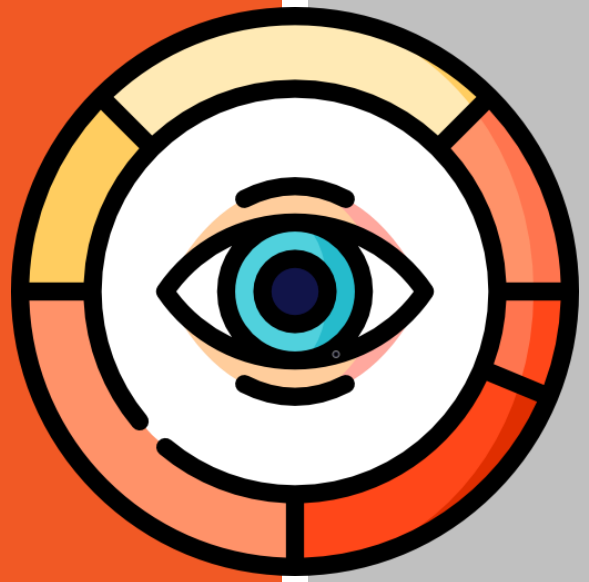
Data Integrity

Concepts and Challenges



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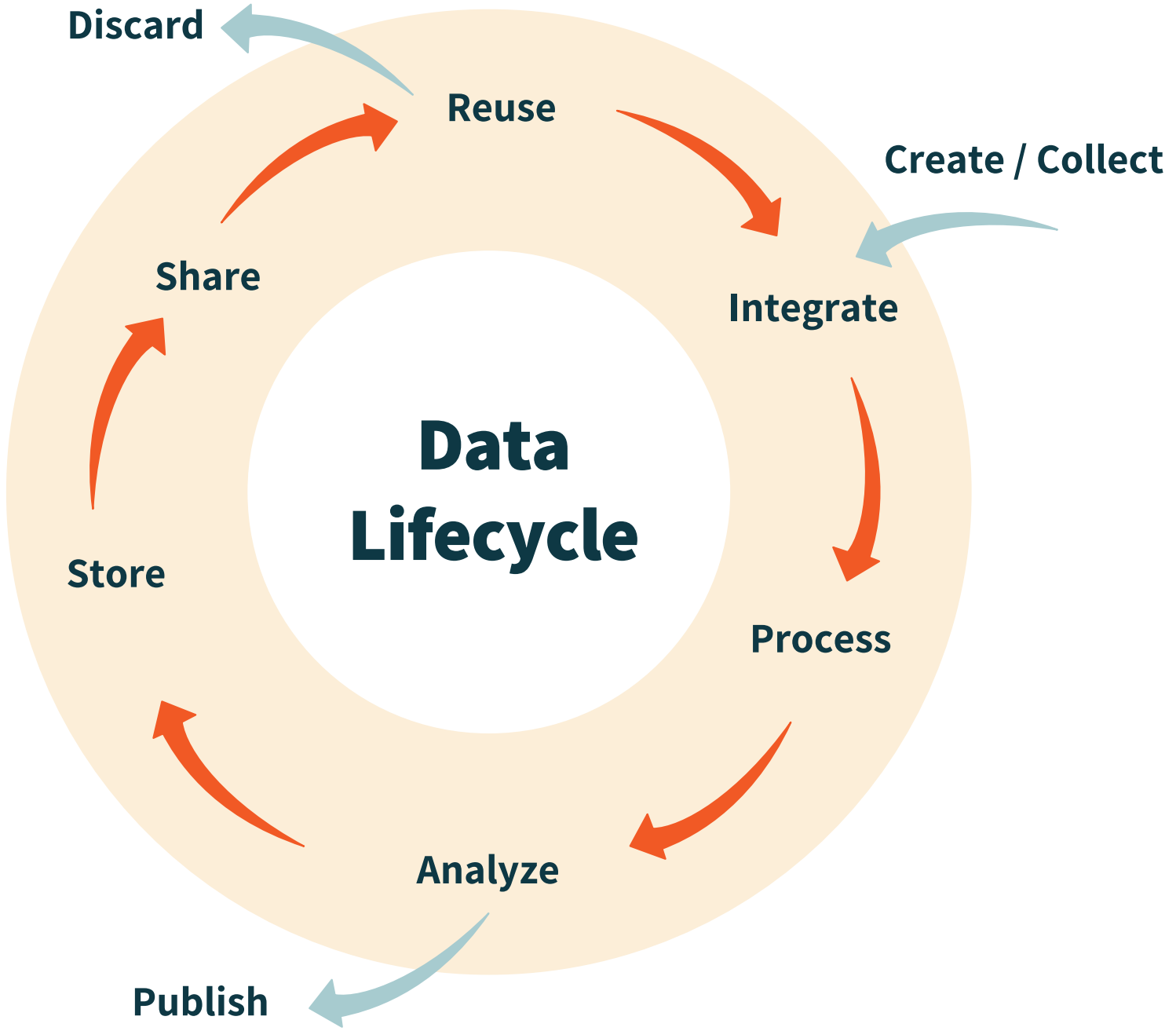
Data Integrity Concepts

Conceptual and Practical Models

ALCOA

A	Attributable	Who, what, when?
L	Legible	Clearly and permanently readable
C	Contemporaneous	Real-time recordings, date and time records
O	Original	Raw data maintained untouched
A	Accurate	Consistent and complete Mistakes and updates reported and recorded

Data Lifecycle



Risk Management

Golden Triangle - Quality Culture

Data Integrity & Quality Culture

The traditional approach:

Manufactures claimed they had difficulties adopting manufacturing excellence because of regulatory requirements.

Solution: a risk based quality paradigm

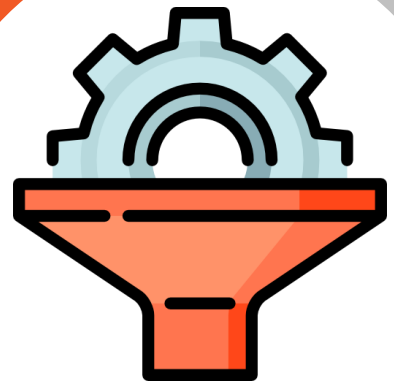
As a results –continuous improvements

Building the necessary motivation:

Tying quality to core values, distributing a code of ethics, and providing a transparent and open environment for reporting problems.

Way of action- implement Data Integrity principles.

ALCOA +

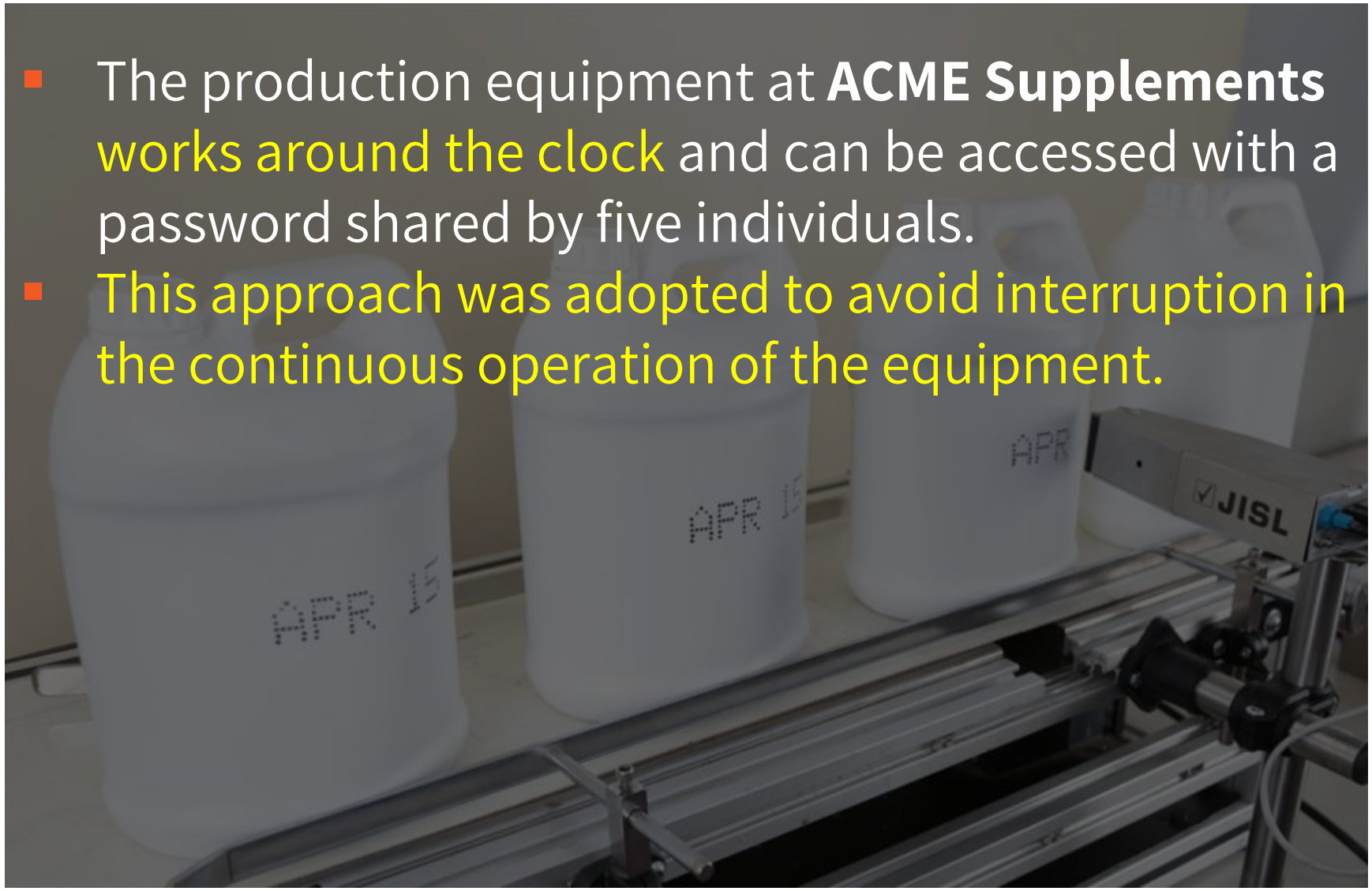


Attributable

The challenge: legacy instrument

Case #1

- The production equipment at **ACME Supplements** works around the clock and can be accessed with a password shared by five individuals.
- This approach was adopted to avoid interruption in the continuous operation of the equipment.



Case #1

What ALCOA aspect of DI is compromised?

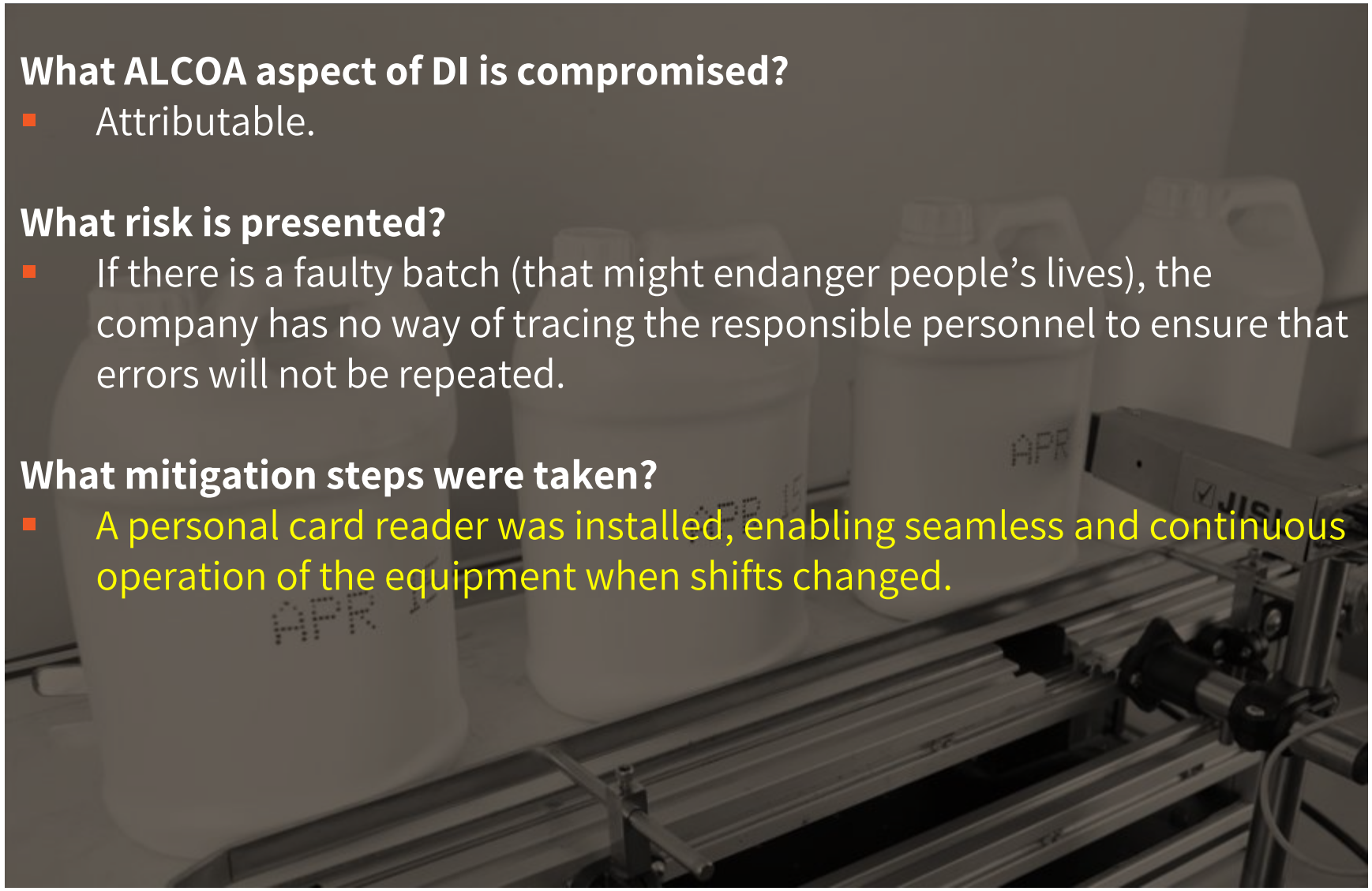
- Attributable.

What risk is presented?

- If there is a faulty batch (that might endanger people's lives), the company has no way of tracing the responsible personnel to ensure that errors will not be repeated.

What mitigation steps were taken?

- A personal card reader was installed, enabling seamless and continuous operation of the equipment when shifts changed.



NOTE: Case details have been changed to ensure company confidentiality.

Legible

The challenge: System upgrade

Case #2

- **ACME Food** upgraded its ERP system.
- As the project progressed, the Head Food Technologist understood that the new system was unable to read old logs.
- He decided (by himself) to exclude the old logs from the available database.

1. What ALCOA aspect of DI is compromised?
2. What risk is presented?
3. What mitigation would you propose?

Case #2

What ALCOA aspect of DI is compromised?

- Attributable, Legible, Original.

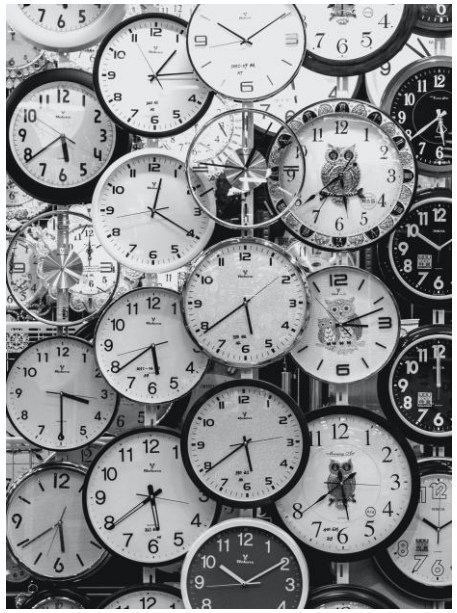
What risk is presented?

- The company cannot trace the responsible personnel to ensure that errors will not be repeated.
- The company loses valuable original data and metadata.

What mitigation steps were taken?

- All the old logs were saved in a virtual environment that enabled the company to access old logs and files when necessary.
- A special migration project was designed for logs that were tagged as important.

NOTE: Case details have been changed to ensure company confidentiality.

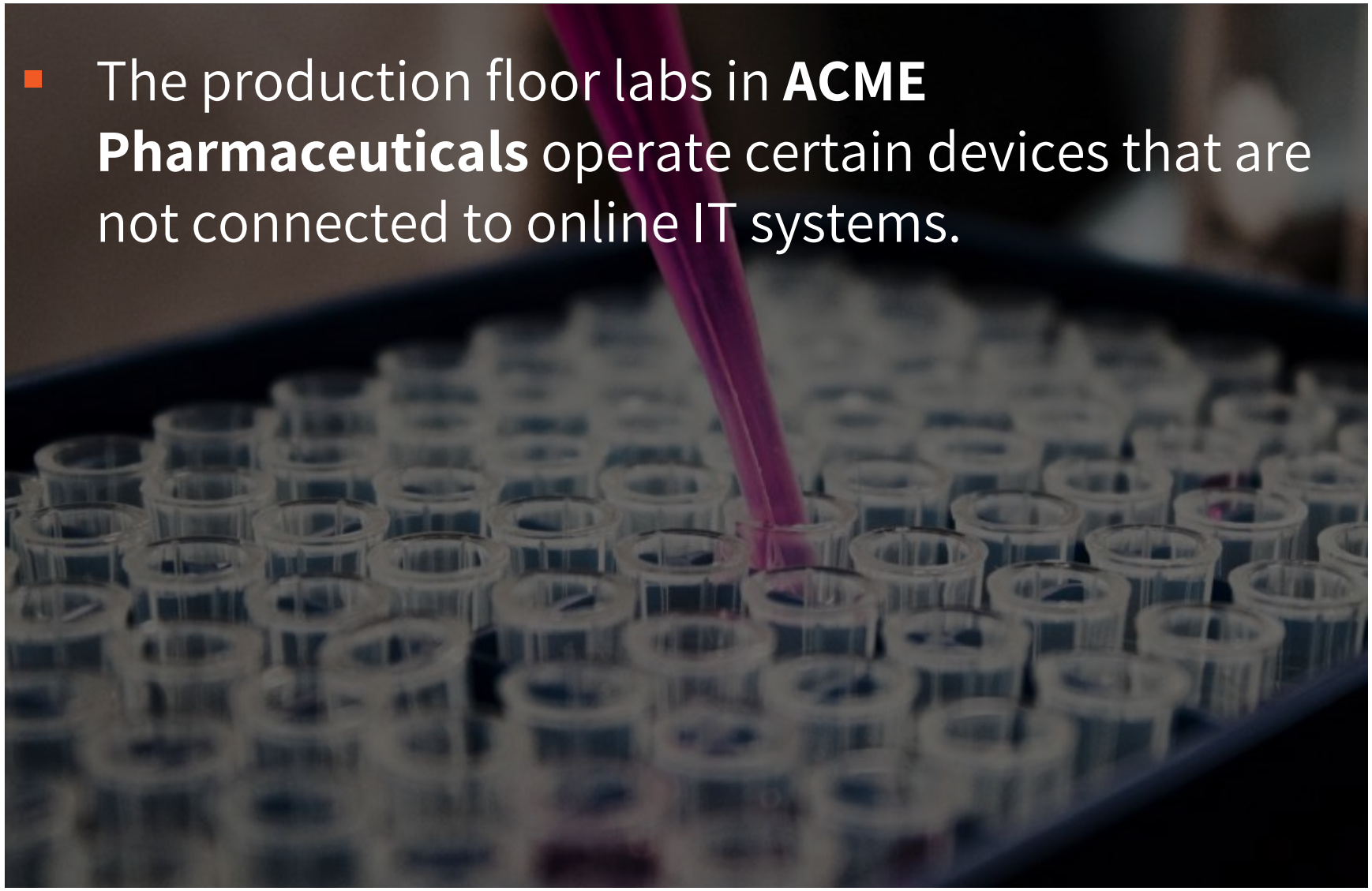


The challenge: Documentation

Contemporaneously

Case #3

1. What ALCOA aspect of DI is compromised?
2. What risk is presented?
3. What mitigation would you propose?



- The production floor labs in **ACME Pharmaceuticals** operate certain devices that are not connected to online IT systems.

Case #3

What ALCOA aspect of DI is compromised?

- Contemporaneous, Accurate, Attributable.

What risk is presented?

- The DI process required many human interventions and caused mistakes, e.g.: backups required the use of memory sticks which failed to function properly.
- Information security updates were compromised, leading to loss of data.

What mitigation steps were taken?

- Connection of the devices to computers.
- Assignment of a team responsible for manual backup and orderly synchronization of data.

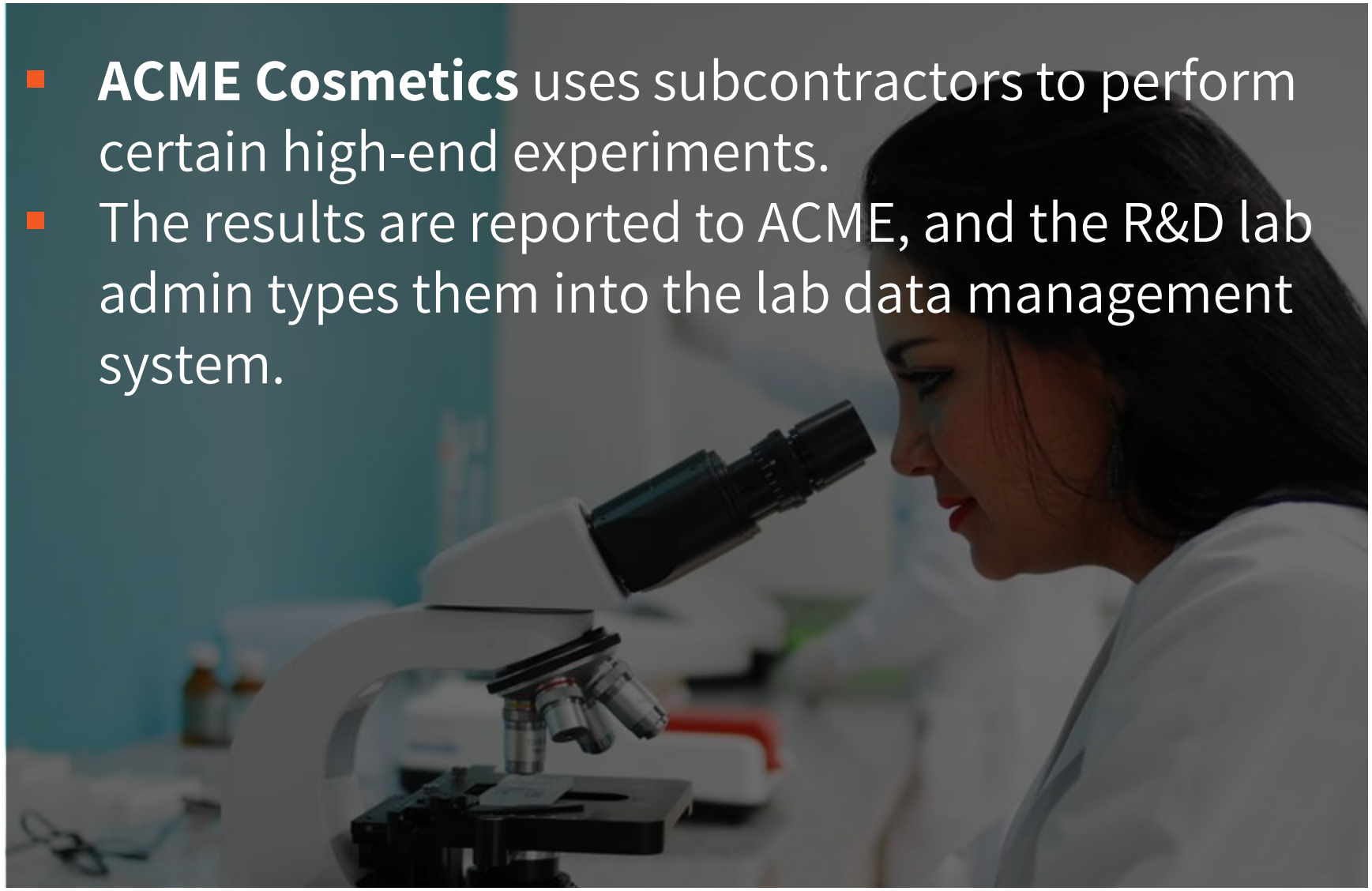
NOTE: Case details have been changed to ensure company confidentiality.

The challenge:

Vendors management

Case #4

- **ACME Cosmetics** uses subcontractors to perform certain high-end experiments.
- The results are reported to ACME, and the R&D lab admin types them into the lab data management system.



1. What ALCOA aspect of DI is compromised?
2. What risk is presented?
3. What mitigation would you propose?

Case #4

What ALCOA aspect of DI is compromised?

- Original & Attributable

What risk is presented?

- If there is a faulty batch (that might endanger people's lives), the company has no way of tracing the responsible personnel to ensure that errors will not be repeated.

What mitigation steps were taken?

The DI failure exposed deficient conduct that occurred in many places in the organization.

- The Compliance Officer, along with IT and HR, initiated a campaign to regulate work with subcontractors. They developed a certification program for system admins and integrated it into QA administration.

NOTE: Case details have been changed to ensure company confidentiality.

Accurate

The challenge: Validation vs. Qualification

Case #5

1. What ALCOA aspect of DI is compromised?
2. What risk is presented?
3. What mitigation would you propose?

- **ACME Breweries** failed to restrict changes in master production and control records to authorized personnel only.
- The company received a warning letter instructing executive management to systematically improve their oversight of manufacturing quality to ensure sustainable quality assurance.

Case #5

What ALCOA aspect of DI is compromised?

- Attributable, Original, Accurate.

What risk is presented?

- FDA determined that audit trails or other sufficient controls to facilitate traceability of the individuals were not established.
- The example records were considered serious CGMP violations.
- The quality system did not ensure the quality, safety and effectiveness of the company food products.

What mitigation steps were taken?

- Data Integrity implementation plan

NOTE: Case details have been changed to ensure company confidentiality.


WARNING

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document *Data Integrity and Compliance With Drug CGMP* for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry.

We strongly recommend that you retain a qualified consultant to assist in your data integrity remediation. In response to this letter, provide the following:

• A comprehensive investigation into the extent of the inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.

• A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.

• A management strategy for your firm that includes the details of your global CAPA plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, manufacturing records, and all data submitted to FDA.

"Until you correct all deviations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new drug applications or supplements listing your firm as a drug manufacturer."

The goal

Thank you!

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