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Electronic Validation in the Pharmaceutical Industry

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Executive Summary

The authors investigate whether or not companies within the pharmaceutical industry still have a hard time effectively designing and following an electronic validation system. With increased data integrity issues from electronic systems, the FDA introduced 21 CFR Part 11 in 1997 to allow for the use of electronic signature and records for processes within the pharmaceutical industry. This regulation also required that the computer and electronic systems be available for audits and inspections by the FDA. In order to comply with 21 CFR Part 11 and adapt to new technology, companies must have an electronic validation system. The electronic validation system requires that the company provides documented proof that regulatory standards are met and electronic procedures have been tested and can assure quality results. A review of current literature examines how the industry utilized electronic validation after the introduction of 21 CFR Part 11. Finally, a case study is presented to see how a current company maintains its electronic validation system. The objective of this study is to look into a current company's knowledge of regulatory compliance as well as its strengths and weaknesses of its validation system.

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I. Introduction

Despite the fact that nearly twenty years have passed since the FDA introduced key regulations regarding electronic validation, the pharmaceutical industry still struggles to meet compliance regulations and adapt to new technology while trying to continue to deliver products safely and in a timely manner. The electronic validation process makes sure that a company's computer processes produce quality results (Stause, 2009). The validation process within the pharmaceutical industry requires that companies have documented proof that quality and regulatory procedures are being followed during every step of the manufacturing and distribution process (Peters & Ferrence, 2013). One of the most important FDA regulations that companies have to be in compliance with is 21 CFR (Code of Federal Regulations) Part 11.

In 1997, FDA introduced 21 CFR Part 11 for companies that chose to maintain and submit records electronically to FDA. 21 CFR Part 11 lays down the regulations for electronic signatures and electronic records to be considered reliable and trustworthy "and essentially equivalent to paper records and handwritten signatures" ("Meeting the FDA's Requirements", n.d.). The purpose of 21 CFR Part 11 was to allow companies to take advantage of using electronic technology while consumer safety was upheld based on standards set forth by FDA ("FDA to Conduct Inspections," 2010). The FDA introduced 21 CFR Part 11 out of concern for consumer safety regarding electronic and computer processes that were emerging in the mid to late 1990s. During the 1990s, FDA discovered that software failures and defects accounted for 7.7% of medical device recalls with a majority of these defects occurring when changes were made to software after initial installation and distribution (Bendale et al., 2011). As a result of their findings, the FDA dictated that validation for all processes from buildings and equipment to computer systems would be required to show that quality standards can be met. For electronic validation, all computer software and hardware required documentation to prove that processes meet standards, that proper testing of software was done, and verification through inspection and review had been conducted. In addition to the use of electronic signature and records, an important part of 21 CFR Part 11 also dictates that computer hardware and software system, controls, and documentation be maintained and made available for FDA inspection ("Part 11 – Electronic Records; Electronic Signatures," 2015). This piece of the regulation underlines the need of a validation system.

II. Electronic System Validation

In his article, Yin (2010) mentions that the FDA believed that the introduction of 21 CFR Part 11 would encourage companies to adapt to new technology through deployment in different operations—from research, manufacturing, and marketing to the validation process. However, some barriers were experienced while attempting to use this new technology. The main premise of 21 CFR Part 11 assumed that the industry had the right software infrastructure, capabilities, and validation system to comply with regulations. Yin believes that when the FDA first introduced 21 CFR Part 11, they were not aware that there was a gap between how the industry perceived the utilization of available technology and how regulatory concerns would actually be addressed. While regulatory demands to adopt electronic signature processes were expected by the FDA, many areas in the industry did not have a full understanding of this technology and how to use it within the validation process. They also did not have great knowledge on the software systems available.

To take advantage of emerging technology, companies would have to have an effective electronic validation system in place that could accommodate and adequately document changing technology. The introduction of 21 CFR Part 11 presented companies with the opportunity to update their business strategy. Companies could create business strategies to create or improve upon processes that would take advantage of new technology and also make sure that their documentation and validation system would keep them compliant. The industry had to be educated on how to make use of technological advances that could help improve processes and product quality while enabling them to respond to consumer expectations and demands (Budihandojo et al., 2007).

Yin (2010) mentions how many pharmaceutical companies did not consider validation of their electronic system as a high priority or even as part of their organizational culture. While pharmaceutical companies were used to validating their manufacturing steps, they did not worry too much about their electronic system and usually had outside vendors to maintain their electronic systems. The FDA assumed that companies would validate their electronic systems and processes similar to the way that they validated their manufacturing processes. This misunderstanding of the need for electronic system validation and a focus on specific parts of the 21 CFR Part 11 regarding just electronic records and signatures resulted in some companies spending millions of dollars trying to meet regulatory demands without establishing a reliable electronic validation system that produced adequate documentation or had the ability to adapt and accommodate new technology. For instance, Procter & Gamble established Electronic Records Electronic Signature (ERES) teams to make sure different regulations were being met by each department (Siconolfi, 2005). While the approach did address regulatory concerns, it did not produce a new and more efficient electronic validation system for the company. Instead the teams proceeded to focus on specific processes that used electronic signatures. While many companies focused on ways to utilize current technology, a new approach was needed within pharmaceutical companies to ensure that their validation system would help to keep them in compliance and able to adapt to technological advances and changes from year-to-year. The validation of electronic systems had to be prioritized and considered an important part of the culture of the company (Richman, 2005).

II.A. Electronic System Validation Expectations

Some companies have started to realize the need to focus on the validation system rather than just regulatory requirements. One of the main parts of the validation system is the documentation of procedures and system components (Ferris, 2000). A good validation system consists of adequate documentation to ensure that if there is a change in technology or regulatory procedures, the right information can be tracked down and adjustments can be made. Additionally, this process ensures that records and information do not get lost when moving from an old system into a new system.

A challenge that companies have faced over the past two decades is that not all processes have become totally paperless. Some companies use hybrid systems that include both paper records and electronic records. Both processes have to be validated with documentation and security measures to ensure data integrity. In 2005, Able Laboratories ran into major compliance issues when a major inconsistency appeared between their paper records and their electronic records resulting in massive FDA enforcement measures (McCulloch, Woodson, and Long, 2014). Able Laboratories had to stop all production and recall its entire product line. The FDA found specific members of the quality assurance and quality control staff to have violated good manufacturing practices (GMPs) with accusations of data manipulation. Violations of standard operating procedures (SOPs) was also evident due to the lack of record keeping as well as allowing for continued distribution of the drug products after bad laboratory results. Able Laboratories ended up filing for bankruptcy and going out of business (Taylor, 2012).

Data integrity is essential for pharmaceutical companies as the FDA and other regulatory agencies are concerned about the whole product life cycle. McCulloch, Woodson, and Long (2014) discuss how research laboratories need to consider the different parts of their processes that generate data that will be under FDA scrutiny. Equipment and facilities need to not only have gone through qualification processes and testing, but these activities should be well documented either in logbooks or an electronic system. Other record keeping could also include the life cycle of product samples, testing, and disposal. Records need to include a great amount of detail on the origination of all raw materials, lot numbers, and equipment used. The company should establish processes and SOPs that are consistently followed during testing and studies. These protocols should generate valid data and also have procedures on how to handle output that deviates from the norm. All data needs to be recorded in a timely manner either electronically or in designated logs and notebooks. This information should be reviewed by personnel and any deviations from the norm should be addressed. All records either in paper form, electronic, or a hybrid of both need to be archived safely in a location that can be accessible for review by both the company and any regulatory parties.

McCulloch, Woodson, and Long (2014) point out that to maintain compliance with 21 CFR Part 11, data within a hybrid system must be synchronized so that consistency exists between paper and electronic records. Any data being maintained within an electronic format must have the "integrity of the record assured" (McCulloch, Woodson, and Long, 2014). Data integrity issues within an electronic system can stem from both human error as well as intentional data manipulation. In addition, while audit trails and other features such as built in time-stamps and electronic signatures can help, some type of data verification process needs to be employed after manual entry of critical data occurs. These features can also point out if any data had been entered outside of the expected work-flow or was not entered right after a testing procedure was complete. A verification process can help to catch errors or raise red flags over potential data manipulation issues. Different interfaces and systems used during various stages must be able to successfully migrate data as well as have specific verification plans that are adjusted for the needs of that system.

II.A. 1. Models

Different models of validation have been discussed in pharmaceutical and FDA literature, specifically the V-model and the O-model (Stage, 2005). The traditional V-model for validation has different documentation at each step and may not share documentation from one part of the process to the other. Each step funnels down to the end result. But once the procedure passes one step, there is no or little feedback given to a previous step with the documentation. As a result, if there is a change made at one step due to new technology or regulatory demands, other areas and units may not be aware of this change.

In the O-model there is more integration and sharing between the stages with the documentation. The O-model allows for the newest versions of documentation and allows electronic records and signatures to move from one part of the process to the other. So if changes in documentation and procedures take place at one step, the other units involved in other steps or procedures are notified so there is no disconnect between procedures or ignorance between steps (Stage, 2005).

II.A.2. Security

According to Lopez (2003), the security requirements for electronic signatures must include privacy, authenticity, reliability, and non-repudiation. Data encryption refers to the scrabbling of messages and the use of specific passwords or keys to generate the output. Authenticity, reliability and non-repudiation can be done through digital signatures, certificates, and hash algorithms. Digital signatures are implemented through software to include the use of public and private keys as a way of verifying who modified or approved a record. Hash algorithms condense messages and records into a fixed length so that the message cannot be easily recovered. A system that has a reliable audit trail is essential to ensure authenticity of data and to show if there has been any tampering or who was involved in the process. A reliable audit log should be able to show when each record was created, deleted, or tampered with and also the user associated with each of these changes. If the audit log looks clean without any abnormalities or appearances of data manipulation, there can be some confidence behind the integrity of the data. The electronic signatures and other features must be up to FDA standards as the FDA can request to look at the system during an audit or an inspection. Being able to follow up on issues that come up during a consumer complaint or a recall of a product is also important. Documentation for each of these features is an essential part of the electronic validation process. An effective electronic validation system would have a way of organizing the documentation and also keeping track of the changes through audit trail and other system indicators (“System Validation for 21 CFR Compliance,” n.d.).

II.A.3. Validation Plans

The models followed by the companies along with system specifications help to ensure that the company is able to have a validation plan that will keep it in compliance. According to Peters and Ferrence, “the Federal Food, Drug and Cosmetics Act Section 501 (a)(2)(B) which states that ‘a drug is deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or were not operated or administered in conformity with Current Good Manufacturing Practices (CGMPs),’ serves as the legal basis for the practice of validation" (2013). Ferris (2000) discusses how various system requirements need to be looked at. He describes a full life-cycle analysis starting from the different components used, the operating system in place to the applications installed while stressing the importance of documenting all the components. When trying to implement new procedures or technology, an effective validation system can help to reduce time and costs while ensuring the integrity of the end product reaching the market.

The validation plan is based on the user requirements specifications (URS) which is determined by the company and the clients the company is serving. This URS highlights the needs for the computer validation system that are essential for carrying out the goals and business processes for the organization. In addition to the URS, there needs to be a project plan, functional and design specification, as well as user testing. The project plan sets forth the timeline for the project. Functional design specifies expected functionality while the design specifications explain how the system is expected to perform. The needs of the company dictate how these features are set up and utilized. In terms of testing new software and hardware, there is a three-level structure for user testing that should be followed: Installation Qualification (IQ); Operational Qualification (OQ); and Performance Qualification (PQ). Additional important procedures for testing include Hardware Design Specifications (HDS), Software Design Specification *(*SDS), and Change Control (STSV Consulting, n.d.). These procedures are always conducted and tested under the supervision of the Quality Assurance department.

II.A.3.a. Installation Qualification (IQ)

IQ occurs when a new product or instrument is installed for the first time. The main objective of IQ is to ensure that the installation has been done as per the user's requirement. Documentation includes the type of model, vendor that the model came from, and other data on the origin of the product. Any additional software or hardware needs for the product are also included within the documentation. During this time, the product is assessed to look for any damages that may have occurred during transportation or perhaps during the installation process ("Installation Qualification and Operational Qualification", n.d.). For instance, IQ will test that the operating system has the appropriate processor, RAM, etc., that all files required to run the system are present, or that all documentation required to train system personnel has been approved (Ofni Systems, n.d.).

II.A.3.b Operational Qualification (OQ)

Once the product is installed OQ takes place to ensure that the product is functioning as expected and that operations can continue. Testing is done to make sure basic and expected functions work appropriately ("Installation Qualification and Operational Qualification", n.d.). Documentation on this process is necessary to ensure that testing was successful and also to ascertain that the expected outcomes should not be negatively affected. Operational qualification is defined in the Functional Requirements Specification. Depending on the needs and the complexity of the system, OQ can be combined with IQ or Performance Qualification. For instance, OQ may test that each screen accepts appropriate data, that system security has been properly implemented, that all technological controls for compliance with 21 CFR Part 11 are functioning as expected (Ofni Systems, n.d.)

II.A.3.c. Performance Qualification (PQ)

PQ is a similar step to OQ in terms of testing but rather than just testing basic functionality, PQ tests how the product does when working with a heavy load ("What Are IQ, OQ, and PQ, and Why Are They Required," n.d.). The purpose of PQ is to make sure that the product can function during a realistic work environment. Successful testing with a heavy load indicates that the product will be able to perform during peak hours or may be also able to handle unexpected increases in activity. PQ should be approved before protocol execution. For instance, PQ can determine if a system can handle multiple users without significant system lag or that a laboratory test correctly identifies a known material (Ofni Systems, n.d.)

II.A.3.d. Hardware Design Specifications (HDS)

HDS identifies and delineates the control equipment requirements of the functional description and agreed control methods. HDS includes detailed equipment specifications like manufacturer, model number, serial number, and system configuration.

II.A.3.e. Software Design Specification (SDS)

In the context of software, design specification includes a document that describes all data, architectural, interface and component level design for the software. While an HDS document will include information about a product and how it can be put together, SDS is designed to meet the unique needs of customers.

II.A.3.f. Change Control

Change Control refers to how processes are managed to make changes within a controlled system. Change control demonstrates to regulatory authorities that validated systems remain under control during and after system changes. The following steps may be included in a change control project: request a change, assess the impact of change, system development in a safe environment, system testing and re-validation, and implementation of the change (Ofni, n.d.)

II.B. Compliance Failures

When companies fail to effectively validate their electronic system, the FDA issues "tickets" for violation of FDA rules through Form 483. McCulloch, Woodson, and Long (2014) point out that violations of 21 CFR Part 11 points towards data integrity issues and infractions on current Good Manufacturing Practices (CGMP). In 2008, the FDA found issues with data quality and banned 30 products from the market. Companies faced massive fines with a few of them having to file for bankruptcy. The FDA found Leiner Health Products to have issues with data manipulation and inadequate testing resulting in a $10 million fine. In another instance, the Department of Justice issued a decree on behalf of the FDA on the Indian generic drug manufacturer Ranbaxy due to multiple violations (McCulloch, Woodson, and Long, 2014). These violations included incorrect testing procedures and inconsistent data records (“FDA AIP Letter to Ranbaxy Laboratories,” 2009). Ranbaxy had to hire outside auditors and agree on making fundamental changes to their processes. Ranbaxy decommissioned one of its facilities in the United States due to the findings from the decree (McCulloch, Woodson, and Long, 2014). In their article, McCulloch, Woodson, and Long (2014) mention how the FDA decided to raise the enforcement profile on 21 CFR Part 11 in 2010 due to data integrity issues. The authors mention that within the last three years, the FDA has issued over thirty Warning Letters and Form 483 inspection observations.

II.B.1. Which violations does 483 include?

Form 483 is drafted after an inspection if the FDA inspector feels that any violations had taken place within a facility that is supposed to be under regulatory compliance. FDA regulations are structured so that companies can take a broad regulation and apply it in a process that works for the particular business being conducted in a given facility. However, the main aim of the regulations is to guide companies in making policies and procedures that will make the end products as safe as possible for the consumers. The regulations require checks and balances throughout the development and production processes, as well as very thorough documentation and recordkeeping. “When product is produced that does not meet its specifications, the regulations require that the occurrence be investigated to determine why the product did not turn out as expected. Were all of the production procedures followed? Were all of the raw materials and/or components manufactured to their specifications? Did any conditions exist in the environment that could have contributed to the nonconformity? By answering the question of how the deviations happen, they can be prevented from recurring, and from nonconforming product potentially reaching customers" (MedMarc, n.d.). According to Medmarc (n.d.), in 2013, the top five observations cited in medical device facilities were inadequate procedures for corrective and preventive actions (CAPAs); inadequate complaint handling procedures; inadequate documentation of CAPA activities; inadequate process validation; and inadequate Medical Device Reporting (MDR) procedures. The three companies mentioned earlier were all guilty of one of these five violations. Among their violations, Able Laboratories was guilty of inadequate process validation when the FDA found that their products did not meet established standards, specification and quality control criteria ("Able Laboratories Inspection Observations, 2005). Ranbaxy was found to have inadequate MDR procedures since appropriate controls were not established over their computerized system. Leiner Health Products' data manipulation is an example of CAPA.

Once a Form 483 has been issued, the company must make the decision to respond. However, the FDA only considers responses from the company within a fifteen-day period. The company must show that it is taking steps to address the violations found within the Form 483 that was produced after the inspection. If the violations are relatively minor and if the company indicates within its response that it is taking the right steps to address the violations, then the FDA is likely to feel the matter resolved and close the case. However, if there is no response or if the FDA feels that the response was inadequate, warning letters and further sanctions may follow (MedMarc, n.d.). In order to remedy a violation involving a recall, companies have to report back to the FDA district office within ten working days after the firm initiates any recall incase a risk was involved. However, no report is required if there was no risk involved, but a record of recall is required to be maintained. Actions taken by manufacturers to improve the performance or quality of a device includes market withdrawals, routine servicing, and stock recoveries ("Recalls, Corrections and Removals", 2014).

II.C. New Technology: A Virtualized, Cloud Environment

In addition to maintaining data integrity, pharmaceutical companies must make sure that their electronic validation system can be effective in the event of changes and/or the introduction of new technology (Wingate, 2004). A validation plan must be in place to allow records from old legacy systems to be checked. Over the past few years, virtualization and cloud technology has started to become a more popular choice for businesses. Virtualization is the software that manipulates hardware, while cloud computing refers to the service that results from this manipulation. So, in other words, virtualization is the basic element of cloud computing that helps deliver on the value of the cloud computing. Mostly, the concepts of virtualization and cloud computing are confused because they work together to provide different types of services as in the private cloud. For instance, the cloud can, and quite often includes virtualization products to deliver the compute service. According to the vice president of compute solutions at IT firm, Weidenhammer, the difference between a true cloud and virtualization is that "a true cloud provides self-service capability, elasticity, automated management, scalability and pay-as you go service that is not inherent in virtualization" (Angeles, 2014).

Bowers (2011) mentions how cloud technology is attractive to many organizations due to the ability to process, store, and access data through the cloud. Companies may find this option attractive if they are confident in the security being offered by the cloud. The convenience of the cloud does have appeal for companies. A cloud based infrastructure ensures that employees are securely accessing and exchanging the same data from the same location in the cloud while possibly being in different physical locations. Additionally, cloud technology offers a low cost model since there are fewer maintenance needs and use of physical hardware is reduced (Sommer, 2013). However, Sommer (2013) mentions that possibly only non-confidential data should be shared through the cloud. The concern regarding non-confidential data would be important when using a public cloud but companies perhaps may be able to work on private clouds. So what exactly is the difference between a private and public cloud?

II.C.1. Private Cloud

The main feature of private cloud that differentiates it from public cloud is that it is hosted on the company's intranet. All of the data is protected behind a firewall. Private cloud is a great option for companies who already have expensive data centers because they can use their current infrastructure. All management, maintenance and updating of data centers is the responsibility of the company. Over the course of time, the servers will need to be replaced, which can get very expensive. Despite these few drawbacks, private clouds offer an increased level of security and they share very few, if any, resources with other organizations (White, 2016).

II.C.2. Public Cloud

As opposed to private cloud, the company is not at all responsible for maintaining and updating of the servers. The data is stored in the provider's data center and the provider is responsible for the management and maintenance of the data center. The public cloud option is more attractive to most of the companies because it is time effective and also reduces lead times in testing and deploying new products. However, the quality of data security is not as strong compared to that of the private cloud environment. Experts, however, explain that even though companies do not control the security of a public cloud, all of their data remains separate from others and security breaches of public clouds are rare (White, 2016)

While an attractive option financially, the pharmaceutical industry has to figure out if cloud-based technology can be FDA compliant. According to Williams' presentation, "Regulated Applications in the Cloud: Aspects of Security and Validation" (2011), prior to running regulated applications in the cloud, pharmaceutical companies need to figure out ways to assess and mitigate the security risks involving moving to a virtual environment. Some of these risks address data security such as encryption and VPN. Pharmaceutical companies connecting to cloud service providers need to make sure that they have secure and encrypted IPsec VPN connection. Traffic traveling between the two networks is encrypted by one VPN gateway, then decrypted by the other VPN gateway. This process protects the data as it travels over the insecure internet. For instance, a pharmaceutical company may desire its employees to be able to work remotely from their homes and while traveling. However, this may pose concerns like exposing its intranet to unauthorized access and the possibility that security of sensitive information may be compromised (Microsoft, 2015). Additionally, outside vendors who own and support the software for cloud technology may not have an understanding of pharmaceutical security and regulatory requirements. Sommer (2013) points out that companies do not have much control over changes to and maintenance of their software. The companies have to wait for the vendor to come up with updates and patches to address concerns. These issues may possibly lead to service access issues which may be a major problem on the customer end. The physical server location may cause issues since 21 CFR Part 11 dictates that computer systems must be available for FDA inspection. Since the physical servers would be maintained by the outside vendor, if they are not available for FDA inspection, there would be a definite violation of 21 CFR Part 11. These concerns hold true if the company was looking to utilize an outside vendor and a public cloud. However, some of these concerns may be mitigated if a company decides to go to a private cloud and are able to stay in compliance with FDA regulations.

According to Williams (2011), these issues and concerns regarding cloud technology need to be addressed through qualification and validation. An approach has to be taken to figure out what needs and procedures would address these issues. Similar to the rest of the validation process, documentation needs to be created and maintained to prove compliance with regulatory concerns. To address data security, best practices dictate that the company should look at Virtual Machine (VM) level security; multi-layered defense; patch management; and data protection and encryption.

VM refers to a logical process that interfaces with emulated hardware and is managed by an underlying control program. Applications need to be updated and the infrastructure on which the application is to run should be qualified. Documentation for each of these parts will be needed for the overall validation plan. Multi-layered defense or multi-level security (MLS) refers to the application of a computer system to process information with incompatible classifications, permit access to users with different security clearances and prevent users from obtaining access to information for which they lack authorization. Patch management is an area of systems management that involves acquiring, testing, and installing multiple patches to a computer system. Patch management tasks include: maintaining current knowledge of available patches, deciding what patches are appropriate for particular systems, ensuring that patches are installed properly, testing systems after installation, and documenting all associated procedures.

An advantage of applying patches in VM environment is that snapshots can be acquired prior to the application any new security patches. In case, an issue arises after deploying patches the operating system can be rolled back to the previous stage.

III. Case Study: Encompass Elements, Inc.

According to its public website, Encompass Elements, Inc is a company that provides "support across the categories of integrated direct marketing, fulfillment and distribution, digital technology, and strategy and planning" (n.d.). Working with pharmaceutical companies as some of their clientele, Encompass Elements needs to make sure that they adhere to regulations set forth by the FDA (Encompass Elements, n.d.). They also make it a point to keep in place an electronic validation system that works and meets client needs and expectations. Specifically, the company handles procurement and fulfillment for its clients through the development warehouse management and shipping application. In terms of size, Encompass Elements is a smaller company with a staff of about 200 employees (anonymous employee, personal communication, November 3, 2015). Through an interview process, a few of their employees discussed their views of the company's current electronic validation system. These employees have a different range of responsibilities in the company but all of them are aware of the electronic validation system and are able to comment on how the system operates.

III.A. Strengths

The employees interviewed generally seemed to have a favorable view of the electronic validation system. One employee (personal communication, November 2, 2015) believes that the SOPs for the validation of the controlled environment is critical for the company and well handled. Specific procedures that are performed and documented well include IQ, OQ, and change control. The Director of Quality Control (QA) (anonymous employee, personal communication, November 5, 2015) believes that a high level of expertise exists among the staff involved with validation (anonymous employee, personal communication, November 5, 2015). Additionally, the staff has great familiarity with FDA requirements and the need for documentation. The Quality Control department and the validation team are considered strengths of the company with regard to the electronic validation system. One of the employees (2015) mentioned that the director of the QA department has an open door policy to allow any individuals to stop by with concerns. Additionally, quarterly trainings are held for updates on good manufacturing practices (GMP) and the validation system. The QA department gets updates from the FDA as well as the Product Development Management Association (PDMA) which provide information on issues and concerns that the QA department would need to share with the rest of the company (anonymous employee, 2015).

With a strong validation team and QA department, Encompass Elements employees have a zero tolerance policy with regard to following regulations. Employees who work within the regulatory environment must be aware of what needs to be done and what processes need to be followed including producing and maintaining documentation (anonymous employee, 2015). Additionally, the QA department has set up a “STOP” mail box (anonymous employee, 2015). If any employee notices any issues and needs to report an incident, they email a description of the issue to the mail box. The emails are reviewed by the QA department, which determines what the next steps are, who needs to get involved, and what should be done to ensure there is no violation of regulations.

To ensure that software and hardware are well maintained and FDA-compliant, Encompass Elements has a strong technology staff from the developers to the database and network teams (anonymous employee, 2015). The in-house developers are able to develop and customize code in order to make changes for maintenance or to remediate issues during or after the validation process (anonymous employee, personal communication. November 4, 2015). The technology staff understands that there are technological updates and continues to seek more training as well as qualification to ensure that the company can keep up with any changes.

III.B. Balancing System Requirements and Expectations for Production

One employee (2015) mentions that the system works and runs as expected without much need for downtime. The steps put in place through the validation process reduce unexpected surprises which is critical for day-to-day operations and client relations. Additionally, the client base expects that the company is up-to-date and aware of regulatory changes and concerns. New regulations or updates from the FDA do not excuse any type of delays to meet production expectations. The company has to make financial choices to ensure compliance concerns and client expectations are met (anonymous employee, 2015).

Upper management within Encompass Elements fully supports both the validation process as well as the maintenance of current technology standards (anonymous employee, 2015). Superiors fully understand the risks involved in the event of the company falling out of compliance, and they also realize that the utilization of technology is essential to improve performance and meet market demands. Upper management encourages the development of internal applications that can be maintained and adjusted to meet regulations (anonymous employee, 2015). Additionally, with the need for compliance, concerns with traceability and having systems with good audit trails is considered of high importance (anonymous employee, 2015).

III.C. Weaknesses

While the company's QA department is strong and is very concerned about being on top of regulations, one of the employees mentioned (2015) that the director of the department is still not satisfied with where the validation system is and believes that there is still room for improvement. Specifically, the director of QA believes that there could be more comprehensive testing with more thorough reviews of access levels. These two features are considered among the threats to processes supported by the validation system. The employee also pointed out a few specific processes that need improvement due to limited resources. These process include pick and pack processes and inventory classifications. Limited technology leaves the pick and pack process in a hybrid form. This particular employee would like to see this process moved to being completely paperless. If classification of inventory was done better, there would be faster processing because capturing the product in the right area would be done more efficiently.

Outside of the QA department, employees (2015) believe an additional challenge with the current validation process includes the fact that the change control and testing processes can slow implementation of new functionality and hardware. On one end, QA believes there should be more testing but there need to be changes to ensure that the testing is more efficient and that there is no delay getting the end product to the clients. QA would need to have conversations with the employees who are working with the clients to get an understanding of the type of deadlines that exist to ensure that if any testing procedures are taking place they can all be done within a reasonable timeframe.

Based on the response earlier that Encompass Elements only has about 200 employees making it a smaller company that does not have unlimited financial and personal resources. The limitation of resources may prove to be a threat for the company down the road. These legacy systems pose a threat in terms of proper validation (anonymous employee, 2015). Another employee (2015) believes specifically that some of the physical servers are getting obsolete as well and that there is need for upgrades and further research for these servers. There are performance concerns with these servers that would have a negative effect on company processes. A possible solution could be to move the servers to a VMware platform and have the servers in a remote connection. One employee (2015) points out that location connectivity is a threat that the company has to address. If these servers crash or something else happens that requires significant maintenance downtime, customers will be highly inconvenienced and may negatively impact customer retention.

III.D. New Technology

While many of the weaknesses of the organization seem to point to a need for more investment in technology, upper management of the organization understands the need to stay ahead of technology but is also concerned about the costs and resources needed (McCool, 2015). Additionally, state of the art technology is recognized by key decision makers. Standards to perform at this specific level of technology is recognized and the company works to maintain its ability to operate at this level until a reassessment determines a need for a change or an upgrade (anonymous employee, 2015). This current state of technology includes consideration of a virtual environment. The company is currently running 90 percent of its servers on VMware virtual environment (anonymous employee, 2015). The physical servers have to remain due to FDA compliance including 21 CFR Part 11 because the FDA has to be able to inspect the electronic systems during an audit or inspection. Once the company determines a way to stay in compliance, Encompass Elements will likely move to a completely virtualized environment.

If costs have to be reduced and processes have to be improved, staying ahead of trends and determining ways to continue delivering high quality products are essential. Overall, the respondents interviewed seemed to believe that the company did a good job for some of their processes and is adapting to new technology. Due to its smaller size and infrequence FDA and client audits, Encompass Elements is incented to stay within regulatory compliance as well as ways to improve processes. One of the employees (2015) points out that the company tries to maintain appropriate technology levels and stay a step ahead of current demands. This practice explains why Encompass Elements is considering ways to go to a completely virtualized environment to improve processes and save on costs. However, based on current client needs and the technology available at this time, there is no immediate threat to the company if it does not move to a completely virtualized environment (anonymous employee, 2015). As long as the company is aware of its current technological capabilities and is keeping abreast with new technological development, it is on the right track. While technology is being embraced by the company, the adaptation of technology has to be balanced between regulatory issues, client needs and expectations, and financial as well as human capital resources.

IV. Conclusion

The original hypothesis of this project started with the assumption that companies still struggle to design and follow effective validation plans that can adapt to changes in technology and regulatory demands. The literature on the development of electronic validation indicates that there was some initial confusion about how to utilize technology when 21 CFR Part 11 was first introduced. Since electronic validation was not something that was regularly followed initially, a disconnect existed between FDA expectations and the industry's capabilities and technology infrastructure. Some companies such as Able Laboratories, Leiner Health Products, and

Ranbaxy ran into major compliance issues that greatly damaged their businesses. Companies must ensure that they are following the guidelines set forth by 21 CFR Part 11 because the FDA is still using this guideline as one of the key pieces for audits and is issuing warning letters based on non-compliance of this regulation.

The case study on Encompass Elements shows a company that is very aware of compliance issues as well as its own limitations while maintaining a good validation system. Three specific themes can be pulled from the case study that can help drive compliance and the maintenance of electronic validation: embracing technology, ensuring high-level quality assurance, and aligning with business strategies.

Embracing Technology

Encompass Elements through the organizational ranks has embraced technology and wants to stay ahead of technological changes. Encompass Elements is looking towards moving to a completely virtualized environment. Additionally, those interviewed mentioned weaknesses that need to be addressed such as old servers or certain processes that need to be modernized. The strength of the technical team and in-house programmers who continue to look for more certification and training highlights how technology plays a key role for companies within the industry. The awareness of technology limitations and mindfulness about what technological trends need to be adopted help to keep the company on track in terms of complying with regulations, maintaining data integrity, and producing a high quality end product. Additionally, the understanding of the need for good documentation on the technical side can help with any moves or adaptation to new technology.

High Level Quality Assurance (QA)

Based on the feedback from the employees interviewed at Encompass Elements, the strength and competence of their QA department was evident. The responses from those interviewed seemed to indicate that the QA department is considered an important part of the overall organizational structure. With the zero tolerance policy, the QA department is empowered by the organization to educate those involved within the regulatory environment. Encompass Elements show that when a strong QA department exists that really helps to keep a company compliant and able to meet regulatory demands.

Alignment with Business Strategy

Encompass Elements is an example where electronic system validation is recognized as being an essential part of the business culture or the company. Upper management is aware how not being able to meet regulatory requirements can prove to be detrimental to and a liability concern for the organization. They strongly support traceability and systems with reliable audit trails. The strength of the QA department within the organizational structure also indicates how meeting regulatory demands is considered an essential part of the company's business strategy. Additionally, the company recognizes the importance of technology. By agreeing on a certain technology standard, the company understands the level of commitment that is needed to maintain systems. While those who were interviewed did mention possible improvements with additional technological resources, financial limitations may be part of the reason why these issues are not yet fully resolved. The alignment with business strategy makes sure that the commitment to technology and validation is kept in mind when discussing the use of resources.

Future Research

Contrary to the original hypothesis that many companies struggle with electronic validation, Encompass Elements appears to be a company that has a sufficient electronic validation system and support for utilizing new technology. Encompass Elements is fully aware of its current limitations but also has an understanding of regulations, the need for validation, and the importance of looking towards technological changes. Future research with other companies is needed to see if they are similar to Encompass Elements or if they do struggle to figure out how to meet regulatory demands and technological changes. It would be interesting to see how the three themes of embracing technology, high level QA, and the alignment of business strategy affect electronic system validation for other companies. With emphasis on the importance of regulations such as 21 CFR Part 11 and the introduction of technological changes (such as cloud technology), pharmaceutical companies will have to create a balance between addressing these concerns, their financial resources, and consumer expectations to remain competitive within the industry.

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