Paper TT08

PhUSE is Moving Cloud Adoption Forward in Life Sciences

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1. ABSTRACT

We shall provide a brief review of this past year with respect to significant advances with the PhUSE Framework for the Adoption of Cloud Technology in the Life Sciences Industry. In particular, we shall provide information around the regulatory landscape that touches GxP workloads that engage with cloud-based solutions and, importantly, outline the framework extension that deals with the practicalities of implementing, deploying and operationally sustaining such workloads. Additionally, we plan to highlight the outcomes from recent discussions with regulatory agencies and how the framework helped guide those discussions.

2. OUR WORKING GROUP

Our working group, which was formed under the Emerging Trends and Technologies (ET&T) stream within the PhUSE Computational Sciences Symposium (CSS) in mid-2013 when the PRISME (Pharmaceutical R&D Information Systems Management Executives Forum) requested PhUSE to take on an analysis of why the adoption of cloud technologies in the Life Sciences sector was slow (compared with other industries), has grown to include 12 members. The membership comprises subject matter experts from Life Science companies as well as vendors with business as well as IT backgrounds. The Group interacts and maintains an active weekly agenda providing for lively discussion of the many aspects of Cloud Adoption across the Life Sciences. The original premise that our sector was missing out on the numerous benefits (see below) that *Cloud* could bring to R&D in general continues to be of concern/interest although we are observing the establishment of clear *Leaders* and *Laggards*. These will remain un-named!

The past couple of years have seen continued and enhanced focus and attention to drug pricing and the rising cost of developing new medicine. This was reflected during the recent US elections and echoed by governments and politicians across the US, Europe and beyond. The trend of doubling the cost of drug development every nine years or so (known as Eroom's law, or the reverse Moore's law) continues. The quest for treatments to more and more sophisticated diseases is likely a contributing factor. Nevertheless, this is still a challenge begging for solutions.

It is widely believed that adoption of Cloud Computing can help reduce the cost of R&D, and make available computing power that would certainly aid in driving new efficiencies in Life Sciences, be it via economies of scale as well as new capabilities such as Machine Learning, AI, and Natural Language Processing that can leverage the computing power made available in the Cloud via sophisticated, configurable apps operating on commoditized services from Amazon Web Services, Google, Microsoft Azure or others.

Over this past year, working group members initiated several interactions with regulatory agencies to influence the establishment of further guidance, which we consider will aid in driving the further adoption of Cloud Computing. It is our belief that the absence of a clear and concise position adopted by the regulatory agencies is inadvertently contributing to the slow adoption of Cloud due to the associated uncertainties and risk perceptions. Or, perhaps, such *guidance* merely needs to say, words to the effect that "we're not focused on the technology per se; rather focus on the predicate rules (from GxP as well as from NIST, IEEE and other frameworks) and existing demands for controls around the way you operate". We can draw parallels to the accelerated adoption of Electronic Records and Electronic Signatures (ERES) in the early 2000's post the issuance of ERES Guidance as well as the enactment of 21 CFR Part 11 and Annex 11.

So, our working group continues to strive to educate and enlighten its members and the broader Life Science community about the benefits.

3. KEY CONCEPTS AND ASPECTS OF THE CLOUD ADOPTION FRAMEWORK

3.1 IS THIS SUSTAINABLE?

FDA Commissioner Scott Gottlieb shared some sobering messages at a recent regulatory conference reminded us that "[We need to be] driving efficiencies into the biomedical R&D model." We all share in Gottlieb's aspiration for targeting drug development costs - "We need to make sure that our approach to regulation is efficient." FDA also wants to modernize, via advanced computing tools, how sponsors can evaluate clinical information.

Back in 2012, we saw an article in Nature that discussed the concept of Eroom's law. This is Moore's law spelled backwards and is the concept, based on analysis of data relevant to the cost of developing medicinal products since the 1950's, that the number of drugs approved per one billion dollars spend on R&D is halved every nine years. This means that based on today's estimate of about $2.6 Billion dollars per molecule we will reach a whopping cost of $32 Billion by about 2050. This is not sustainable and to avoid the situation of medicines being available only to the richest of the rich we must radically change our approach. We must consider and leverage all technological advances available to us today to secure a safe and efficacious health system in the future.

Several trends govern the advancement towards this future. We should consider the broad adoption of cloud-based technologies to be a critical component and one of the most crucial factors. Other general trends include:

- The shifting and eventual amalgamation of Pharma, Medical devices, Healthcare and Technology
- The empowerment and engagement of patients via utilization of smart, mobile devices, big data and artificial intelligence in preventing, intercepting and management of medical conditions
- Leveraging customer excellence platforms
- Embracing the disruption from software companies such as Qualcomm, Google, Microsoft, Apple, Samsung and others.
- Shifting from sick care to well care.
- And personalization of medicine at scale.

3.2 REAL AND PERCEIVED ISSUES

The first endeavour of the working group back in 2013 was to identify – and quantify - the key obstacles associated with the slow adoption issue that had been flagged by PRISME. A number of brainstorming workshops were undertaken in the latter part of 2013 and early 2014 and those obstacles were encapsulated and summarised as follows:

- In a negative sense, it was NOT the technology itself!
- There was poor, general understanding of what *Cloud* actually meant compared with past technology
- There was resistance – for multiple reasons – to the likely outsourcing of technologies (and associated roles and responsibilities) to other parties especially when the supply chains associated with those other parties could become complex (when compared with legacy approaches that mostly involved *on-prem* solutions running home-grown applications and/or licensed application software
- Unlike other industries, no standards existed for technology generally with GxP-regulated domains within the Life Sciences sector
- There was general concern around the concept of service providers utilising applications that were shared by multiple customers – even though there were robust delineation mechanisms
- Above all, the Quality Management Systems within Life Sciences organization tended to be highly geared to the more traditional on-prem based operations described above. This was especially vivid in the domain of computer systems validation (CSV) approaches.
- And, finally, the advent of Cloud has highlighted core underlying issues that have existed for a long time – mostly in the areas of information confidentiality and privacy controls, information

security more generally as well as the utilization of information technology in a truly internationalised manner.

In reading this paper, we ask you, for now, to park these obstacles and reflect upon them in the context of the following sections.

These issues were initially shared with the CSS conference that took place in Silver Spring, MD in March 2014 and huge interest, discussion and engagement from attendees (both PhUSE and FDA) was generated. Moreover, it was at that conference that the idea of a *Framework* was conceived.

So, in essence, the Framework (the subject of this and past papers) would address the obstacles described above and, further, would propose new models of thinking that would allow the obstacles to be overcome.

So, what's changed? Cloud technologies have matured and developed rapidly and in many different ways - Moore's law again. We have definitely observed greater adoption of cloud technology – or, at least, a change in commitments to address the adoption barriers highlighted above.

We also observe, however, a still-strong continuation of the obstacles/issues described above. In some ways, this is to be expected; many organizations have large legacy technology investments tied up in older systems and it is likely to be many years before such systems naturally attain "retirement" modes. On the other hand, reduction of fixed costs, cost in general and improvements in overall efficiency and value are, as already mentioned, increasingly viewed as paramount across the Life Sciences sector. So, perhaps, continued cloud adoption – and the benefits of such – will accelerate such retirements.

3.3 TECHNOLOGY EVOLUTION

Suffice it to say that so-called cloud technology is, as described in our Framework, a word of jargon that's been attached to technology of recent times. That technology embraces advances in hardware and software and, above all, the "power" of the internet.

Above all, however, we must contemplate the notion that every company today should consider itself a software company to a certain extent. Information is king yet knowledge is power. Distillation of knowledge from information will only be achieved at meaningful scale with the leveraging of Cloud Computing capabilities.

3.4 FRAMEWORK TENETS

Our Framework has a number of fundamental tenets or design concepts as follows:

- Unlike many guidance-like documents that are published and updated very rarely, our Framework document is more of a "living" entity. It is updated on an ongoing basis by the members of the working group and made available into the public domain. Almost, wiki-like!
- Whilst the Framework inevitably builds upon the capabilities of today's technologies and past traditions and practices within the Life Sciences industry, it attempts to be agnostic in terms of such technology. In particular, it challenges the traditions built up in the past couple of decades that were largely built around the technologies of those times. Our key proposition therefore is that approaches to be taken should avoid being tied to specific technologies. Especially because those technologies will continue to develop and evolve – rapidly!
- We have avoided re-inventing concepts and terms! Hence, we have deliberately adopted terms and standards from NIST and ISO, both of which are not specific to Life Sciences.
- And, finally, we very much gear the Framework to the objective of helping stakeholders to have awareness of and, as appropriate, to conform the GxP predicate rules. In addition we demonstrate cognizance of emerging regulatory guidance associated with data integrity, transparency as well as regulations associated with information confidentiality and privacy.

Focusing on the final bullet above, our working group has, over the past several months developed a separate, scalable FAQ document that has been geared toward both complementing the Framework and to provide real, practical advice to address real-world queries that the group has received or heard of.

3.5 A STYLIZED EDC/CTMS SETUP – THE TECH-STACK AND THE ROLES

We use this GCP-area case example to demonstrate the various permutations that can exist across different cloud technology solutions.

It is a domain that includes ***customers*** – typically pharmaceutical clinical trial sponsors, **brokers** – often shaped as Clinical Research Organizations (CROs) – and **providers** – in the form of Software as a Service (SaaS) providers supported (down the tech stack) by Platform as a Service (PaaS) and Infrastructure as a Service (IaaS) providers. And it includes **auditors** – internal, 3rd-parties and, indeed, regulatory inspectors.

Let's look at the ISO definitions of these players:

- Cloud Service **Customer:** In the context of GxP, these are generally the organizations or entities that purchase/use the cloud services to support their GxP-regulated activities. They are generally billed for the cloud services they consume, and depending on the services requested (IaaS, PaaS, SaaS), their activities, use cases and GxP requirements may vary.
- Cloud Service **Provider**: Organizations or entities responsible for providing cloud services to customers. The activities that the cloud providers perform will vary depending on their particular service offerings and can include building, deploying, operating and maintaining the cloud apps, infrastructure and associated service layers.
- Cloud Service **Broker**: These are the organizations or entities that manage the configuration, delivery and use of cloud services on behalf of the cloud customer. For example, cloud managers may perform infrastructure change control activities on the infrastructure built using general purpose, commercial cloud services.
- Cloud **Auditor**: A cloud auditor is a party that is qualified to conduct assessments of the cloud provider and the cloud infrastructure underlying the IaaS, PaaS, SaaS services. The auditor may be an independent third party such as a third party assessment organization (3PAO) or can also be a member of the consumer, provider or manager organization. Or, an inspection-oriented party from regulatory agency.

The final entity is, understandably and by its very nature, somewhat detached from the others. But, it is increasingly important owing to the much greater expectation on the part of inspectors to get hands-on with systems themselves. This, in itself, creates challenges: will the technology still be available?; does an inspector need to be trained?; and so forth.

The key thrust of our Framework is that the contractual and commercial interactions between these players have numerous permutations in terms of roles and responsibilities. And that this, in turn, leads to the need for clarity – a key factor in explaining things to regulators (who are, as mentioned, a form of ***auditor)***.

4 POTENTIAL BENEFITS

There has been much written, discussed and refined on this particular topic. The high-level benefits associated with *Cloud*:

- The use of automated scalability coupled with payment on an usage model – leading to reduction in fixed costs
- Embedded fault tolerance
- Intrinsic high availability
- High levels of commoditization of computing, data storage and networking
- Enhanced speed of deployment
- High levels of monitoring and measurability.

No matter what we extol within our Framework, it is the Cloud Service Customer that has to make these potential benefits become a reality within their own organization. The business pressures to do so are increasingly compelling.

5. CONCLUSIONS

Cloud based technology solutions are here to stay!

There are adoptable ways and means for making these technologies work effectively within the regulated Life Sciences industry.

Education and awareness are key – for customers, providers and regulators.

The jargon, terminology and treatises will change into new eras of technology evolution.

Legacies will persist and must be accommodated.

But, above all, innovations through adoption of cloud technologies are to be encouraged from within customer organizations BEFORE the demands from the business units compel things to happen.

So, a final "checklist" that summarises what can be got from our Framework and what the approach should be to embarking upon a cloud journey:

- Understand *Cloud*; it can be complex!
- Understand options and limitations
- Examine your Quality Management System and understand its limitations – and what may need to change
    - Adequacy/appropriateness of policies and procedures
    - Approaches to qualification and validation – differentiating between validation of the technology and the validation of the *use* of the technology
    - Supplier management.

6. RECOMMENDED READING

- Cloud Services – A Framework for Adoption in the Regulated Life Sciences Industry: https://s3-us-west-2.amazonaws.com/phuse/public/PhUSE+Cloud+Doc+13-Nov-2015.pdf

This quoted edition was published in Nov-2015; at the time of this paper, a new edition is in preparation and by clicking on the link, you will be re-directed to the new edition when it gets published.

Additionally, the FAQ paper (referred to above) will also be published in the near future.

- Nature Reviews Drug Discovery 11, 191-200 (March 2012) | doi:10.1038/nrd3681

7. CONTACT INFORMATION

Your comments and questions are valued and encouraged. Please contact the principal member of the working group:

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