AMDM Focus 2019

Diagnostics in the Cloud

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Global Security Assurance Lead -
Healthcare and Life Sciences, AWS

Agenda

Overview

- What is the cloud?
- How does AWS approach compliance?
- Tech vs. Biotech
- Shared Responsibility Models
- Case Studies

What is the Cloud?

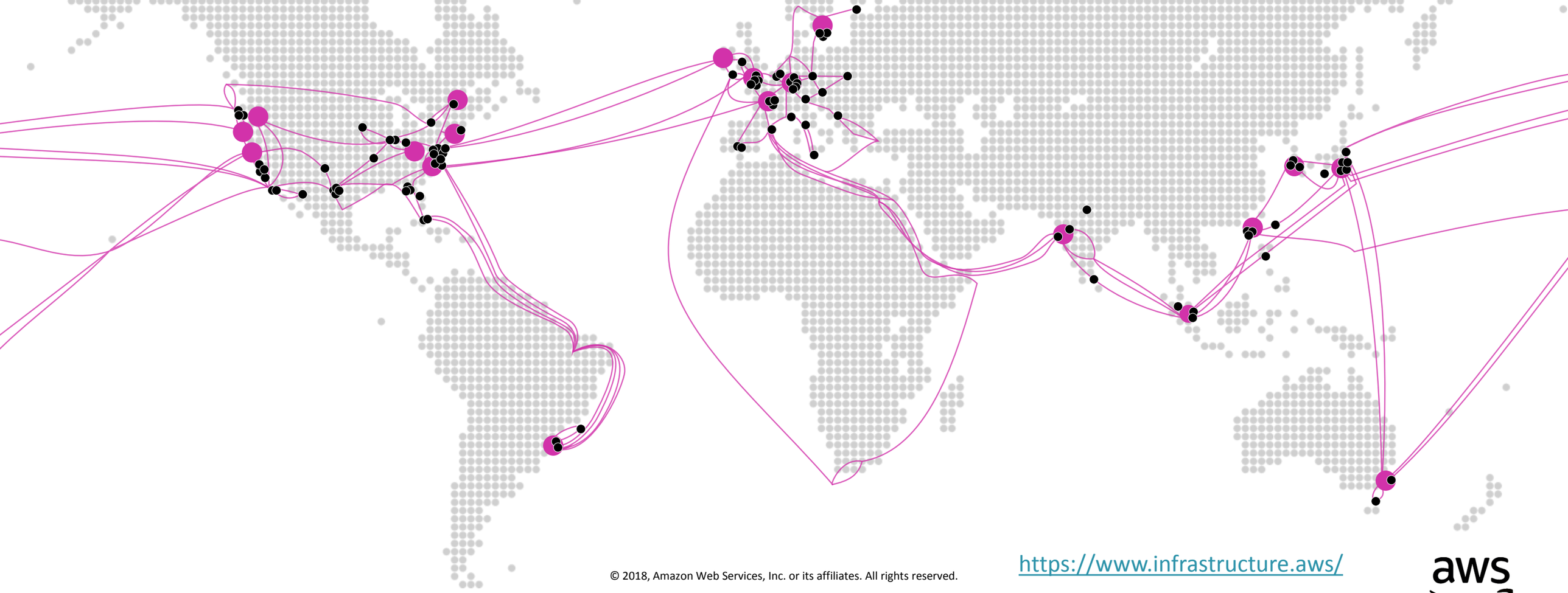
- Cloud computing is the on-demand delivery of compute power, database, storage, applications, and other IT resources via the internet with pay-as-you-go pricing.
  https://aws.amazon.com/what-is-cloud-computing/

  - Agility
  - Elasticity
  - Cost Savings
  - Deploy Globally in Minutes

https://www.infrastructure.aws/

Global Networks, Performance, Localization

AWS has 22 Regions, 69 Availability Zones, with 3 regions planned in Cape Town, Jakarta and Milan



https://www.infrastructure.aws/

aws

Cloud basics: IaaS / PaaS / SaaS (NIST)

- **Infrastructure as a Service** (IaaS): The capability provided to the **consumer is to provision processing, storage, networks, and other fundamental computing resources** where the consumer is able to 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).
- **Platform as a Service** (PaaS): 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.
- **Software as a Service** (SaaS): 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 a thin client interface such as a web browser (e.g., web-based email). 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

https://www.nist.gov/sites/default/files/documents/itl/cloud/cloud-def-v15.pdf

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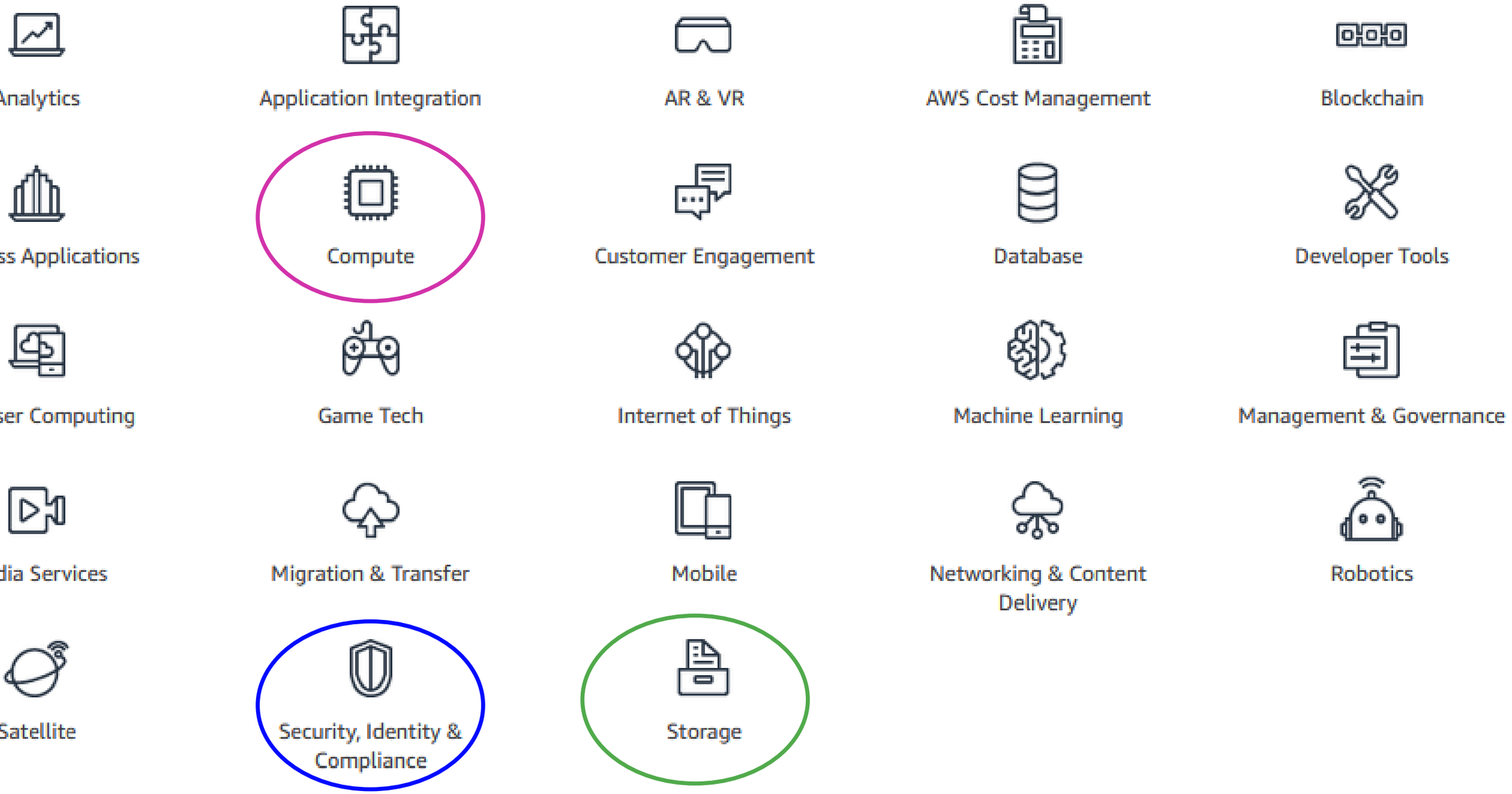
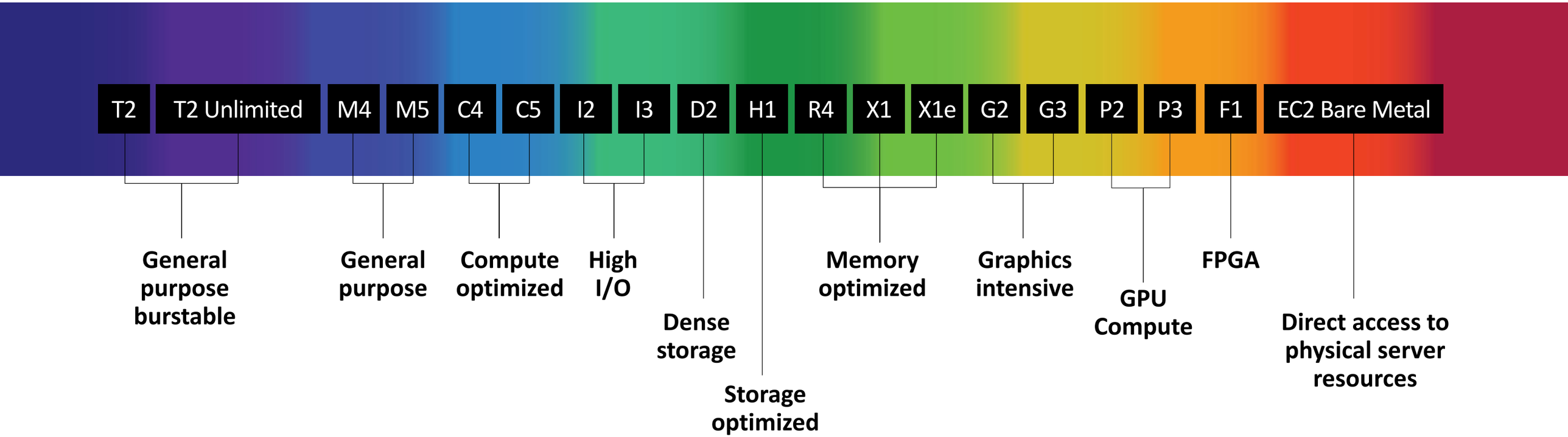
Cloud native = cloud building blocks



https://aws.amazon.com/products/?pg=WIAWS&tile=Get_Started

Compute: Amazon EC2 Instances

Optimize the price/performance with the widest range of compute instances



AWS security solutions

Identity

AWS Identity & Access Management (IAM)

AWS Organizations

AWS Cognito

AWS Directory Service

AWS Secrets Manager

AWS Single Sign-On

Detective control

AWS CloudTrail

AWS Config

Amazon CloudWatch

Amazon GuardDuty

VPC Flow Logs

Infrastructure security

AWS Systems Manager

AWS Shield

AWS WAF – Web application firewall

AWS Firewall Manager

Amazon Inspector

Amazon Virtual Private Cloud (VPC)

Data protection

AWS Key Management Service (KMS)

AWS CloudHSM

Amazon Macie

AWS Certificate Manager

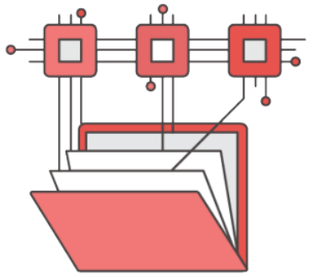
Server-Side Encryption

Incident response

AWS Config Rules

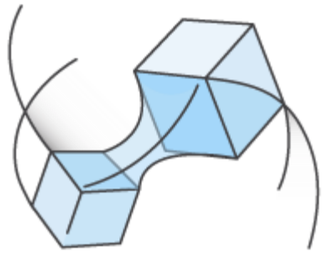
AWS Lambda

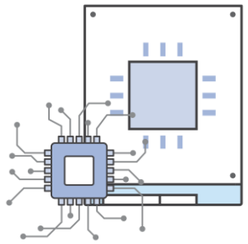
AWS Storage is a Platform



Amazon EFS

File

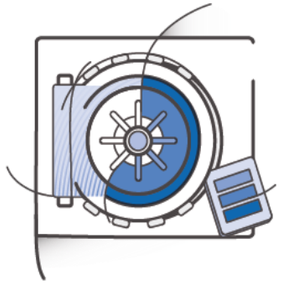




Amazon EBS

Amazon EC2 Instance Store

Block

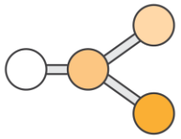


Amazon S3 / S3-IA

Amazon Glacier

Object

Data Transfer



Internet/ VPN

AWS Direct Connect

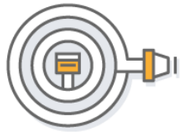
Amazon CloudFront

S3 Transfer Acceleration

ISV Connectors

Storage Gateway

AWS Snowball



Amazon Kinesis Firehose

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AWS Benefits Directly Impact Life Sciences

Accelerated Time to Insight

- Quickly derive actionable insights from research and development data inputs
- No large upfront investments in time, infrastructure, and money

Scalability and Dynamic Resourcing

- Efficiently scale resources to meet shifting demands throughout the product lifecycle
- Encourages unrestricted scientific experimentation, product launches, and manufacturing runs

Compliant and Secure Environment

- Streamlined and repeatable test environment
- Traceability helps organizations satisfy regulations and audits

Global, Fault-Tolerant Infrastructure

- 69 AWS Availability Zones in 22 Regions worldwide means high availability
- Allows for seamless information-sharing between global stakeholders

You executive leadership assessed the business case and decided to…thoughts?

- Store our supplier management solution in the cloud
- Move a critical to quality manufacturing analysis (storage, process, compute) to the cloud
- Put PHI work streams in the cloud
- Migrate half of our data center(s) to the cloud
- Move a few processes within our Class I device to the cloud
- Build our Class II device as cloud-first technology
- Change our Class III device data aggregation and transmission of results to the cloud…

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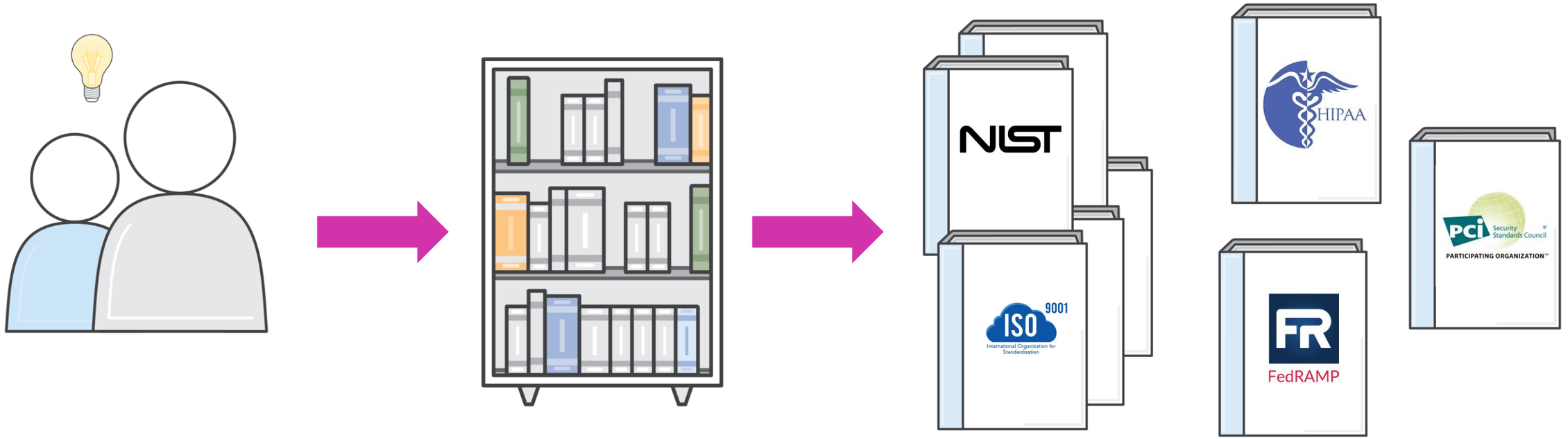
Tech = Biotech, so how to approach compliance?

- Combination of AWS Certifications, resources and support, in addition to customer due diligence



Customer Compliance programs Verticals

Tech =\Biotech, so how to approach compliance?

- IT Industry Standards / certifications
- Health Data Privacy / certifications
- GxP
- Global considerations

Diagnostic-relevant Compliance Programs

Certifications / Attestations

ISO 9001 International Organization for Standardization

ISO 27001 International Organization for Standardization

ISO 27017 International Organization for Standardization

ISO 27018 International Organization for Standardization

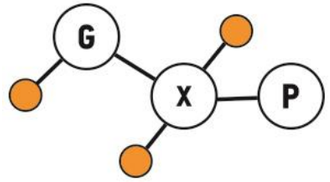
AICPA SOC aicpa.org/soc4so SOC for Service Organizations | Service Organizations

Laws / Regulations / Privacy

HIPAA

HIPAA compliance does not equate to GxP compliance

Alignments / Frameworks (industry / function)



NIST

https://aws.amazon.com/compliance/programs/

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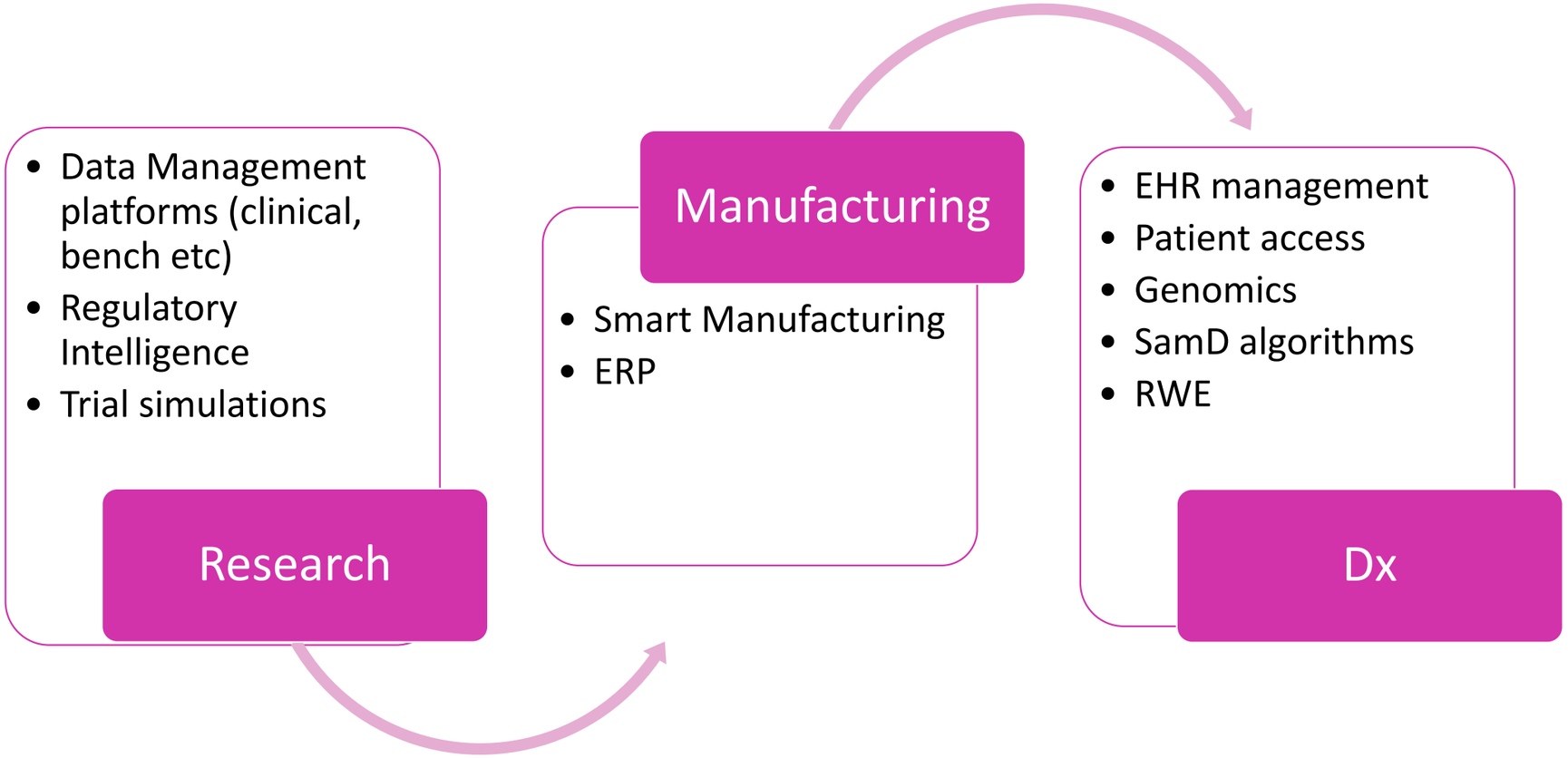
Diagnostic life cycle where cloud can be used



The importance of GxP

Pharma

Med Devices

Biologics

Diagnostics

GxP does not have a standard definition -

- …collectively GMP, GCP and GLP (each defined) as guidelines and regulations to ensure BioPharma and Medical Device products are safe and effective, and meet their intended use during manufacturing, design, storage, and distribution through various stages of development (pre-clinical, clinical, marketed product)

- Reproducibility
- Geography matters
- Violations may hurt you

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GxP: Quality Management System considerations

- Compliant QMS includes supplier evaluation
- AWS ISO 9001 International Organization for Standardization certified since 2014
- BioPharma: range of guidelines for GxP
- Medical Devices: QSR (GxP), ISO 13485

Have you hugged your IT team today?

- SW Development
- IT Support
- Security

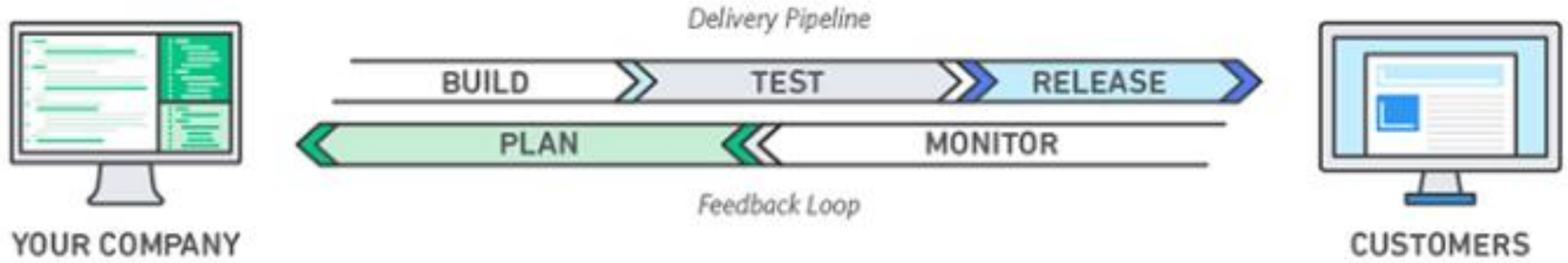
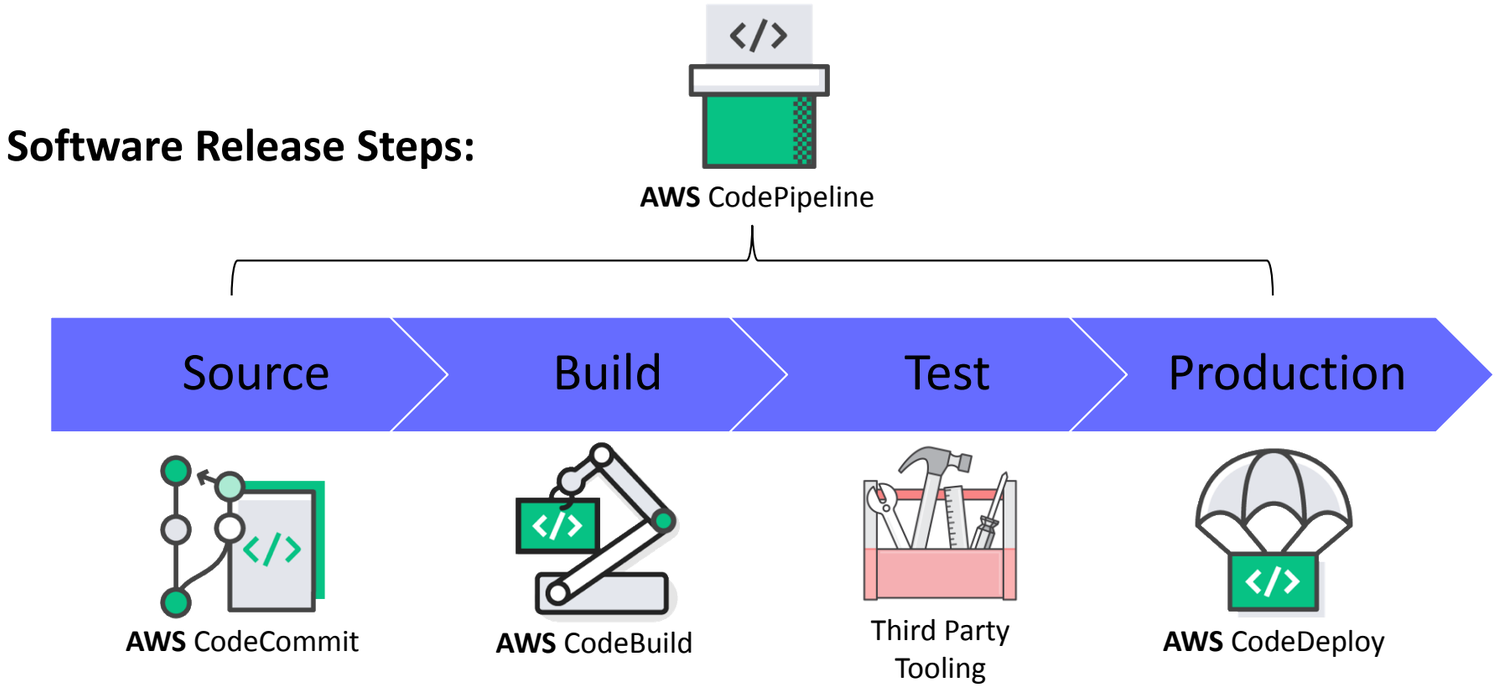


Figure 2: A standard DevOps pipeline

https://www.youtube.com/watch?v=6jHd421FXUQ&feature=youtu.be

GxP: Validation

- Treat Infrastructure as code
- Validate Infrastructure as you would code



Shared Responsibility Model

AWS Delivers

Security **of** the Cloud

Expert guidelines and resources to assist customers with compliant application development

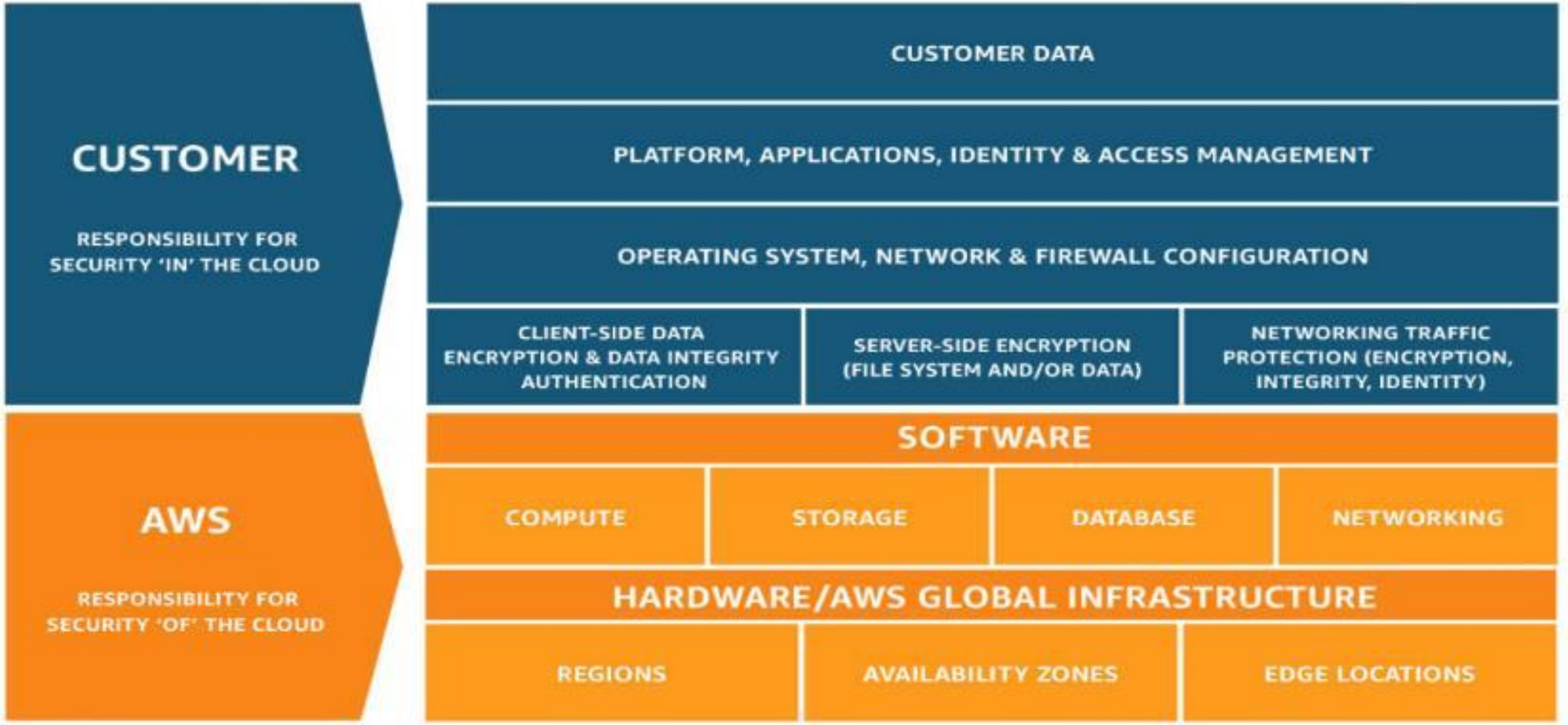
AWS White Paper: Considerations for Using AWS Products in GxP Systems

Customer Responsibility

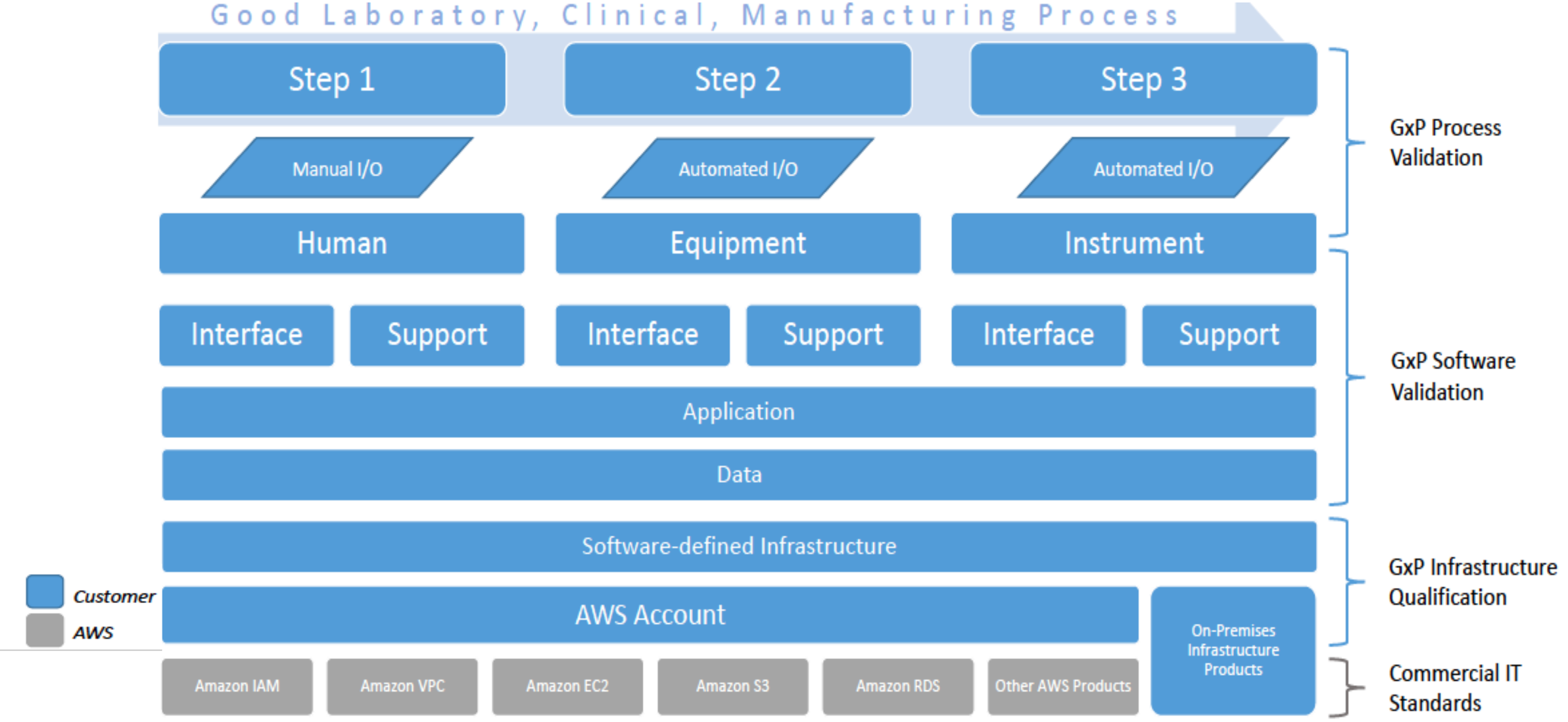
Security **in** the Cloud

Develop, validate, and secure applications based on due diligence and expert consultation

Shared Responsibility Model - Security

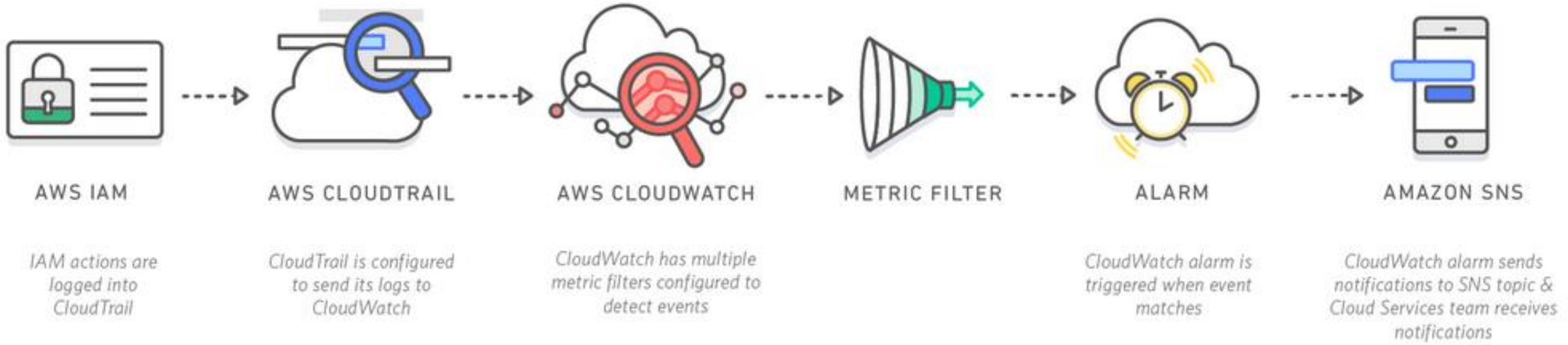


Shared Responsibility Model - GxP

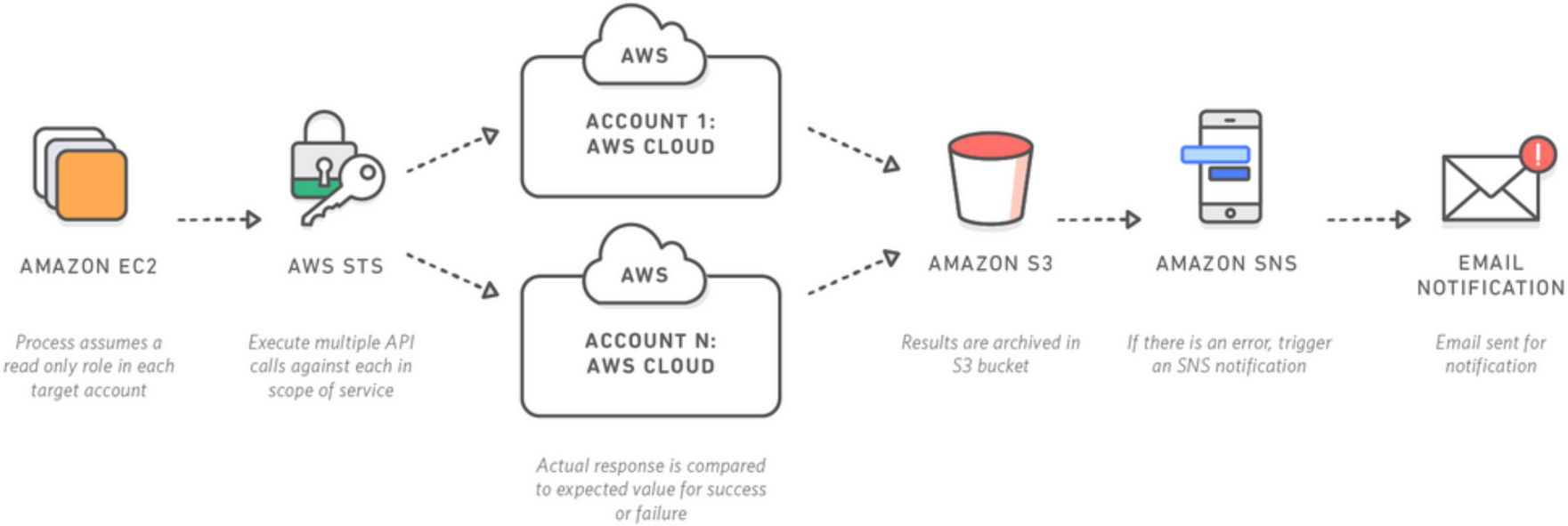


Architecting for GxP in the Cloud – Sample Architectures

Example 1:
Near real-time alerting



Example 2:
Continuous compliance checker



https://aws.amazon.com/health/life-sciences-compliance/architecting-for-gxp/

General Strategies for GxP Compliance

- **Cloud Native**

- Use Management Tools & Automate
  - CI/CD for changes

- Sensitive Data
  - Decouple from processing
  - **Always** encrypt
  - **Separate** from general workflow

Amazon CloudWatch

AWS CloudTrail

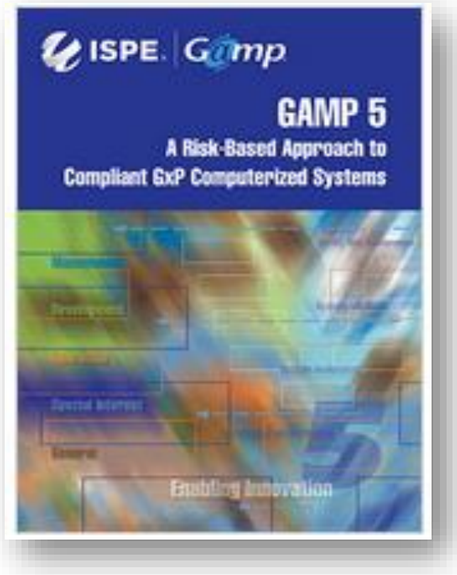
AWS Config

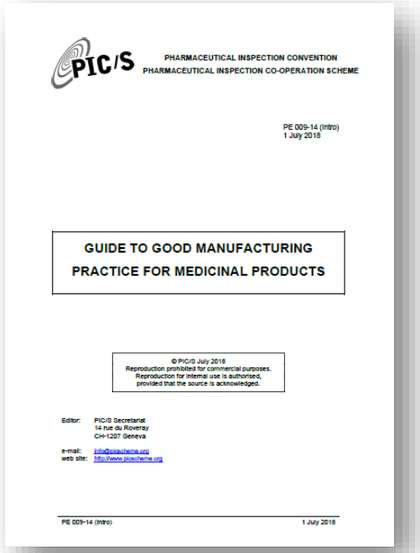
Always Test!

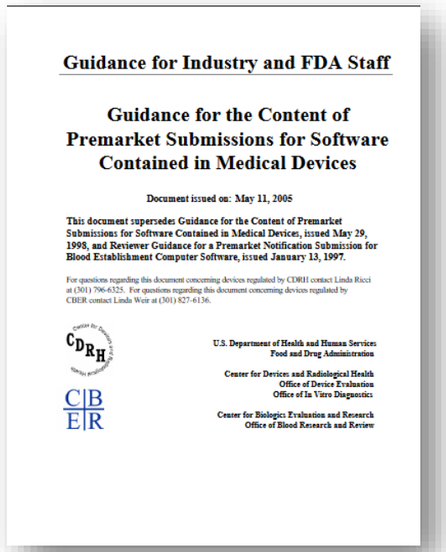
GxP: AWS Classification

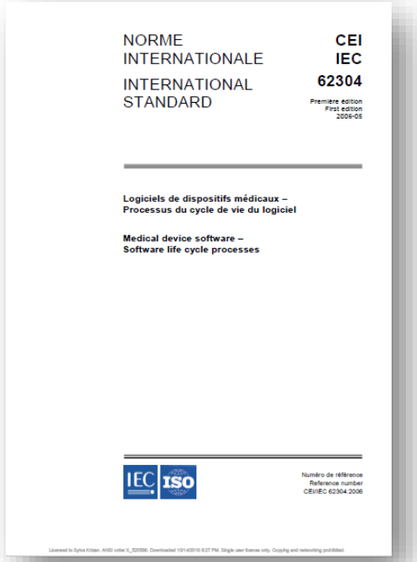
- AWS infrastructure classification - customer designation often COTS – FedRAMP

- Customers with GxP requirements responsible for categorizing AWS using industry recommendations









GAMP PIC/S OTS/LOC SOUP/62304

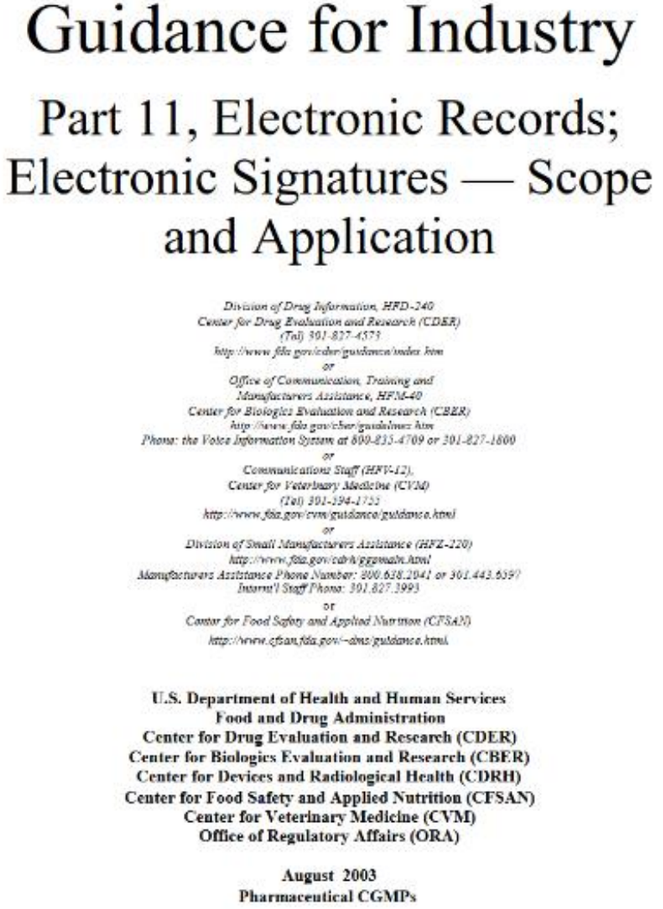
21 CFR Part 11

III. DISCUSSION

A. Overall Approach to Part 11 Requirements

As described in more detail below, the approach outlined in this guidance is based on three main elements:

- Part 11 will be interpreted narrowly; we are now clarifying that fewer records will be considered subject to part 11.
- For those records that remain subject to part 11, we intend to exercise enforcement discretion with regard to part 11 requirements for validation, audit trails, record retention, and record copying in the manner described in this guidance and with regard to all part 11 requirements for systems that were operational before the effective date of part 11 (also known as legacy systems).
- We will enforce all predicate rule requirements, including predicate rule record and recordkeeping requirements.



Guidance for Industry

Part 11, Electronic Records; Electronic Signatures — Scope and Application

Division of Drug Information, HFD-240
Center for Drug Evaluation and Research (CDER)
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
or
Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research (CBER)
http://www.fda.gov/cber/guidelines.htm
Phone: the Voice Information System at 800-835-4709 or 301-827-1800
or
Communications Staff (HFV-12),
Center for Veterinary Medicine (CVM)
(Tel) 301-594-1755
http://www.fda.gov/cvm/guidance/guidance.html
or
Division of Small Manufacturers Assistance (HFZ-220)
http://www.fda.gov/cdrh/ggpmain.html
Manufacturers Assistance Phone Number: 800.638.2041 or 301.443.6597
Internl'l Staff Phone: 301.827.3993
or
Center for Food Safety and Applied Nutrition (CFSAN)
http://www.cfsan.fda.gov/~dms/guidance.html

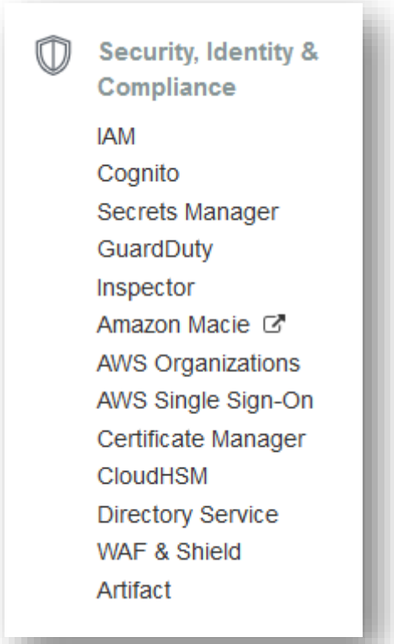
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Food Safety and Applied Nutrition (CFSAN)
Center for Veterinary Medicine (CVM)
Office of Regulatory Affairs (ORA)

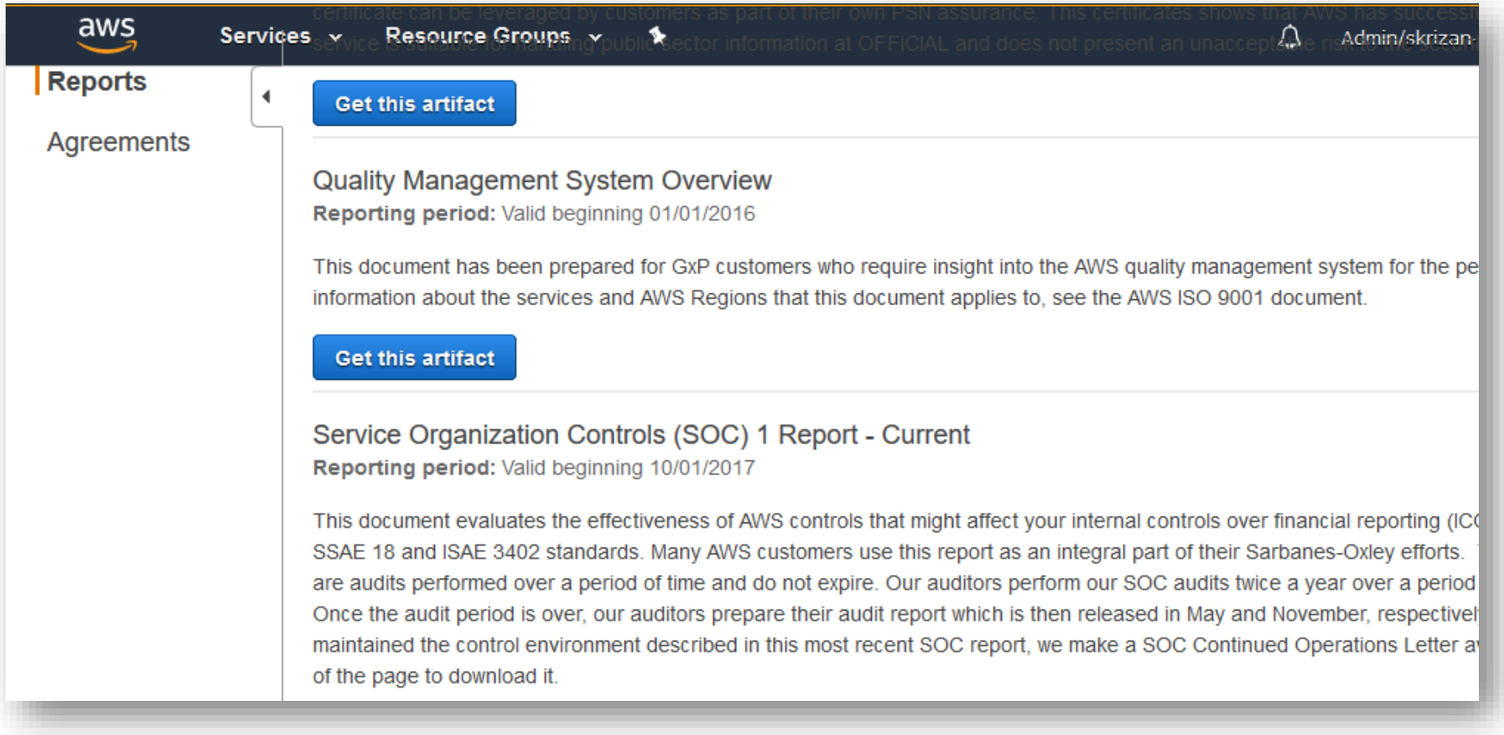
August 2003
Pharmaceutical CGMPs

https://www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm#iiia

Know where the resources are – e.g. Artifact

- Login to AWS account; Security, Identity & Compliance
- Select and accept NDA Agreement





Cloud-specific conversations with FDA

- Review Division (product)
- Technology Programs (manufacturing)
  - CDRH ?
  - CBER Advanced Technologies Team (CATT)
  - CDER Emerging Technology Program (ETT)
  - Small cross functional team with representation from all relevant CDER review and inspection programs
    • Vision: Encourage and support the adoption of innovative technology to modernize pharmaceutical development and manufacturing where the Agency has limited review or inspection experience. Includes: − Innovative or novel product, manufacturing process, or analytical technology subject to CMC review − Existing or planned submission(s) https://www.fda.gov/media/91768/download; https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/emerging-technology-program

FDA Cloud References - definitions

***Cloud**: A device or product with internet-based computing that provides computer processing resources and data on demand. The cloud is a shared pool of configurable resources (e.g., computer networks, servers, storage, applications, and services). Computing and data storage resources include: servers, operating systems, networks, software, applications, services, and storage equipment.*

Examples include:

- SaMD being executed in the cloud.
- A mobile colposcope that stores images taken on the cloud for future retrieval and review in the doctor's office.
- A picture archiving and communications system consists of cloud-based, web-accessible software that analyzes cardiovascular images acquired from magnetic resonance (MR) scanners.

https://www.fda.gov/medical-devices/digital-health/digital-health-criteria

FDA Cloud References - continued

- Q: f. What are the “systems” in “computer or related systems” in §211.68?
- A: The American National Standards Institute (ANSI) defines systems as people, machines, and methods organized to accomplish a set of specific functions. Computer or related systems can refer to computer hardware, software, peripheral devices, networks, **cloud infrastructure**, operators, and associated documents (e.g., user manuals and standard operating procedures) https://www.fda.gov/media/97005/download
- Data Integrity and Compliance With CGMP Guidance for Industry (April 2016)

FDA Cloud References – cross-border use

- "Outsourced Electronic Services" – data management systems –
  - **Q: Does FDA consider it acceptable for data to be distributed across a cloud computing service's hardware at several different geographic locations at the same time without being able to identify the exact location of the data at any given time?**
  - A: If appropriate controls are in place, there are no limitations regarding the geographic location of cloud computing services. However, it is critical for sponsors and other regulated entities to understand the data flow and know the location of the cloud computing service's hardware in order to conduct a meaningful risk assessment regarding data access, integrity, and security. Data privacy laws may differ from country to country. Therefore, sponsors and other regulated entities should perform appropriate risk assessments to ensure that data residing on storage devices outside their country can be retrieved and accessed during FDA inspections.
- *Draft Guidance: June 2017 Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers CBER/CDER/CDRH*
  https://www.fda.gov/media/105557/download

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FDA Cloud References – public workshops

- Food and Drug Administration - Ophthalmic Digital Health Workshop 10/23/2017 –
- *"MS. BOTTORFF: Yep. So of course, GE and also a bunch of our portfolio companies are doing things that are cloud-based and we have discussions every day with, you know, integrated delivery network big systems as well as smaller entities about this very issue, because everyone's quite concerned about moving to the cloud and having it off premise. But, you know,* ***that presumes one thing, that their on-premise security is better than Amazon Web Services. Really? Probably not, you know. Not even for, you know, a big IDN necessarily but certainly not for an individual practice person. Their security is probably not nearly as good as the cloud****."*
- https://www.fda.gov/media/111966/download

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FDA Digital Health Guidance Documents – *9/27/19*

- Clinical Decision Support Software
- Changes to Existing Medical Software Policies Resulting from "Section 3060 of the 21st Century Cures Act
- Policy for Device Software Functions and Mobile Applications
- Medical Device Data Systems, Medical Image Storage Devices and Medical Image Communications Devices
- General Wellness Policy for Low Risk Devices
- Off the Shelf Software use in Medical Devices

"…or upload it to an online (cloud) database"

Examples that are not mobile medical app Manufacturers: "cloud hosting services"

Case Studies for Speed and Productivity

> We processed 800 samples on 100 nodes. Using our competitor's method, this would have taken more than two full weeks. With AWS, we did it in 60 minutes.
>
> Jos Lunenberg -Chief Business Officer

GENALICE
TECHNOLOGY FOR PEOPLE & SCIENCE

The startup's GENALICE MAP Next-Generation Sequencing (NGS) data analysis suite is a data-processing and data-analysis solution that uses smart, algorithm-based software to identify DNA changes.

- Population-scale analysis involves checking entire groups, or 'cohorts,' rather than just one sample.
- "The aim with Population Calling was to perform analysis on 800 Alzheimer's disease samples," says Lunenberg. "We knew that analyzing them using our onsite servers would take too long, so we started looking for a cloud provider that could deliver reliable scale—and speed."

https://aws.amazon.com/solutions/case-studies/genalice/?trk=hcls_case-studies_card

Case Studies for Speed and Productivity

> Using AWS, a single scientist can launch hundreds of compute nodes. That's a capability we just didn't have before.
>
> **Lance Smith**
> Associate Director of IT

- Wanted to improve its high-performance computing (HPC) capabilities
- Needed to enable collaboration between its own researchers and academic research labs
- Reduces HPC computational jobs from weeks to less than one day
- Enables secure collaboration between internal and external researchers
- Gives each scientist the ability to launch hundreds of compute nodes

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FDA clearances – Cloud References

- IDx-DR (DEN180001)
  - Software program that uses an artificial intelligence algorithm to analyze images of the eye taken with a retinal camera called the Topcon NW400. A doctor uploads the digital images of the patient's retinas to a cloud server on which IDx-DR software is installed. If the images are of sufficient quality, the software provides the doctor with one of two results: (1) "more than mild diabetic retinopathy detected: refer to an eye care professional" or (2) "negative for more than mild diabetic retinopathy; rescreen in 12 months." If a positive result is detected, patients should see an eye care provider for further diagnostic evaluation and possible treatment as soon as possible. First medical device to use artificial intelligence to detect greater than a mild level of the eye disease diabetic retinopathy in adults who have diabetes.
- STUDIO on the Cloud Data Management Software (DEN140016)
- CardioFlux FAC Magnetocardiograph (K182571).
- iHealth Cloud (K131203).
- TM eCloud ECG Analysis System (K142349)
- Cloud Smart Thermometer (K160306)

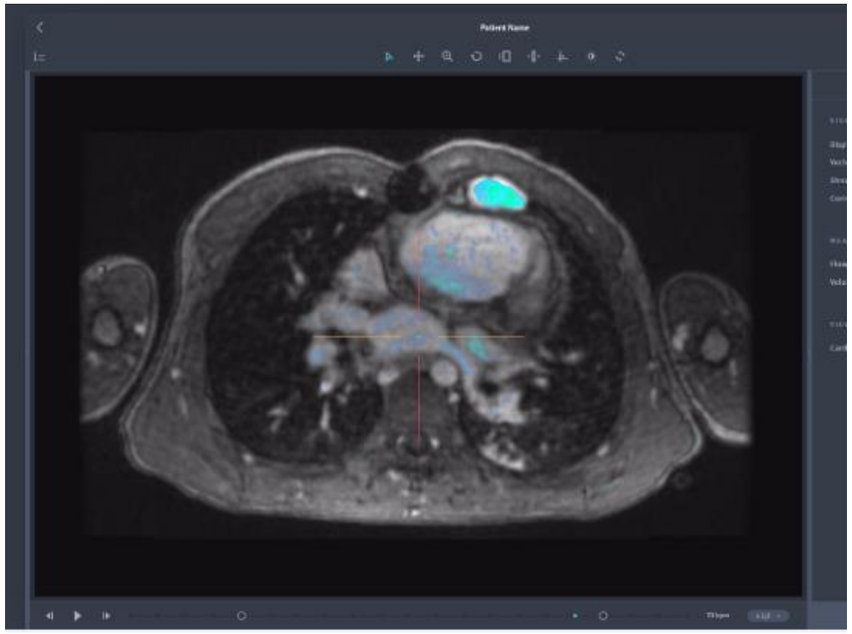
FDA Clearances – Cloud Case Studies

- Novartis-Pear Therapeutics collaboration: Reset-O – to increase retention of patients with Opioid Use Disorder using Cognitive Behavioral Therapy (Rx only digital therapeutic) (K173681): https://www.youtube.com/watch?v=jqKlsRqpQi0&feature=youtu.be

- Viz CTP (Viz.ai): …used to perform image processing, analysis, and communication of computed tomography (CT) perfusion scans of the brain. Data and images are acquired through DICOM-compliant imaging devices. Viz CTP provides both analysis and communication capabilities for dynamic imaging datasets that are acquired with CT Perfusion imaging protocols. ….Results are exported (K180161) https://aws.amazon.com/blogs/startups/deep-learning-viz-ai/

FDA Clearances – Cloud Case Studies

ARTERYS



Arterys® MICA software is a medical diagnostic application that displays, processes, stores, and transfers DICOM and non-DICOM medical data, with the exception of mammography. It provides the capability to store images and patient information, and perform filtering, digital manipulation, and quantitative measurements. The client software is designed to run on standard personal and business computers (K182034).

Arterys uses deep learning for innovation in medical imaging to deliver data-driven clinical patient care.

- Analyzes thousands of cardiac MRI images from global hospitals to understand patients and treatments.
- Enabled seamless visualization of medical images and solved limited computation power available to doctors today by moving from CPU to GPU computing.
- Reduced time for medical imaging analysis from 30 minutes to seconds using deep learning and Amazon G2 and S3.

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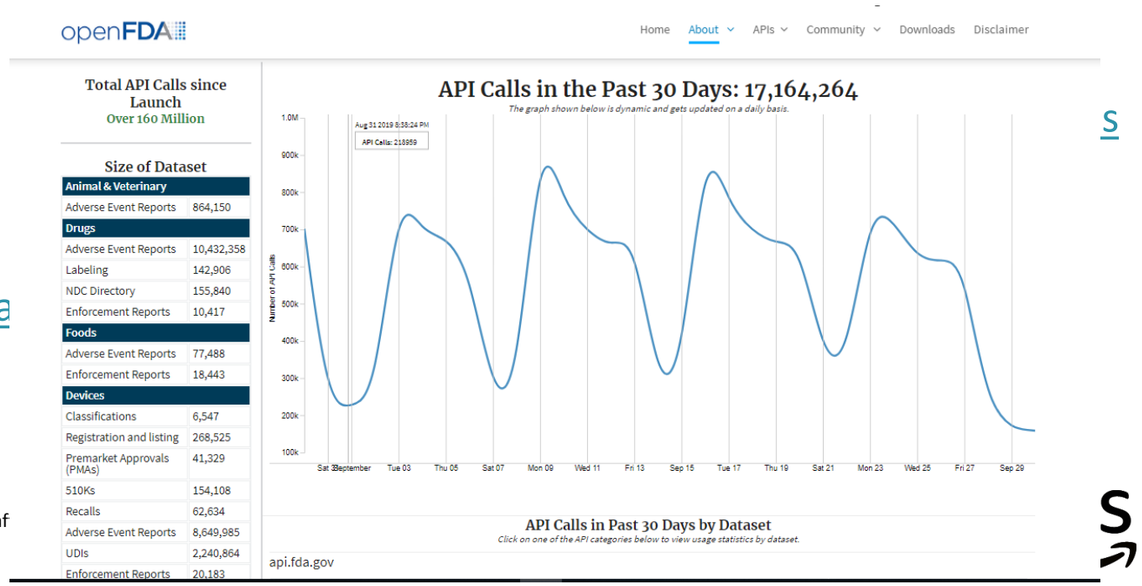
Use of Cloud by FDA

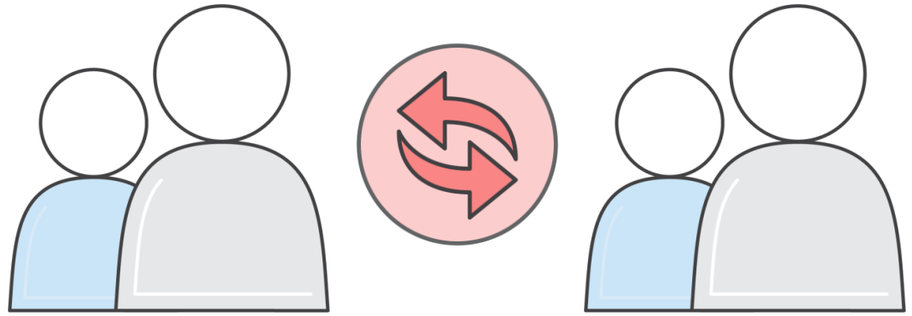
- **FDA MyStudies: An Open-Source, Digital Platform to Gather Real World Data for Clinical Trials and Research Studies** https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/introduction-fda-mystudies-open-source-digital-platform-gather-real-world-data-clinical-trials-and
- **precisionFDA**: community platform for NGS assay evaluation and regulatory science exploration https://precision.fda.gov/docs/intro
- **FDA Innovation Lab:** focus areas include Cloud Services, Mobility, High Performance Computing, Data and Social Computing.
- **FDA databases (openFDA)**:

  FAERS, Medwatch etc https://open.fda.gov/about/sta



Ways to help CSPs better serve you

- Engage compliance (e.g. Quality, Regulatory Affairs, Data Officers)
  - Define requirements for GxP cross-functionally
  - Confirm global requirements
  - Plan for repeatability (scaling)



- Use the cloud adoption framework
  - Engage with cloud center of excellence
  - Ensure plan aligns with enterprise strategy

- Remember others have walked the GxP path before you…

You are not alone

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Thank you!

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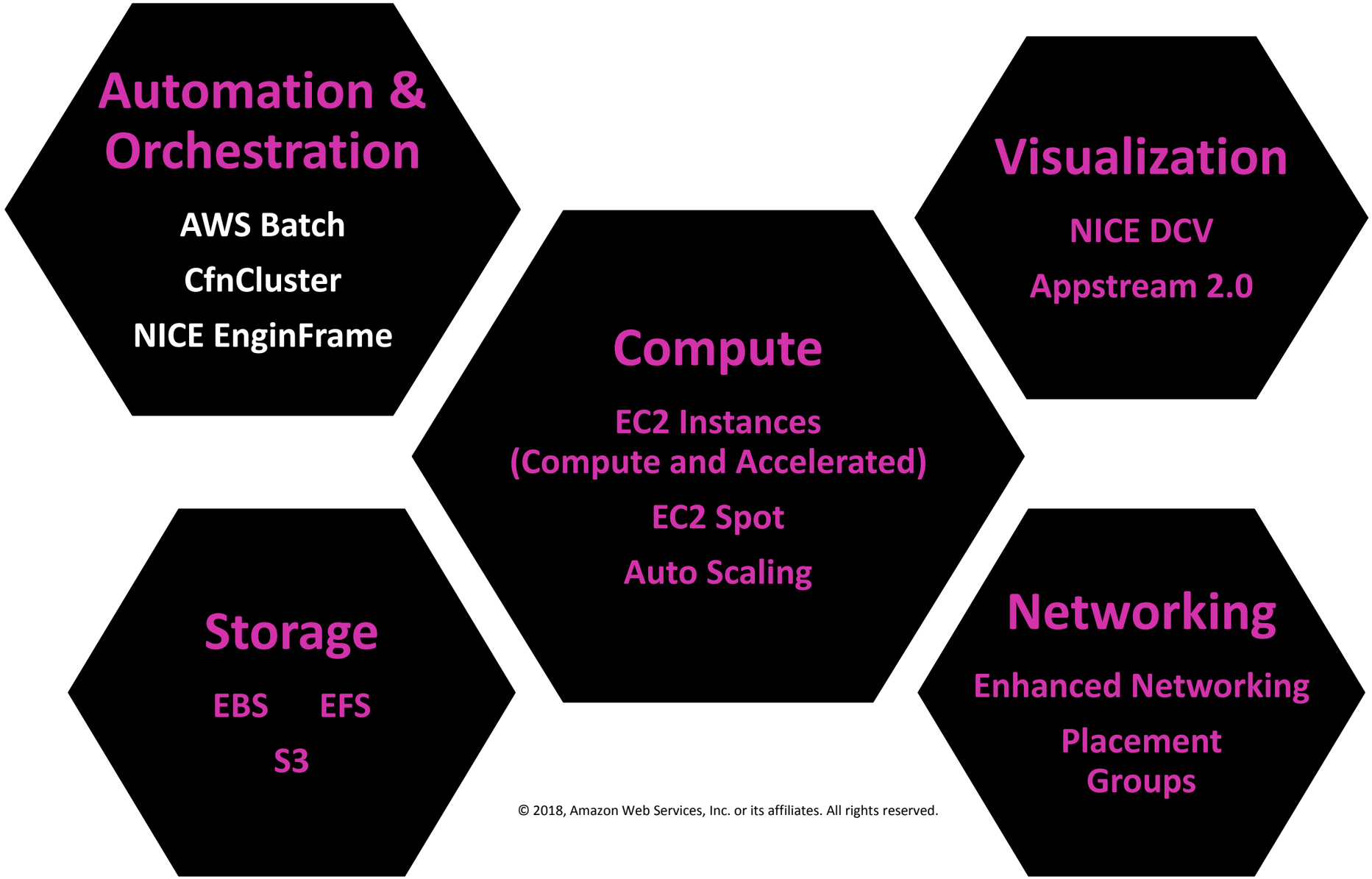
AWS HPC Solution Components



Defining HPC – Example Use Cases

Clustered (Tightly coupled)

- Fluid dynamics
- Weather forecasting
- Materials simulations
- Crash simulations

- Seismic processing
- **Clinical trial simulations**
- Astrophysics
- Deep learning

Data Light

Minimal requirements for high performance storage

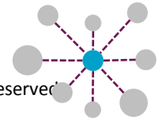
Data Heavy

Benefits from access to high performance storage

- Risk simulations
- **Molecular modeling**
- Contextual search
- Logistics simulations

- Animation and VFX
- Semiconductor verification
- Image processing/GIS
- **Genomics**

Distributed / Grid (Loosely coupled)



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