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GxP Cloud Services in the Pharmaceutical Industry-A Review

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***ABSTRACT**: In the pharmaceutical and healthcare sector role of information technology is vast and most of the operations such as research, production, quality, supply chain, and distribution cannot be imagined without information technology. The pharmaceutical industry not comparatively aggressive in adopting technology when comparing to other industries due to its regulatory compliance and data confidentiality. This industry focuses on compliance-effective technology rather than cost-effective. The compliance norms are established for this industry decades ago anticipating future information technology. Hence the adoption of available technology such as cloud services is very insignificant in this area. There is a wide range of industries already using these services, including the more critical industries such as the banking sector and there are vast Cloud solutions for pharmaceutical industry needs, nevertheless, the pharma industry slowly moving towards cloud services due to a lack of awareness on the advantages and compliance of cloud systems.*

KEY WORDS:- GxP Compliant Cloud system, Life science cloud, Computer system validation, Open system

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I. INTRODUCTION

Cloud computing is the most intrinsic information technology evolved over the years and emerged as an indivisible tool from the human life which helps in collaboration, communication, drives mankind towards innovation irrespective of location and continents.

A simple google search on cloud computing provided more than 47 billion results and this volume indicates the impact and use of cloud computing in the technology world. Though the idea of technology has been originated in the sixteenth century, it was formulated during the second world war with the development of the world's first programmable computer Zuse Z3 which helps in decode the German messages. This invention helps as a foundation for the development and evolution of various technologies in computing, network, data storage, transfer, Internet communications areas, and virtualization of computers.

As per recent statistics, 90 % of companies are using Cloud services in different manners across the Globe. Though private and public cloud usage increasing drastically, the usage of cloud services in the Pharmaceutical and Healthcare industry is insignificant due to traditional regulatory expectations.

Currently, most of the cloud service providers endeavours to fulfil the compliance requirements to get confidence from Pharmaceutical firms. This compliance is known as GxP compliance. Pharmaceutical and healthcare need compliance-effective solutions to adopt the advantages of cloud services.

II. DISCUSSION

i. Significance of Cloud Services in Pharma

Despite having technical competency and technology understanding, the software industry took more than two decades for initiating the cloud implementation and utilizing the services. As many of us know, GxP industries are natively built by research and regulations. In addition to that, the lack of technical understanding and expertise, the progress of cloud technology has become insignificant over the years. Meanwhile, earlier, cloud service providers and other software service companies were mainly concentrated on business improvement and neglected the security and data management aspects of the cloud. The vulnerabilities in the systems lead to breaches in cloud computing and loss the trust of the customers, business. In view of data breaches and vulnerabilities in regulatory companies that are intended to away from the cloud technology regulatory bodies have to revise their policies and impose strict regulations to protect the personal data on clouds.

Over the decade, cloud service providers are working seamlessly on cloud data security & compliance to meet regulatory & business expectations. These significant efforts in the improvement of protection & security of the cloud data made the cloud systems safe, secure, and reliable. These efforts also enhance the trust

of regulators & as well as business customers. Along the way, cloud service providers draw the attention of the pharma and healthcare industries towards cloud technology.

As many of us aware, the establishment of GxP industry would require huge capital, time, and resources. Also, the establishment of its own infrastructure for information technology would require technical expertise, time, and pain of purchasing physical equipment, space, other utilities followed by the construction of data center, installation of equipment, and security.

Early days, industries have taken the pain and established their own IT infrastructure but currently, these industries are struggling to protect and manage the IT infrastructure due to cyber threats and lack of technical expertise.

As per the Mid-Year Report from Risk-Based security, the health care sector is the second and nearly matched the information sector (14.5%) with 14.3% of the reported breaches. A total of 211 breaches were reported in the Q2, 2020. These numbers alarm the lack of awareness and security compliance programs in the Healthcare industries. Cloud service providers are using different cybersecurity tools and implementing advanced programs to protect the systems and data. Hence implementation of cloud services in GxP sector reduces the cyber threats, reduces the implementation and maintenance cost, and provides global standard features.

Figure 1: 2020 Midyear Report Data Breach QuickView from riskbasedsecurity.com

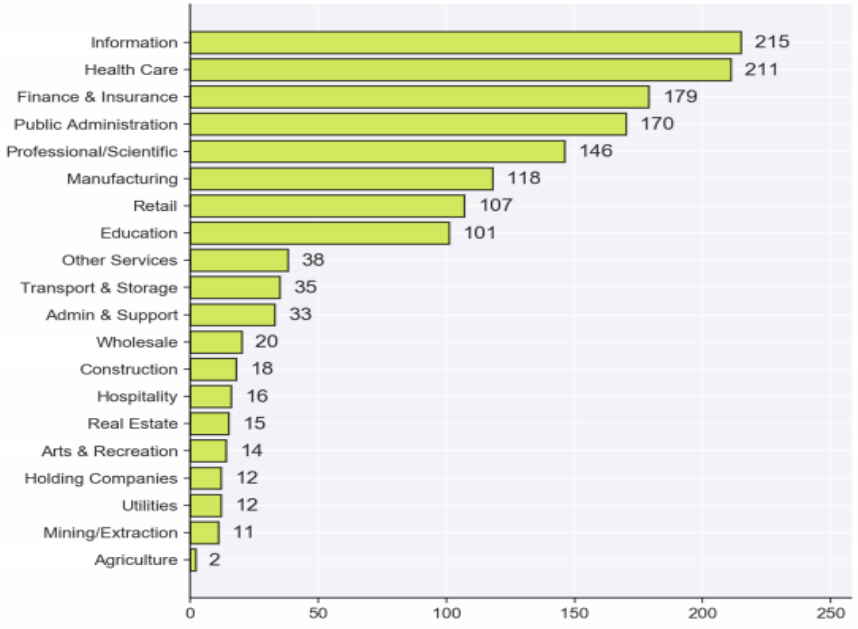
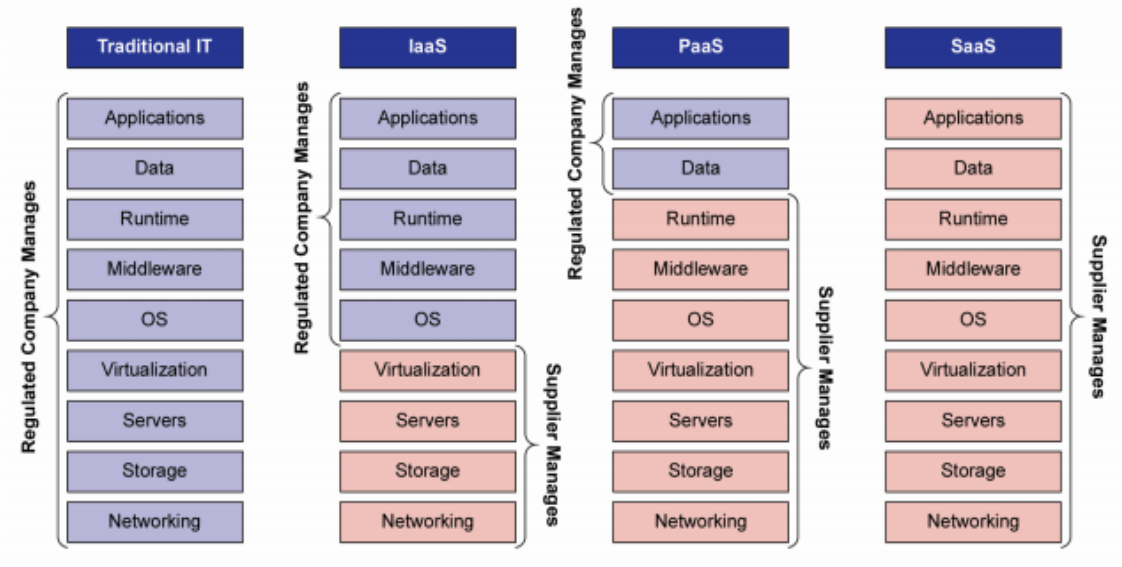


Figure 9: Number of reported Q2 2020 breaches experienced according to economic sectors

ii. Cloud Services distribution and classification

Infrastructure solutions can be implemented as Cloud solutions. Cloud solutions are managed by an external company and will be accessed via the Internet. Different type of cloud solutions is defined as Infrastructure as a Service (IaaS), Platform as a service (PaaS), and Software as a Service (SaaS). [GAMP].

The Figure:2 depicts the above service models in relation to traditional IT Infrastructure (ISPE GAMP® Good Practice Guide: IT Infrastructure Control and Compliance)



a. Classification based on the distribution

The clouds are classified into three types based on the distribution and usage.

Private Cloud

A private cloud solution operates and distributes the services within an organization or individuals. The organizations involved in a larger scale of operations and services utilize private clouds. The responsibility and risk of management of cloud lie with the organization or third party which works for them. The owner organizations will have full authority over the data and security

Public Cloud

Public cloud solution operates and distributes the services for public and business over the internet. The responsibility of managing the clouds lies with the cloud service providers and the user can subscribe to the services as per their needs. The data owners will have limited access to data operating and management..

Hybrid Cloud

This solution operates in the combination of private and public cloud services and remains individual to each other.

b. Classification based on services

The cloud services augmented across the Information technology over the years but majorly segregated as below based on the services.

IAAS (Infrastructure as a service):

The capability provided to the consumer is to provision processing, storage, networks, and other fundamental computing resources where the consumer can deploy and run arbitrary software, which can include operating systems and applications. The consumer does not manage or control the underlying cloud infrastructure but has control over operating systems, storage, and deployed applications; and possibly limited control of select networking components (e.g., host firewalls).

SAAS (Software as a service)

The capability provided to the consumer is to use the provider's applications running on a cloud infrastructure. The applications are accessible from various client devices through either a thin client interface, such as a web browser (e.g., web-based email), or a program interface. The consumer does not manage or control the underlying cloud infrastructure including network, servers, operating systems, storage, or even individual application capabilities, with the possible exception of limited user-specific application configuration settings (e.g. Trace link)

PAAS (Platform as a service)

The capability provided to the consumer is to deploy onto the cloud infrastructure consumer created or acquired applications created using programming languages, libraries, services, and tools supported by the provider. The consumer does not manage or control the underlying cloud infrastructure including network, servers, operating systems, or storage, but has control over the deployed applications and possibly configuration settings for the application-hosting environment. (e.g., SAP platforms)

iii. Pros and Cons of Cloud services in regulated environment

Pros	Cons
Expenditure Every rupee is important for the business, nowadays, building the own data center and management costs way more than for any organization. Cloud services are addressed this issue and provides a wide range of solutions as pay peruse. **Resources and utilities** Colluding and managing resources such as employee, infrastructure, hardware, space, power, temperature, and humidity for data centers can be avoided through cloud service providers. **Focus on Business** While cloud service providers handle the IT problems, the user concentrates on core business goals. **Collaboration** Cloud services help you in collaboration between different groups of people from different continents to improve the business **High Availability** Most of the cloud service provides high availability which helps the organizations to serve their customers 24/7 and improve their business. **Flexible in size** Cloud service helps you to increase or decrease the size of services based on your requirements in hours without charging any additional costs **Disaster Recovery** Cloud based services provide quick data recovery and re-establish the services	**Data Integrity and Security** Data integrity and security is the primary concern in cloud services since the data residing on the third party (vendor) servers and the responsibility of the security solely depends on service providers technical competence and expertise **Security** Cloud platforms handle multiple tenants and their data. Insider threats and vulnerabilities of one tenant may expose the other data on the same platform. . **Vendor Support and Availability** Cloud services are the third-party services hence vendor support and availability may have an impact on the business. **Patch Management** Cloud service providers will evolve and update the platform as part of improvement but the compatibility of the existing applications to be ensured prior to the patch management. **Hardware** Cloud service providers distribute hardware across multiple users. In case of failures, the user may not be able to receive the faulty hardware for further troubleshooting and the vendor may hold the hardware to protects the data of other customers. **Backup and Redundancy** Some of the cloud solutions do not have the backup and redundancy for the data storage. In that case, the user may have to find an alternative or avoid such cloud providers. **Multi-tenant** Cloud services are multi-tenant services and sometimes vendor may not help the user to design as per individual requirement

iv. GxP Compatible Cloud services

GxP refers to the regulations and guidelines applicable to the life sciences industry that make food and medical products such as drugs, medical devices, and medical software applications. There are dedicated regulations applicable to computerized systems and computers, or related systems in the pharmaceutical industry. The overall intent of applicable GxP requirements of IT related solutions is to ensure the integrity of data used to make product-related safety decisions. The pharmaceutical industry especially focuses on 21 CFR Part 11 requirements which are designed for electronic records and signatures compliance. The IT-related applications, services, and hardware known as computers, or related systems and computerized systems. The cloud services used in the pharmaceutical falls under computerized systems or related services based on nature The cloud solutions should be capable of complying with applicable regulations and guidelines for the pharmaceutical industry such as 21 CFR Part 211.68, 21 CFR Part 11, EU Annex 11

v. 21 CFR Part 11 compliance of the clouds:

Multiple regulations are available across the globe for computerized systems and its electronic record and electronic signatures. However, the regulated industry more focuses on 21 CFR Part 11 requirements. There is confusion in the industry that Cloud-based applications are open systems as per the definition provide in 21 CFR Part 11 "Open system means an environment in which system access is not controlled by persons who are responsible for the content of electronic records that are on the system" Though there are open systems

by nature, these regulations are not against for Cloud implementations in the regulated industry. Appropriated additional recommended for an open system in part 11 "Persons who use open systems …… additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality"

Whether cloud systems are "open systems" or "closed systems" these systems have to comply with applicable regulatory norms. Currently, most of the established GxP cloud services/applications are claiming that they are capable of fulfilling these requirements. However, the overall responsibility of compliance lies with the regulated company.

vi. Regulatory norms on Cloud computing:

Currently, there are no well-established and specific regulatory norms for cloud services from any major regulatory bodies. However, in recent years USFDA recognized the necessity of cloud services in regulated and provided certain following recommendations in their draft guidance document "Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers Guidance for Industry DRAFT GUIDANCE". The following recommendations are given to mitigate the risks associated with cloud services. These requirements can be addressed by implementing 21 CFR Part 11 controls over the cloud-based systems.

- Validation
- Ability to generate accurate and complete copies of records
- Availability and retention of records for FDA inspection for as long as the records are required by applicable regulations
- Archiving capabilities
- Access controls
- Secure, computer-generated, time-stamped audit trails
- Encryption of data at rest and in transit
- Electronic signature controls
- Data integrity controls

vii. Key consideration while adopting cloud services

- **Supplier Assessment:** To ensure appropriate quality and compliance procedures, certifications, service life cycle approach, change management, business continuity, disaster recovery, validation, and qualification methodology, GxP knowledge etc.

- **Service Level Agreement (SLA):** SLA is a key risk factor for any outsourced engagement. It can be particularly difficult in a cloud service relationship given the many combinations of providers who may come together to deliver the cloud solution to the regulated company. The level of managed service that can be expected from a service provider should be clearly understood before beginning an engagement

- Support for risk assessments and quality agreements
- Knowledge of GxP Regulations
- SDLC methodology
- Single or multi-tenant environment
- Upgrade frequency
- Qualification scope
- Nature of cloud (public, hybrid, community, private)
- Infrastructure Qualification activities
- Quality Agreement
- Data location(s)
- Certifications: SSAE 16, ISO 9001, ISO 27001, ISO 27017 , PCI , EHNAC , FISMA, FedRAMP , HITRUST, etc.
- Cybersecurity
- Physical security
- Geography
- Redundancy (ISP(s), utilities, generators, emergency power systems etc.)
- Capacity
- Staff qualification and training
- Uptime
- Help Desk support
- Change management

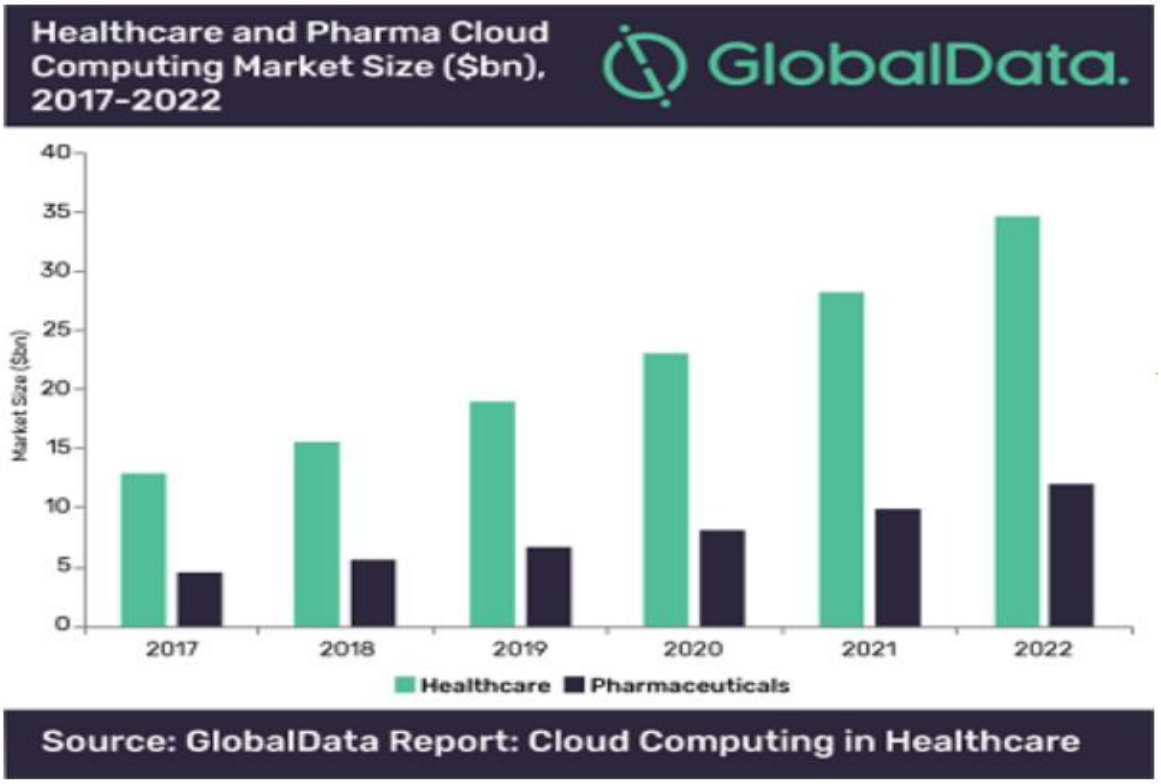
- Termination of the contract and deletion of data, including avoiding lock-in and GxP data retention
- Data processing operation
- Use of third-party subcontractors

- **Certifications:** Certifications from international organizations to ensure data security, data integrity, privacy, trust, and continuity

To support the GxP information technology services in terms of quality and security, the cloud service providers focusing the certain certifications which are following by the regulated pharmaceutical industry such as ISO 9001, ISO 27001, ISO 27017, and ISO 27018. Also, the cloud services providers are complying with NIST 800-53, SOC 2 and FedRAMP standards.

viii. Usage of Cloud computing in Health care and Pharmaceutical sector:

Despite having challenges such as data privacy, regulatory requirements the growth of cloud service usage in this sector going to make a good impact in forthcoming years. This is a good sign to utilize the real flavor of cloud services in the Health and pharmaceutical industry. The below figure shows the expected growth of cloud services in Healthcare and pharmaceutical.



III. CONCLUSION:

As the pharmaceutical industries are moving towards Pharma 4.0, the technical expertise of the cloud service providers and the actual benefits of the cloud helps the industries to achieve compliant digitalization and automation in line with the regulatory bodies expectation. However, the risk of sharing the responsibility of system and data ownership persists and impede the implementation of cloud services in the regulatory industries. Hence, regulatory industries should evaluate and document the necessary agreements for cloud service providers before the implementation. Considering benefits, compliance risks associated and regulations on cloud services pharmaceutical and healthcare industry can utilize the cloud services without any apprehensions. If data security is the main concern, private cloud service best option for the regulated company, or else hybrid cloud service option is the best option considering cost-effectiveness and security, better data management, accessibility.

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