-based qualificaiton approach.

In the pharmaceutical industry, a system's compliance needs and status can be determined when it satisfies the following conditions:

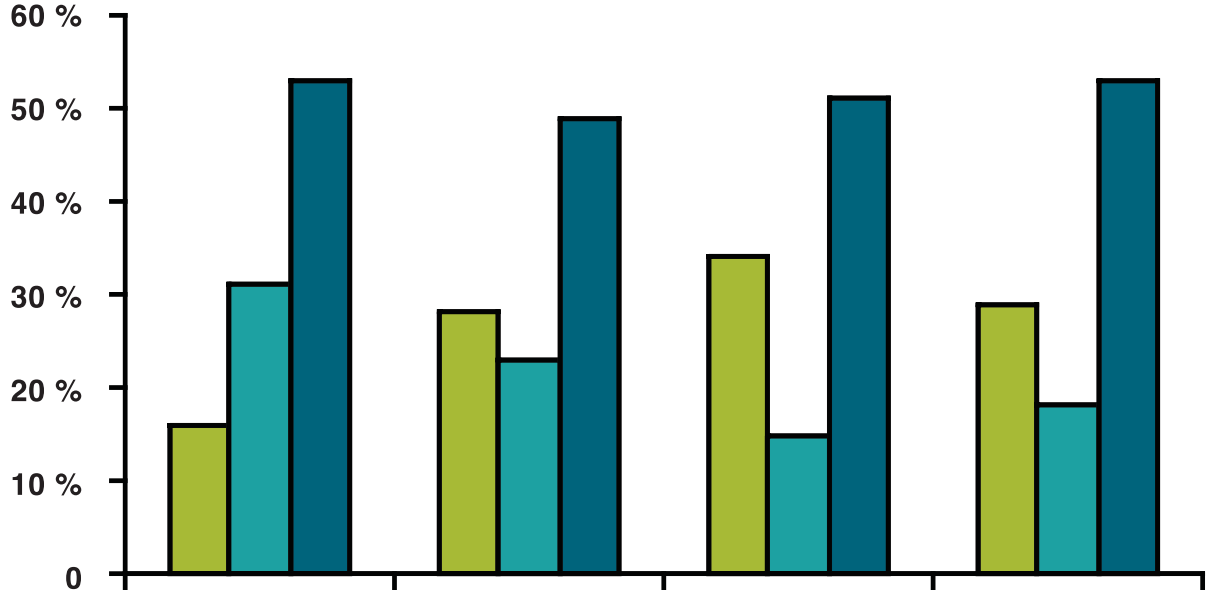
- The system supports business processes that require regulatory compliance
- The IT processes followed to gather requirements, design, build, and manage the system are qualified
- The processes have clearly defined execution roles and documentation to track execution

All these conditions add to the complexity of designing and delivering compliant systems. Unless IT processes are robust enough to capture all these details, downstream IT work may fail in delivering the right functionality, or may cause cost and schedule overruns. For instance, the functional needs of a 21 CFR Part 11 compliant application may be defined by users and effectively captured in User Requirement Specifications, but its non-functional requirements may not be defined very well and may

Figure 2

Source: Chaos report, Standish Group International

Software Project Success Rates



	1994	2001	2003	2004
Successful	16	28	34	29
Failed	31	23	15	18
Challenged	53	49	51	53

Software Project Success Rates for the ten year period from 1994 through 2004 indicate surprisingly high levels of failure and 'challenge' even with the application of User Acceptance Testing.

be left to interpretation. This "open to interpretation" situation causes issues during project execution. The problem increases multifold with other FDA predicate rules such as 21 CFR 210, 211, 221, 600, 610, OSHA, CAPA, or eCDT. Moreover, the process may demand a great deal of review and rework to ensure detailed traceability, infrastructure qualification, user training, etc., and should be addressed during budgeting and scheduling.

The effort expended in completing a traditional IT project is significantly lower than that demanded for a regulated IT system mainly because of the uncertainty in non-functional requirements and the regulatory needs such as, Computer System Validation, Part 11, and so forth. Traditional IT teams do not focus on these details during project planning. They remain undecided on system validation or infrastructure qualification needs, even in the matured state of project delivery, and suffer project risks from client expectation mismatch and incur huge schedule and budget overruns. Further, shortcuts to beat timelines, typically, lead to inferior product delivery.

Across a wide range of pharma IT projects, the success rate has been relatively low – even in the long run. Although IT departments and outsourcing companies have made significant improvements to the way software engineering projects are planned and executed, success rates have not improved significantly, as can be seen in the chart in *Figure 2*.

The Chaos report by Standish Group International (source *Figure 2*) shows that only 52% of the desired functionalities were made available in products delivered to users in 2004. This data may at first seem counter-intuitive because most applications are accepted only after User Acceptance Tests (UAT). And therein lies the rub – non-functional requirements such as application performance, audit trail, user authentication, data encryption, etc., are key aspects of regulatory compliance, but these aspects of the applications are often not tested in UAT. Non-delivery of these functionalities is a big risk in regulated applications, i.e., without testing audit trail functionality, an application cannot be claimed to be Part 11 compliant.

ARE THE CURRENT PROCESSES ENOUGH?

The main reasons for project failures are as follows:

- Incomplete or improper requirement specification
- Lack of process standardization
- Ineffective change management

The success of a project depends on executive sponsorship, project resource skills, technology selected, and the process for capturing system requirements. The process must help in developing a system that provides all functionalities needed, thus bonding the user and project teams. A change management process helps users adopt the system and be part of the system development initiative, not just its recipient. No project can be successful if its users are not a part of the execution team.

Most mature IT companies have adopted the Capability Maturity Model (CMM). CMM Level 5 companies have a different stature in process excellence. The goal of the CMM is to reduce project risk and drive program productivity and the quality of deliverables. The CMM framework strengthens basic IT processes and drives maturity, but it does not address pharma-related regulatory requirements described earlier. CMM helps set quality goals, provides process guidance, and sets priorities on the to-do list. It also helps define the measurement criteria and creates awareness about process standardization. However, it cannot help in defining how things must be done or who performs which tasks, which are vital in the pharma industry where specified tasks must be performed by defined roles. This sets the stage for robust methodologies that focus on execution of tasks. The methodologies should consider all areas of risks – regulatory, business, and system – and the design framework for execution.

The industry has always been undecided on the level of rigor to be put in place to be able to meet all regulatory requirements and yet be cost-effective. This must be considered along with policy definitions around segregating regulated and non-regulated systems or validated and non-validated systems. The FDA supports executions with a risk-based

approach as against fit-for-all processes.

The industry is also facing a challenge in consolidating various regulatory needs and handling them comprehensively. The GXP, computer system validation, and 21 CFR Part 11 requirements are being handled by one group and IT security by separate groups in the organization, even though all the groups share significant amounts of IT system-level information.

SO WHERE DO YOU STAND?

You can evaluate your current processes by answering the following questions:

- Does your process segregate validated systems from non-validated ones?
- Does your process clearly identify regulated systems?
- Is your process robust enough to handle different business situations?
- Can your process adopt smarter executions and react quickly to ever-changing business and regulatory needs?
- Does your process have well-defined execution roles?
- Does your process have a well-defined self-calibration mechanism?

The evaluation report will look very similar for most companies. Most of the processes will be either very weak, with no defined roles, or will be too rigid to be executed in varying business situations.

WHAT IS THE SOLUTION?

It is obvious that pharmaceutical IT projects must look beyond IT requirements while delivering the needed software. Regulatory complexities make the requirement elicitation process vulnerable. This increases the non-functional requirements so much that it causes project schedule and cost overruns, and the non-acceptance of functionalities.

Most downstream problems can be resolved if the IT team gets the requirements right. However, this is not an easy task and the pharma IT industry has not yet shown the desired maturity. Understanding the user requirements, the regulatory needs – direct and indirect – applicable to the business domain, and the non-functional IT requirements is a daunting task that needs multiple skill sets. The key challenge lies in getting the entire team to operate in sync. The following eight steps will enable pharma companies to better handle these challenges.

STEP 1: Create a robust process architecture

Companies must define the quality goal and identify the required processes and process aids. The process architecture must have four layers:

• Quality Policy:	• Describe organizational quality goals and the organizational structure to meet them
• Process Layer:	• Design processes that support the quality goal journey
• Process Supports:	• Process execution details in the form of SOPs, checklists, guidelines
• Process Deliverables:	• Predefine templates to create deliverables that support the processes

STEP 2: Open the door for executers to create processes

The best process is the one that can be executed easily. Processes are successful only when executers find them easy and efficient. Cumbersome processes always fail. The process team must be open to suggestions from executers to tailor

baseline processes. A robust change control mechanism must be institutionalized to make the changes more efficient and to eliminate *ad hoc* changes that put projects at risk.

STEP 3: Focus on requirements capture

The most significant value of a process is in delivering it right at the first instance. This sets the quality goal and minimizes IT process gaps between user specifications (documentation) and user needs (expectation). Process supports in the form of SOPs, work instructions, and checklists bridge gaps between the two. Both functional and non-functional requirements are important.

STEP 4: Standardize regulatory requirements

Most FDA regulations are open to interpretation. Companies can have their own viewpoint of a rule, but it is important to have a consistent interpretation across projects. Companies must create a standardized list of requirements for various needs, e.g., a list of requirements for a Part 11 compliant application, a list to comply with CDISC, etc. This helps the project team to quickly validate with users and comply with regulations. If it is not predefined, the business analyst of the project team must define them, which may cause project failure from too much dependence upon an individual.

STEP 5: Use tools to manage projects

IT service providers are coming up with mature processes that enable technology-driven productivity enhancements and drastically reduce the overall cost. These processes also help manage requirements, create forward and backward traceability, and better manage test results. As the FDA is increasingly laying more emphasis on tool-based risk management as a strategic program to reduce product risk, it applies more pressure onto pharma IT to be able to demonstrate greater value to business in regulatory risk management.

STEP 6: Create an enterprise risk management process

Enterprise compliance management processes help in combating a risk before it becomes a problem. A robust organization with strong process support will help eliminate program execution risks. The enterprise view will ensure effective participation from all stakeholders to make the project a success.

STEP 7: Train IT talent in business and regulatory domains

Lack of domain knowledge prevents IT teams from asking the right questions of users, leading to incomplete understanding of requirements. A lack of regulatory knowledge also hinders the ability of IT teams to address key requirements adequately. A well-defined process framework and robust training of all resources will improve project discipline, make teams more productive, and reduce the number of failures.

Article Acronym Listing

CAPA	Corrective and Preventive Action
CDISC	Clinical Data Interchange Standards Consortium
CFR	Code of Federal Regulations
CMM	Capability Maturity Model
CSV	Computer System Validation
eCDT	Electronic Common Technical Document
FDA	Food and Drug Administration
GXP	Good Clinical, Laboratory, Manufacturing Practice
HIPPA	Health Insurance Portability and Accountability Act
IT	Information Technology
OSHA	Occupational Safety and Health Administration
SOP	Standard Operating Procedure
UAT	User Acceptance Test

STEP 8:
Create process measurement framework

Key process execution steps should be monitored for performance to make the process more agile. Process performance measures should be defined followed by regular data analysis to help improve performance and make the execution more productive. Process measurement should be done at the execution step level to avoid redundancy in collecting these data separately.

CONCLUSION

As IT takes center stage in pharmaceutical companies for technology-driven productivity, the traditional way of executing IT is no longer acceptable to business. IT must shift from "we work for business" to "we work with business." This requires a paradigm shift in process execution to enhance IT service delivery and reduce project failures. The ever-increasing regulatory pressure makes processes more complex. But companies need to constantly focus on making processes smarter to be able to react to various changes. Success depends upon developing a robust process model, monitoring its execution efficiency, and making it nimbler for better acceptance. ❑

ABOUT THE AUTHOR

Kamal Biswas is a Principal with Life Sciences Consulting in Infosys Technologies Limited. Kamal is an expert in Pharma IT strategy and regulatory compliance in FDA regulated industry. He has over a decade experience in pharmaceutical manufacturing operations and IT. He is a thought leader in pharma IT strategy, IT enabled productivity in pharmaceutical manufacturing operations, and regulatory compliance transformation. Kamal can be reached at kamal_biswas@infosys.com

REFERENCES

1. Chaos report, Standish Group International
2. Infosys Internal Research
3. FDA, fda.gov