LEVERAGING YOUR VENDORS TO SUPPORT DATA INTEGRITY:

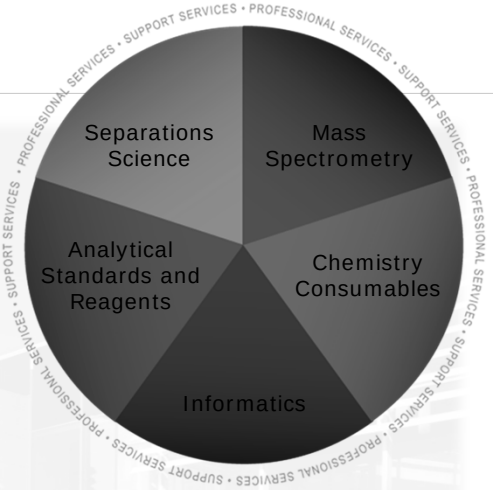
QUESTIONS TO ASK AND RESPONSIBILITIES TO DOCUMENT

Heather Longden

Boston Chapter Educational Meeting

April 2018

About Waters Lab Informatics



Informatics development and service centers

Milford, MA, USA, Manchester, UK, Brasov, Romania

>550 employees focused on Informatics

Installed Base

> 4,000 Empower networks installed worldwide

> 425,000 Empower licenses

> 10 languages

All Top Pharma uses Empower

> 50,000 NuGenesis licenses

Gathering & Sharing Regulatory Information

Regulatory Bodies
FDA/MHRA etc

Industry Groups
ISPE/GAMP

Customer & QA

Sales and Specialists

Professional Services

Product Functionality and Design

Data Integrity Guidances

U.S. FOOD & DRUG ADMINISTRATION

Website Q and A 2015,
DRAFT Guidance April 2016
DRAFT: Use of ER and ES in Clinical Investigations June 2017

OECD

For GLP, April 2016

MHRA Regulating Medicines and Medical Devices
Medicines & Healthcare Products Regulatory Agency (UK)

GxP Data Integrity, *March 2018*

World Health Organization

Released June 2016, as WHO_TRS_996 Annex 5

EPA

EPA QA/G-8, November 2002

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Q and A: August 2016
Annex 11 and Chapter 4 revision 2018

PIC/S
Pharmaceutical Inspection Co-Operation Scheme

PI-041-1 (DRAFT 3), coming April 2018

PDA Parenteral Drug Association

Points to Consider Series:
Conduct: March 2016
Fundamentals: Sept 2016
Data Integrity: In Progress

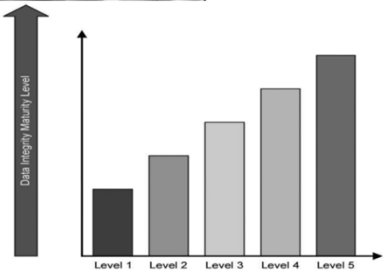
ISPE

GAMP: RDI Guide Published April 4th 2017

ECA ACADEMY

Coming Soon

ISPE Records and Data Integrity



- **RDI Guide is the 'sister' guide to GAMP 5**
  - Computer System Lifecycle
  - Data Lifecycle
  - Additional detailed GPG's will be released under the RDI Guide
- **Main Body**
  - Introduction, Regulatory Focus, Fata Governance Framework, Data Lifecycle, Quality Risk Management
- **Appendices**
  - Management
    - Corporate Data Integrity Program
    - Data Integrity Risk Management
  - Development
  - Operations

What is involved in Data Integrity?

People
- Culture for data integrity
- Governance and data review
- Unique user accounts
- Scientific skill
- Training
- Safeguards against fraud

Quality Separations
- Quality standards & reagents
- Instrument calibration & maintenance
- Qualification
- Method validation
- System suitability
- Quality Columns

Laboratory Computerized Systems
- Built-in data integrity controls
- Computerized system validation
- Maximum Automation
  - Minimum Human Intervention
- Traceability
- Periodic review

IT Components
- Secure centralized storage
- Network qualification
- Disaster recovery plan
- Backup and restore process
- Archiving electronic data

THE RIGHT APPLICATIONS AND TRAINING

For GxP Environments

Technical Controls

“Is your software compliant?”

> Does your software have all the technical controls to meet part 11?

> Why wasn't it configured to work correctly in my regulated environment?

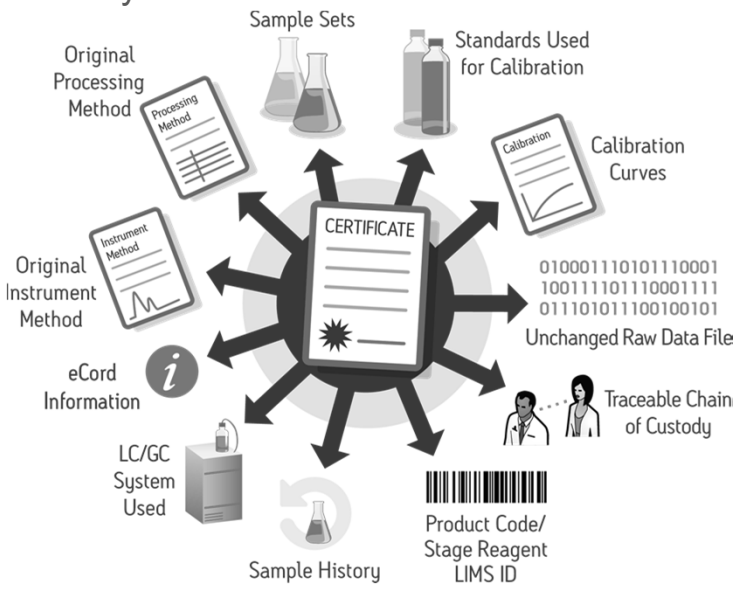
“Is it OK if we share one user account so I don't have to buy more licences?”

“Do you have an audit trail in your software?”

> If there is one... why should look at it all the time?

“Why do I have to enter a reason/comment every time?”

Empower Traceability



Technical Controls

Does your software have…

Part 11 compliance?

Audit trail?

Backup and restore?

"Yes …but…"

> Have you configured, tested and locked configurations to match your SOPs?
  – (passwords on a sticky note… backup that happen sporadically or were never tested)
> Can you explain and show that you understand and have "challenged" these technical controls?

Help me Deal with Regulators

Can you please speak to this investigator and explain how this works?

Could you tell the auditor why we do it this way?

Can you write a response to this 483 observation we just received?

Can you guarantee I wont get any 483 observations in my next audit?

Please tell the FDA how this software works?

Please would you NOT tell the FDA how this software works?

And you are on speaker phone…with the FDA

Why you should not invite /demand your vendor takes part in your inspection

Vendors do not know your product, procedures or SOPs

Vendors have not been trained in how to participate in audits at your company

Customers use the same software in different ways, may connect to LIMS or ELNs in unknown ways.

Calling the vendor indicates you do not know your equipment /tools

It could be very easy for your vendor to say something contrary to your procedures

What do I have to do for validation and training?

"Can you send SOPs on how to use this equipment?"

"Can you train users on how to use those SOPs?"

"Can you train QA on how they should review my data?"

"I need you to tell me what is the minimum I have to do to meet my regulatory requirements"

Key services to train and support

User Training

- **Analysts, supervisors and managers**
- **QA reviewers**
- **Data Integrity questions preparedness**
- **Administration teams**

Periodic Review Services

- **Leverage vendor tools and expert advise**
- **Computerized System Validation Support**

Vendor Qualification services for instruments and software

Leverage vendor QMS evaluation testing and CSV professional services

THE RIGHT APPLICATION VENDOR / CSV CONSULTANT

Computer System Validation

Computerized System Validation

“Please send me a user requirement specification for this computerized system?”

“Where is my validation certificate?”

“If you've tested the software, why do I have to do it?”

“You qualified the equipment, isn't that enough?”

“How can I prove the numbers/ calculations are right?”

“I need copies of all your test cases...”

“I'm not sure I if I should trust the vendor testing, so I'm going to test every function and button just in case…”

The onion layers of "validation"

System Suitability	•Prior and During analysis •Post Analysis (ISR)
Method Validation	•On a qualified system •Exactly as you intend to use it
Performance testing	•After maintenance •"periodically"
Software Validation	•To YOUR user requirement •Using your SOPs
Extended Software Qualification	•Functionality you will use •Especially Data Integrity
Vendor Qualification	•Software (Basic) •Instrument
Vendor testing	•Software •Instrument

Leveraging Vendor Testing

- **Supplier Assessment**
- **Regulatory FAQs**
- **Release Acceptance Tests: Test Summaries**

> Unlikely to have access to actual Test Documents, except in a live audit under NDA

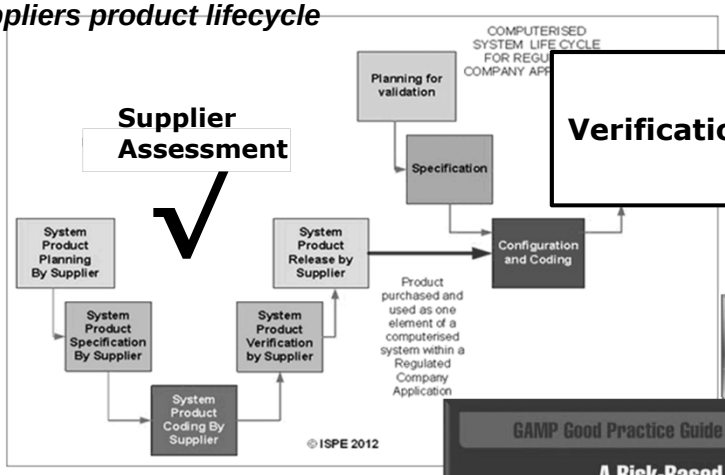
> Compare to EU Annex 11 requirement to share 3rd party supplier assessment documentation

> Consider sharing the overall assessment report

- **ISO /Lloyds certificates**
- **Examples of your own escalation and resolution through your vendor**

GAMP Good Practice Guides

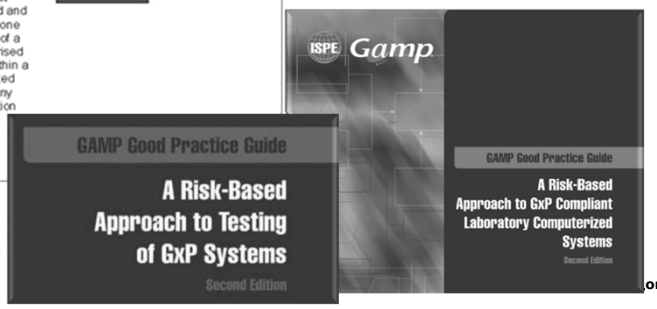
Leveraging work already done in the suppliers product lifecycle



Supplier Assessment √

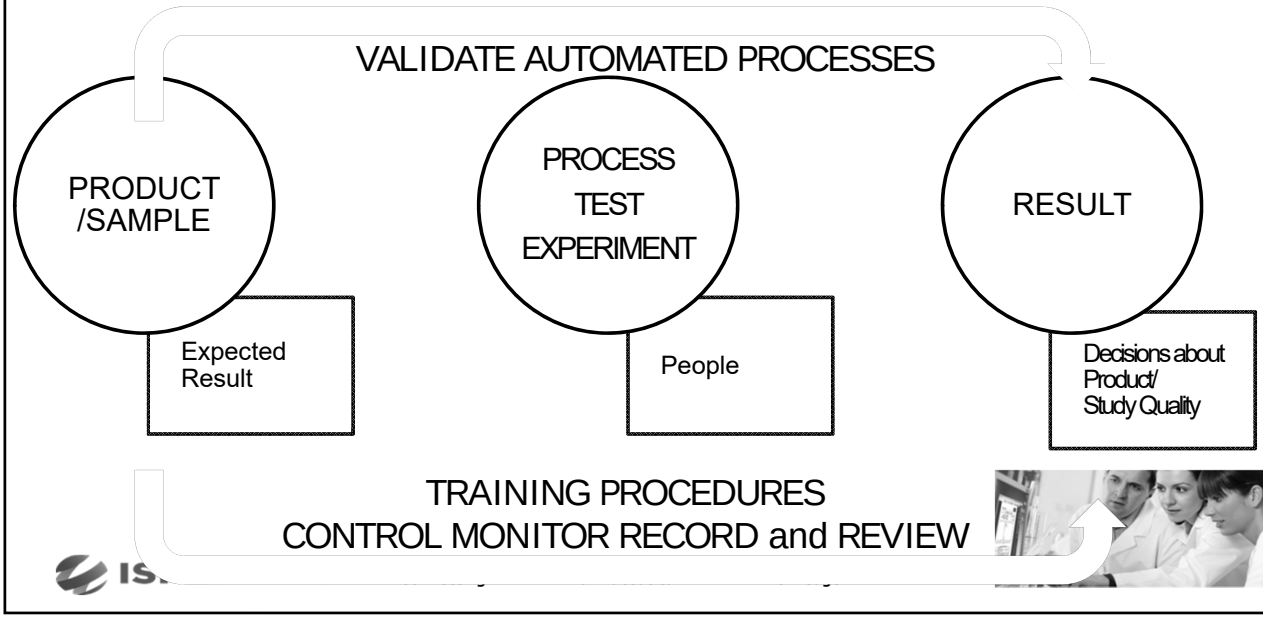
Verification

- **FOCUS ON USER REQUIREMENTS TESTING**
- **Vendor Instrument and Software Qualification**
- **Vendor Verification Testing**
- **3rd Party Testing**
- **User Acceptance Testing**



ISPE. Connecting .org

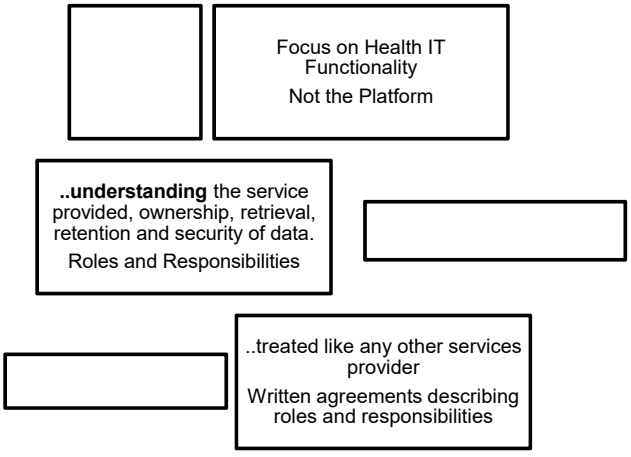
Addressing Technical and Procedural Controls



THE RIGHT CLOUD HOSTING VENDORS

Roles and Responsibilites

Regulators Guidance about Cloud Hosted Services



ISPE :Cloud technologies associates RISK

ISPE Infrastructure Control and Compliance Good Practice Guide 2nd edition 2017

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Examples | Risk Consideration Chris Reid: ISPE GAMP

	Increased RISK	Decreased RISK
Outsourcing		
Surrendered control	↑	
Outsource company has better processes		↓
Virtualization		
If a physical machine fails, the image finds new hardware to live on		↓
Data in the Cloud		
Better disaster recovery protection		↓
Data is not on the regulated company's asset	↑	
Provider selection: Amazon Web Services		↓
Responsibility for performance & application management	↑	
Responsibility for security	↑	
Contracts and service level agreements Service Provider business failure	↑	

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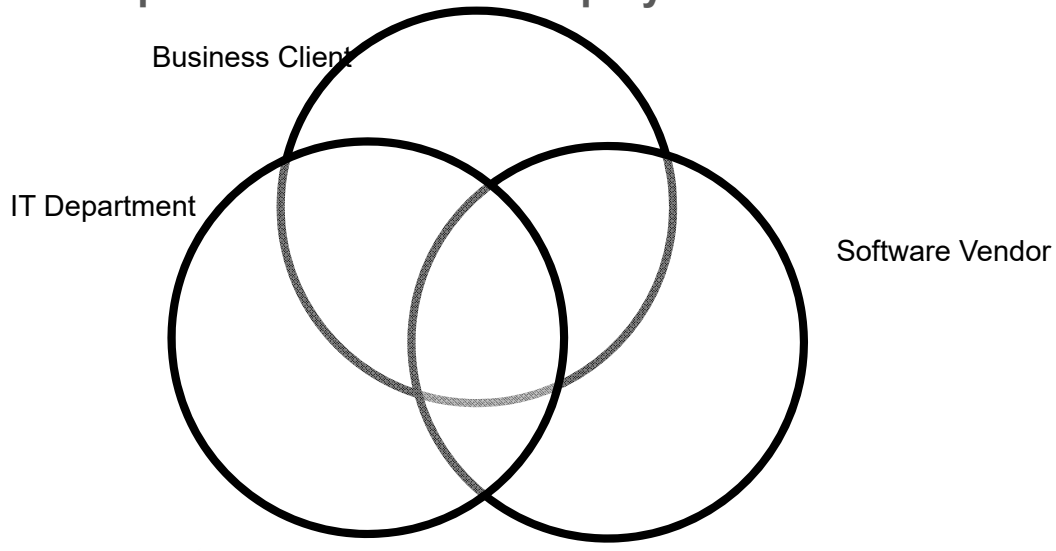
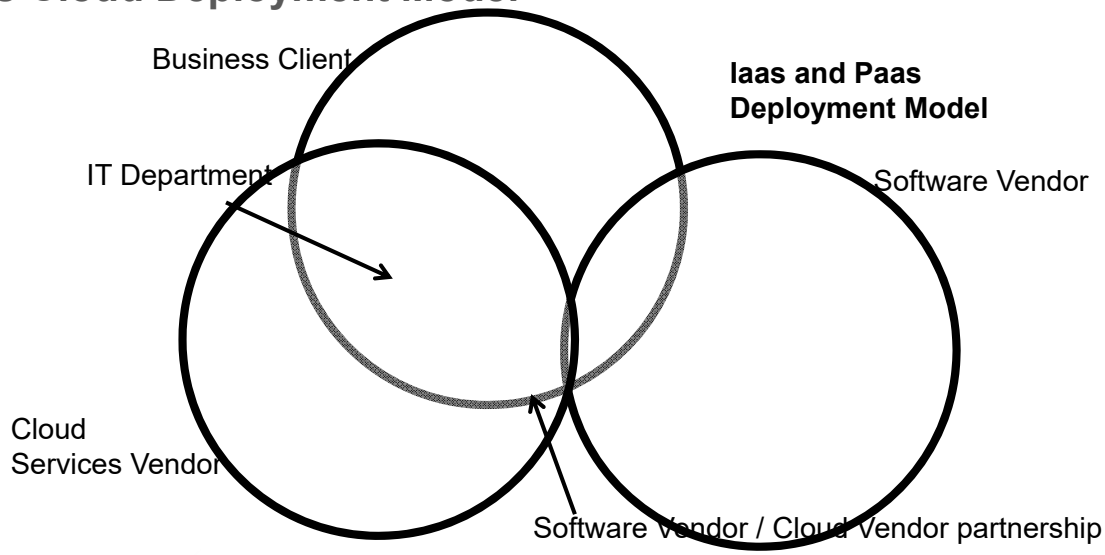
Real Life Responsibilities

Defining Vendor and Client
Traditional on-premise Datacenter Deployment Model

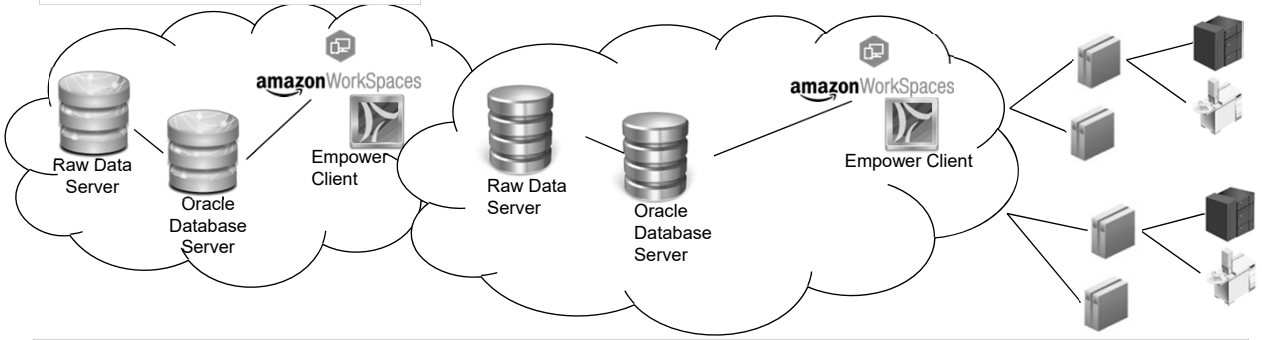


Defining Vendor and Client in a Iaas Cloud Deployment Model

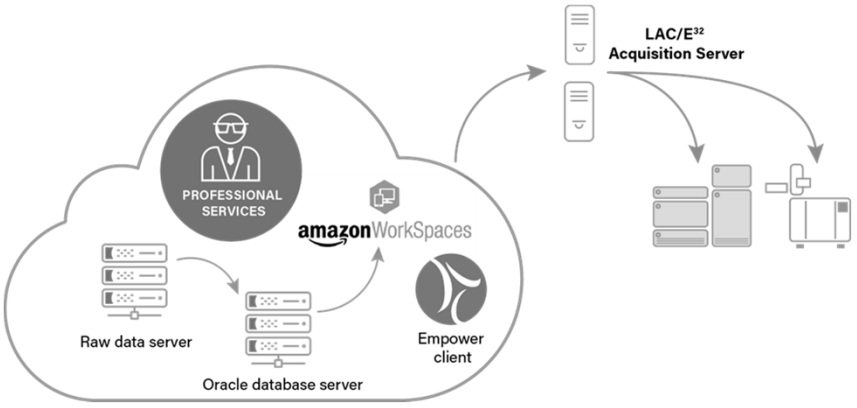


Empower Cloud

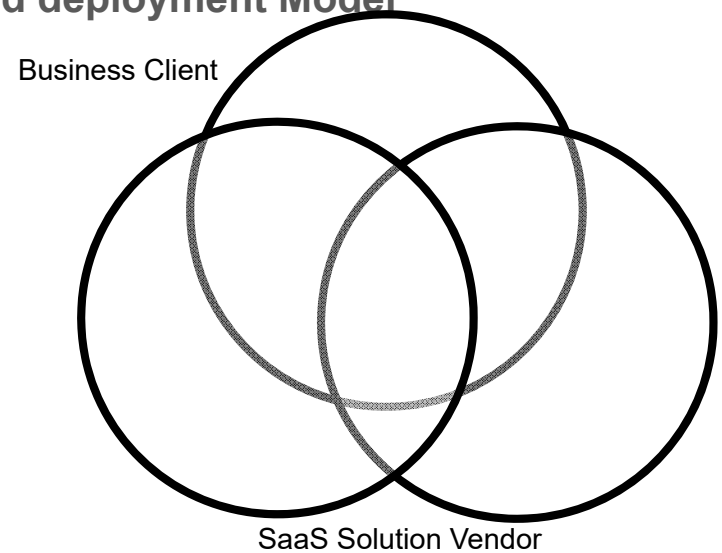
Waters Tested Templates and Deployment Procedures



- Waters design, evaluate and provide templates under Waters Quality Management Systems (QMS)
- Waters Professional Services assist customers to design, build and validate appropriate Amazon infrastructure
- Use automated deployment tools to replicate Waters templates onto their cloud infrastructure
- Minimizes variation and risk



Defining Vendor and Client in a Saas Cloud deployment Model



ISPE GAMP COMMUNITY OF PRACTICE ACTIVITIES

The GAMP CoP Mission

- GAMP® CoP Mission The ISPE GAMP® Community of Practice (CoP) exists to **promote the understanding of the regulation and use of computerized systems, control systems and intelligent instruments** .. …within the **pharmaceutical, biopharmaceutical, medical device** industries or other regulated healthcare institutions
- The GAMP® CoP will work with other ISPE CoP's to ensure a consistent ISPE message. Whenever possible, the GAMP® CoP will form relationships, coordinated through ISPE, with like-minded industry associations and competent regulatory authorities to create **globally harmonized quality standards and approaches to implementation and operation of computerized systems**.
- Furthermore the GAMP® CoP **will partner with suppliers to identify and share best practices in order to have a positive influence on the quality of computerized systems used in the industry.**

SOC2+ for Life Science Companies
GAMP Task Team with extensive experience in Auditing and SOC2+

How to assess a supplier who won't let QA auditors in the door?

Look to compliance with another federal law: Sarbanes-Oxley

Solution: The finance sector has a process wherein suppliers

- Engage an independent third-party audit firm to conduct an audit supported by testing of controls
- Management responds to the audit, implements corrective actions
- Audit results and management response are made available to user companies

Life science companies

- Get an independent assessment of companies they have not been able to audit
- For traditional GxP suppliers, they may not need to audit or may be able to do a quicker, more focused audit

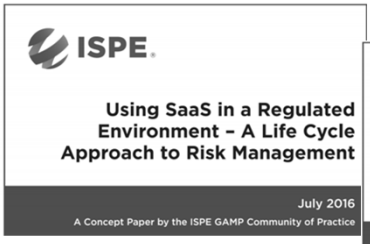
Regulators know that an independent audit supported by test evidence has been done

The existing finance process covers better than 90% of the controls expected for data integrity!

The GAMP team is working on closing that gap and developing a trustworthy GxP process

ISPE GAMP: Cloud Special Interest Group (SIG)

Continue to provide education and guidance documents for IaaS, PaaS and SaaS deployment models



ISPE GAMP: DI SIG

Further GPGs planned for 2018 and beyond

- **Key concepts**
- **Manufacturing Systems**
- **Lab Systems**
- **Data Lifecycle**
- **Clinical**
- **ERP**

Always looking for volunteers to plan, write, review and revise content

Separate Quarterly Education Meetings

- **Open to all SIG Members**
- **Volunteer speakers always welcome**

THANK YOU!

HEATHER LONGDEN

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