Data Storage Methods and Examples under Japan's GLP Regulations

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Japan Society of Quality Assurance (JSQA)

Introduction of Presenter

- 6 years as a student at a university and graduate school specializing in pharmaceutical science
- 7 years as pharmacokinetics researcher
- 15 years as QA personnel for non-clinical studies
- 14 years as QA personnel for computerized system validation
  - Concurrently working for 5 years with the business above.

Introduction of Presenter

The 2nd Asia Quality Assurance Forum

The 6th Global QA Conference

Agenda

- Background
- Status of Data Storage in Japanese Laboratories
- Possible Measures to Address Issues Related to Data Storage
- Further Considerations for Storage of Digitalized Records
- Conclusions

BACKGROUND

Background

- Japanese non-clinical research facilities store data and records in accordance with GLP and other Japanese regulations. With the development of information technology, these facilities have begun to store some of their materials electronically.
- We surveyed the status of data storage in Japanese non-clinical research facilities and discussed countermeasures to address the issues found.
- I will introduce the examples of data storage methods in Japan, including the above.

Japanese Regulations for nonclinical studies

Good Laboratory Practice (GLP)

Good Laboratory Practice (GLP) is a quality system concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.
(Refer to paragraph 1 of section 2.1 of OECD GLP CD No. 1.)

Japanese Reliability Standards in Ordinance for of Pharmaceutical and Medical Device Act (JRS)

When applying for a new drug or medical device, Pharmaceuticals and Medical Devices Agency (PMDA) checks the consistency between the application materials and the supporting documents to confirm the reliability of the application materials.

Regulations for Electronic Data

OECD GLP Guideline AD No.17 Application of GLP Principles to Computerised Systems

This guidance defines how to manage data collected by computerized systems that include analytical devices.

Ministry of Health, Labour and Welfare (MHLW) Guidance on using electronic records and electronic signatures

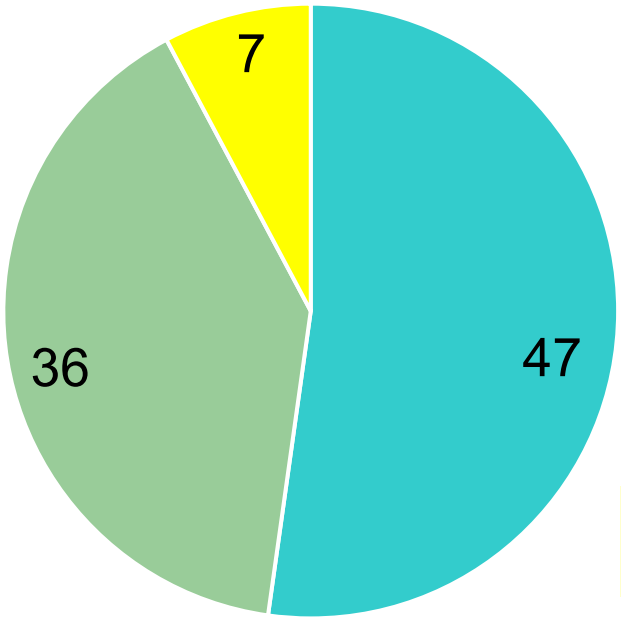
Japanese guidelines on how to ensure the reliability of electronic records/electronic signatures about the supporting documents for application materials and electronic records required to be stored under GLP and other good practices.

STATUS OF DATA STORAGE IN JAPANESE LABORATORIES

Overview of Questionnaire Survey

- Survey period: August 19 to August 30, 2024
- Survey target: Corporate members of JSQA
- Number of respondents: 91 (61%)
- Purpose of survey:
  - To confirm the current method of storing data subject to inspection by the authorities at non-clinical laboratories in Japan

Background of Respondents



Facilities that follow both GLP and JRS* were asked to respond based on GLP operations.

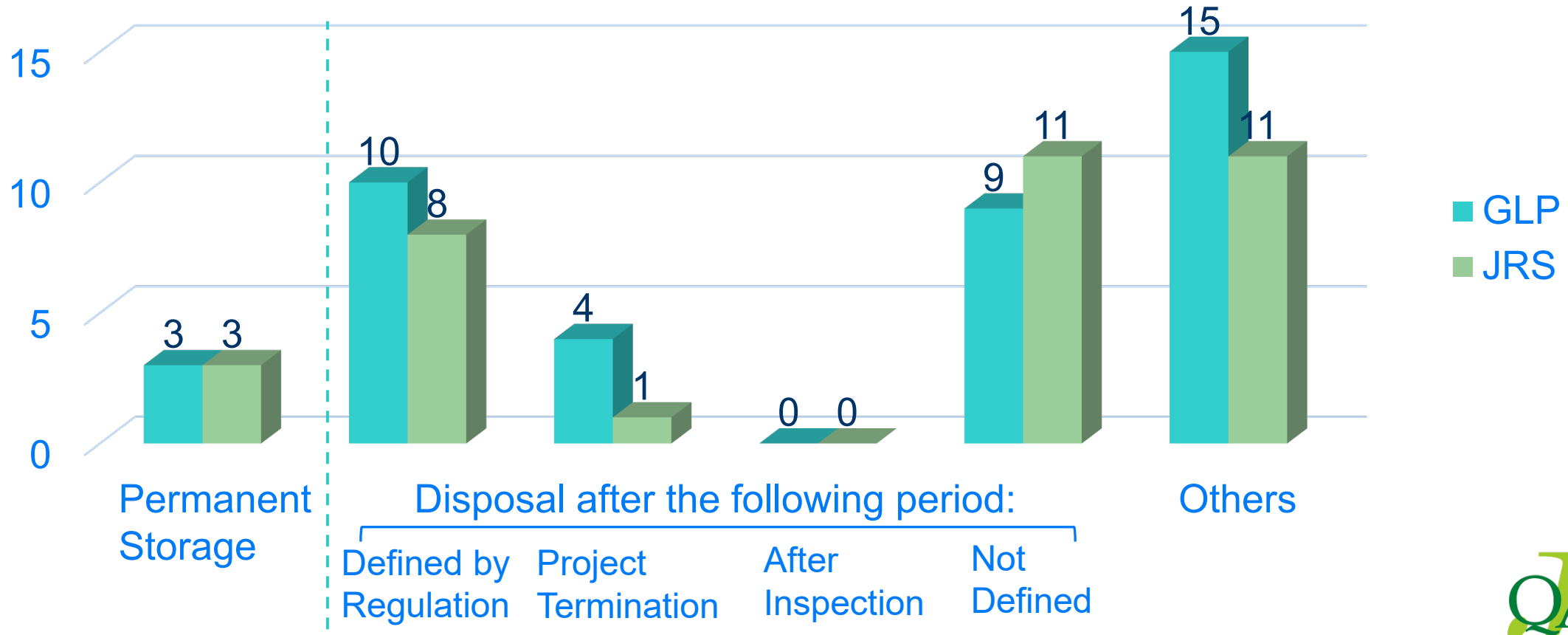
Facilities that did not follow either GLP or JRS.

Excluded from further surveys.

* JRS: Japanese Reliability Standards in Ordinance for of Pharmaceutical and Medical Device Act

Retention Period for Test-Related Electronic Data

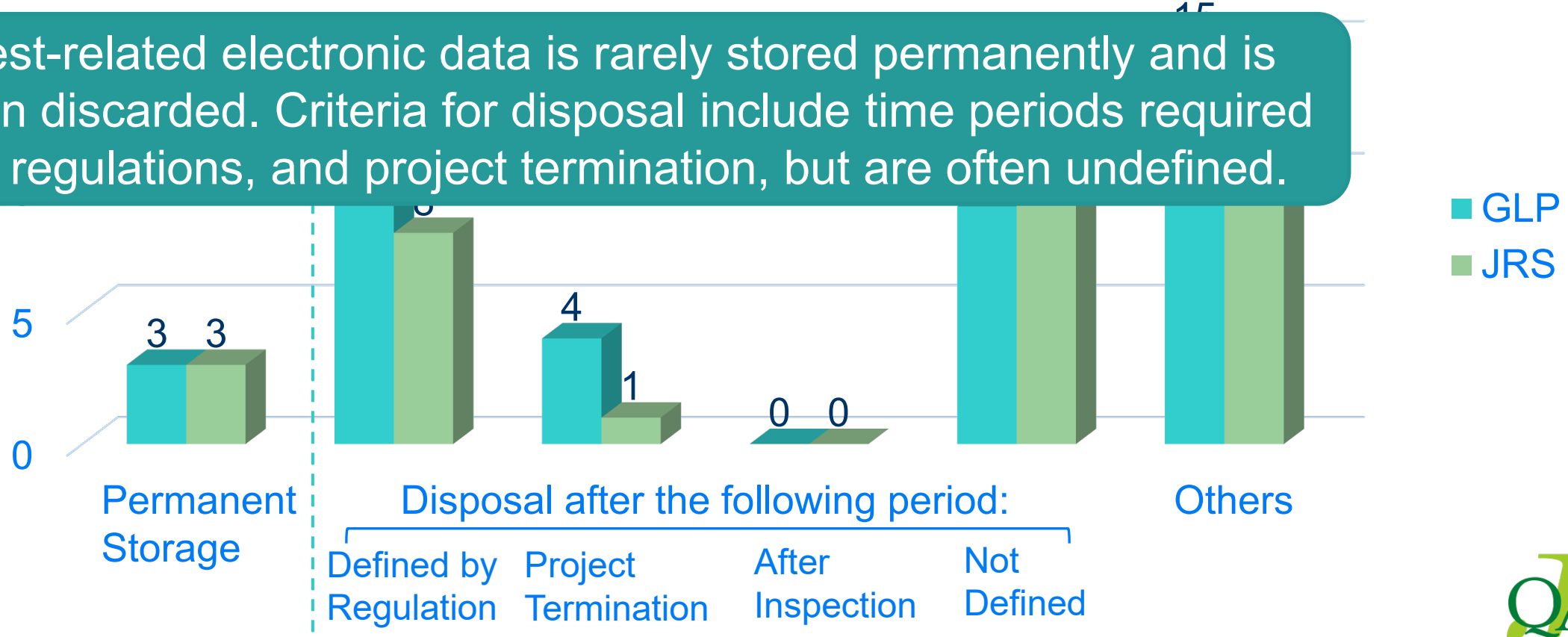
Is there a defined retention period for electronic data obtained during testing?



Retention Period for Test-Related Electronic Data

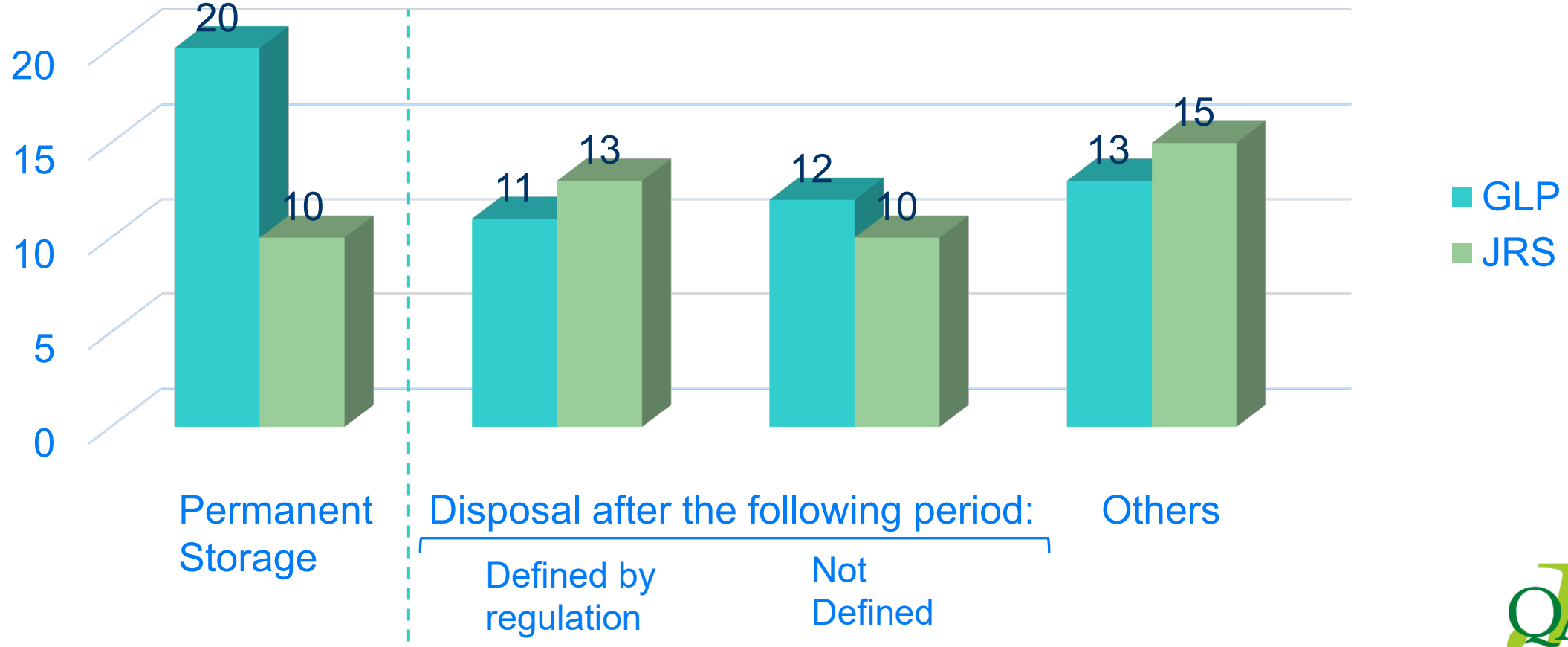
Is there a defined retention period for electronic data obtained during testing?

Test-related electronic data is rarely stored permanently and is often discarded. Criteria for disposal include time periods required by regulations, and project termination, but are often undefined.



Retention Period for Facility-Related Electronic Data

Is there a defined retention period for electronic data captured per facility?



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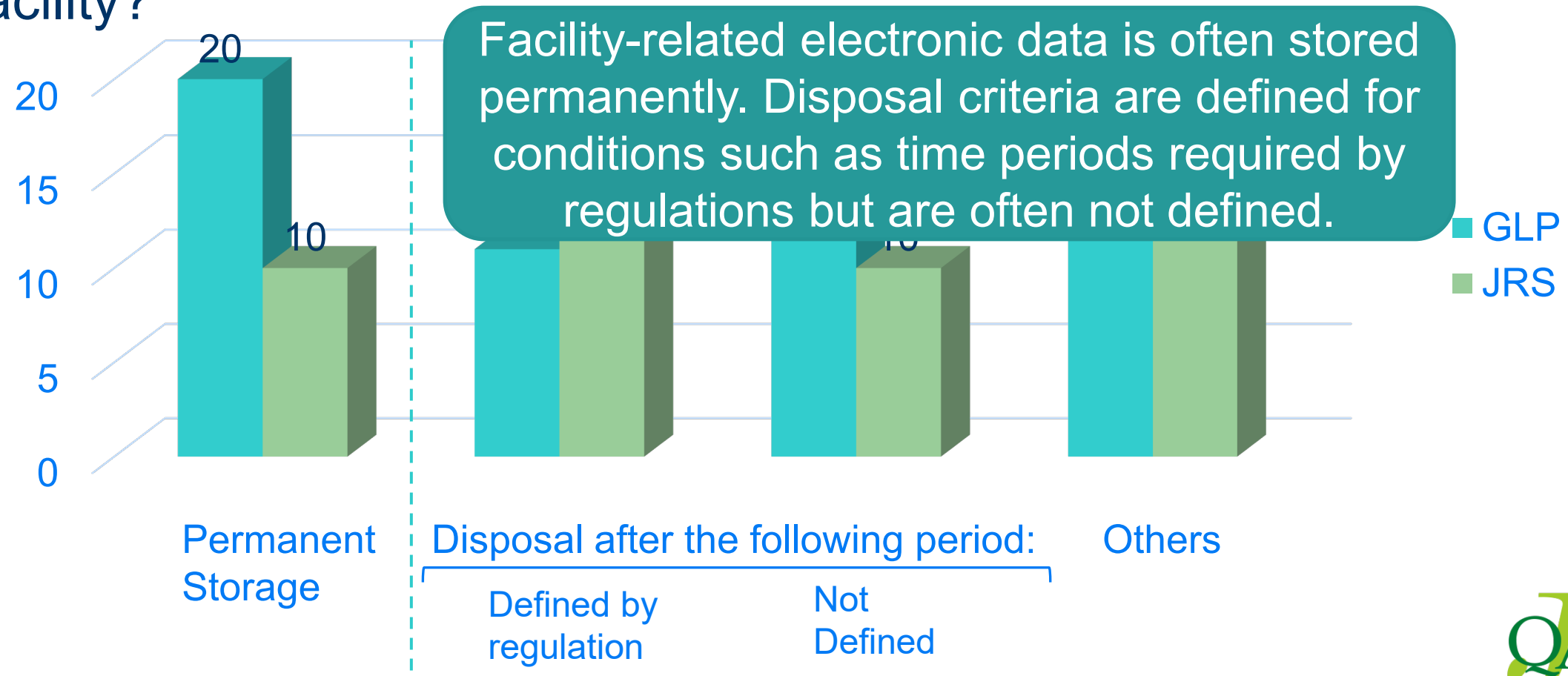
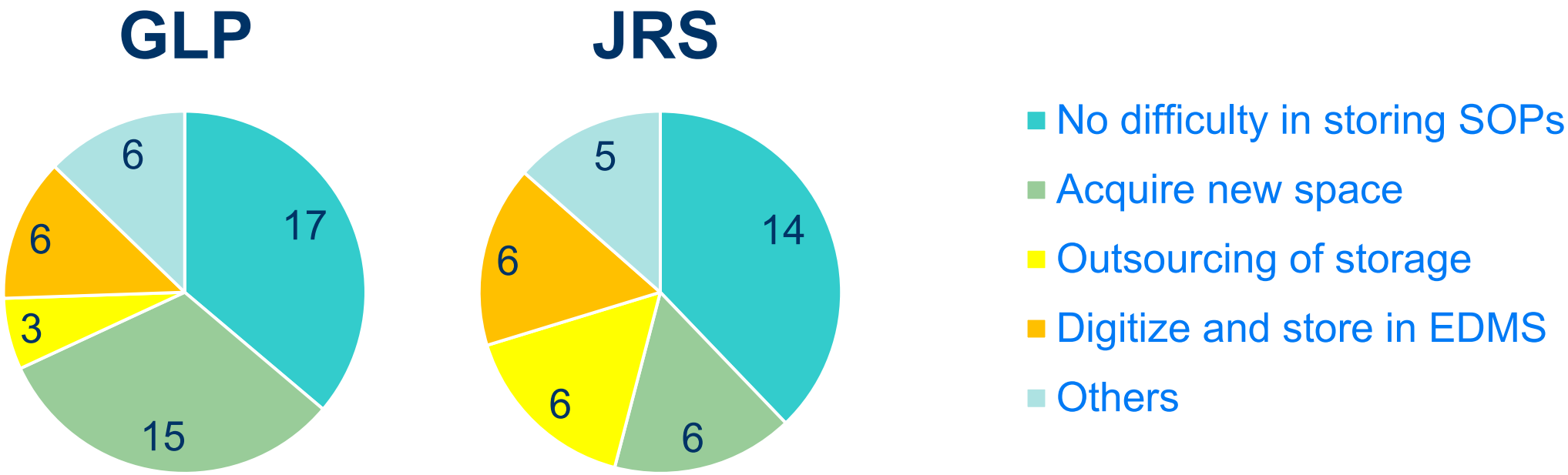


Solutions for Insufficient Storage Space for SOPs

Do you have any difficulty in securing space for storing SOPs?
If so, how does your institution handle this problem?



JRS: Japanese Reliability Standards in Ordinance for of Pharmaceutical and Medical Device Act

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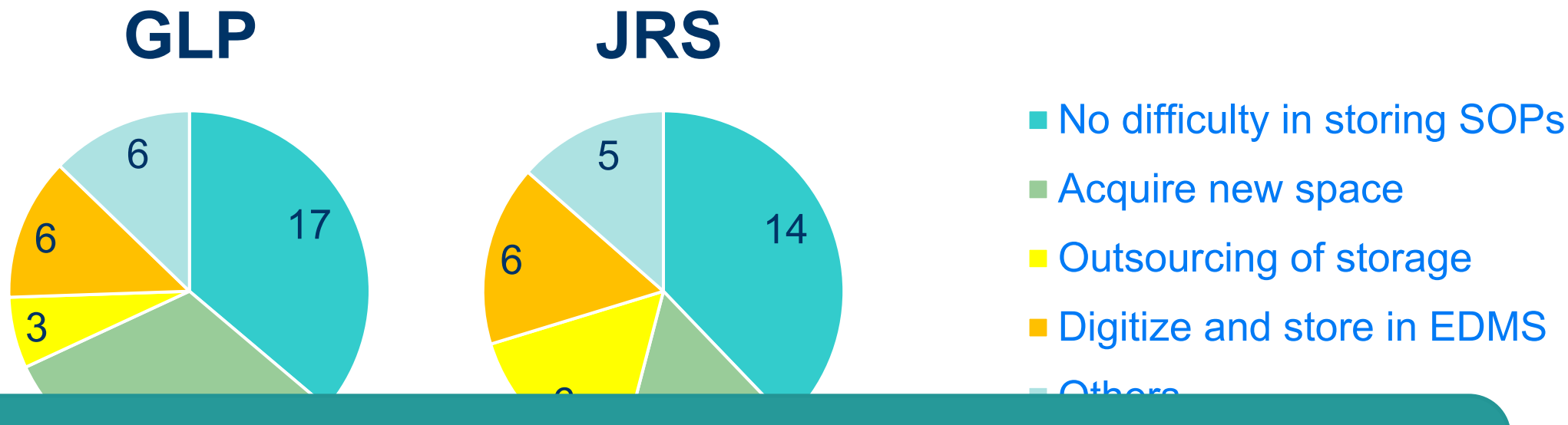
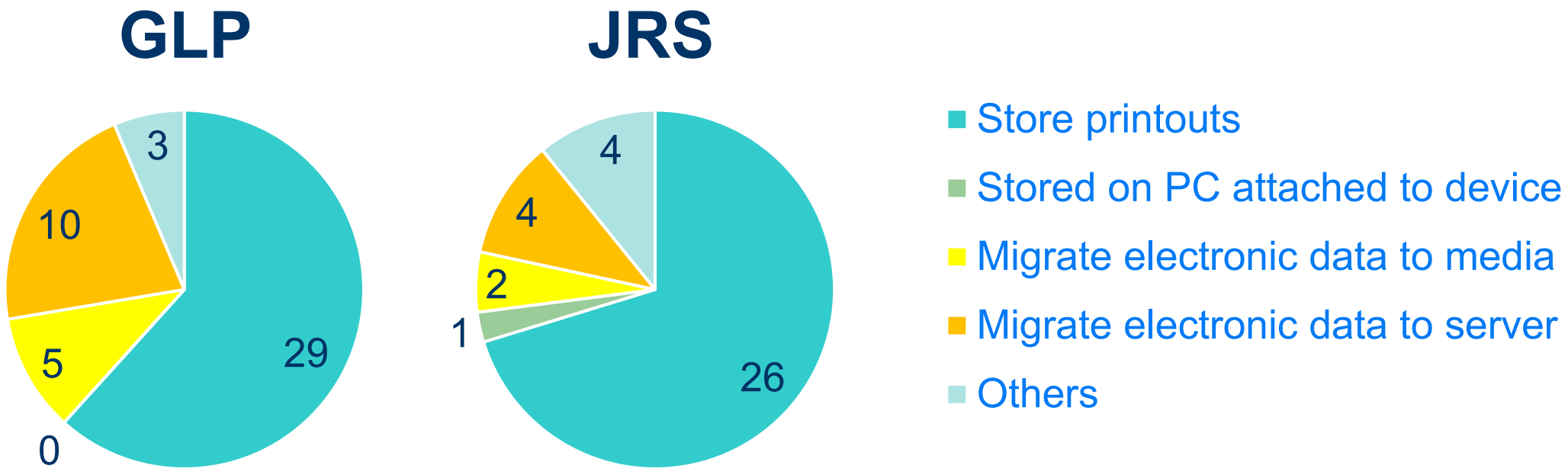


Many non-clinical laboratories in Japan have no difficulty in finding a place to store SOPs in-house. If they have difficulties with storage locations, storage is either outsourced or stored electronically.

How to Store Analytical Device Data

How is analytical device data stored? Depending on the type of analytical device, what is the main method of storing the data?



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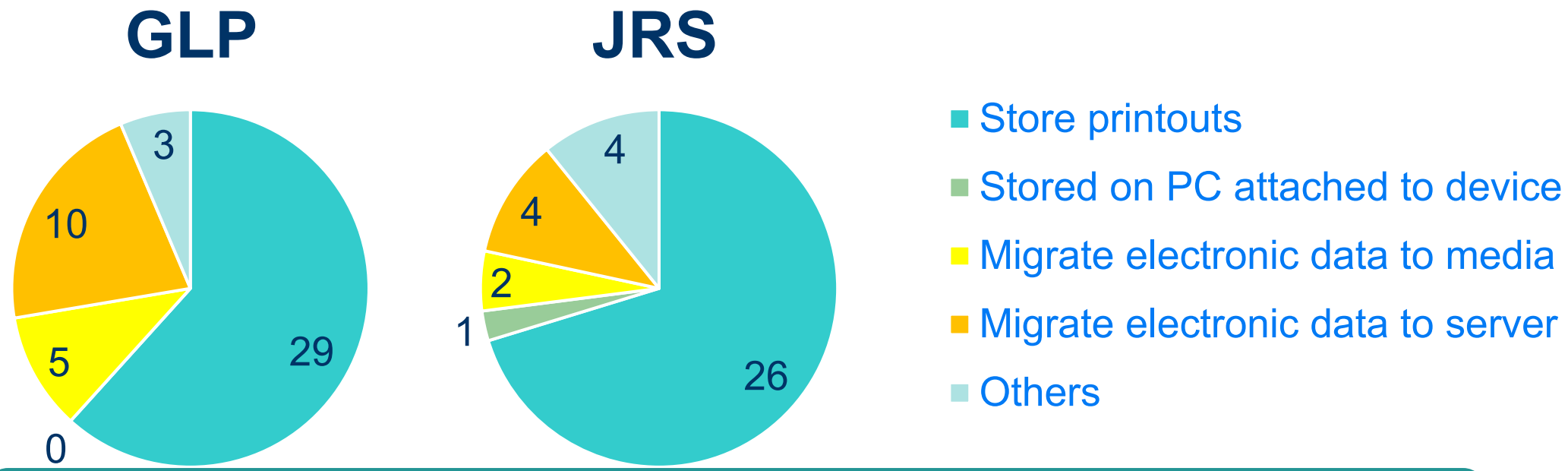
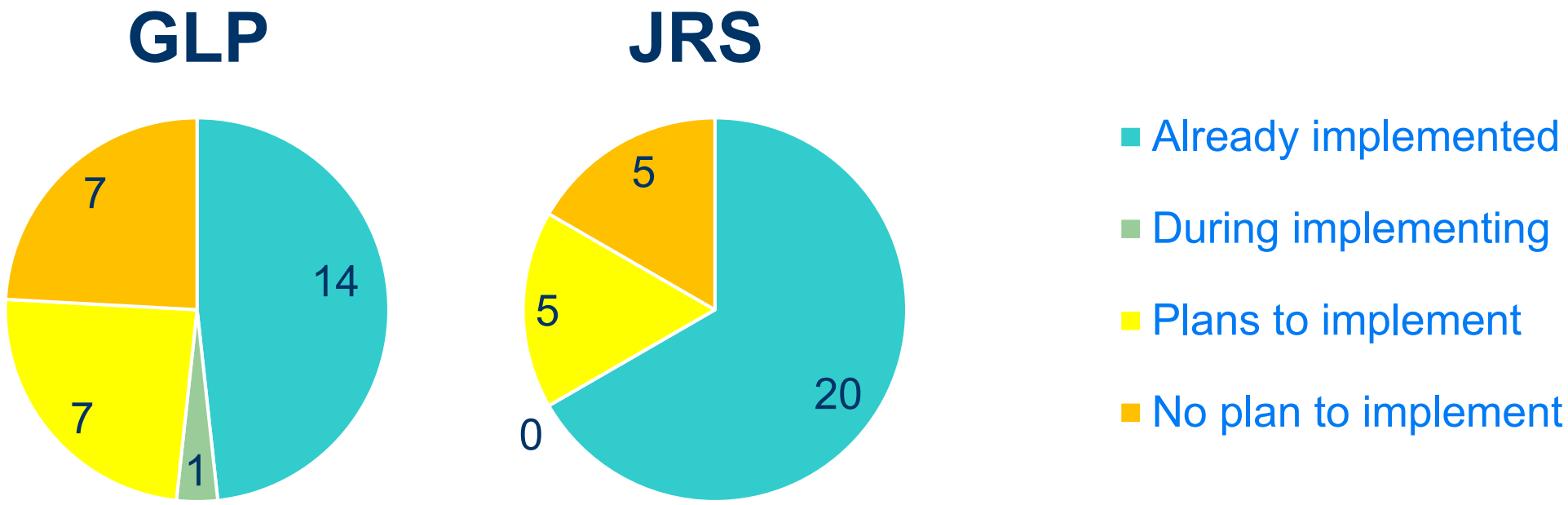


In many facilities, analytical device data is printed and stored, whereas in some facilities, the data is stored in media or on servers.

Implemented Status of Electronic Signature System

Has your facility implemented an electronic signature system for signing electronic documents related to GLP and JRS?



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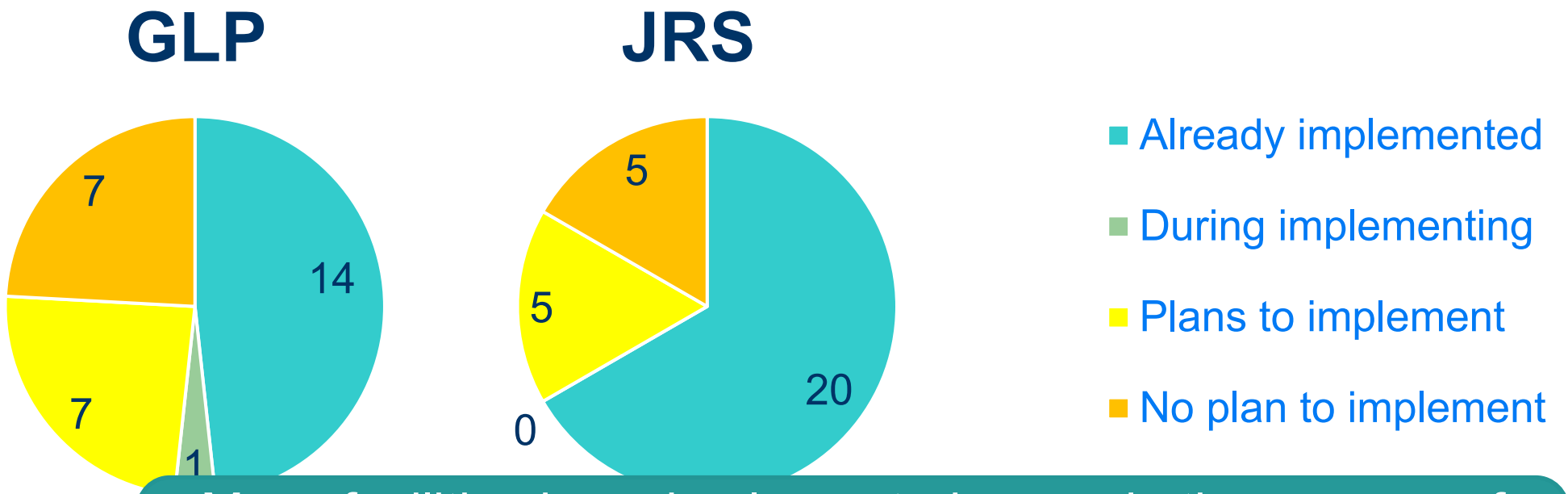
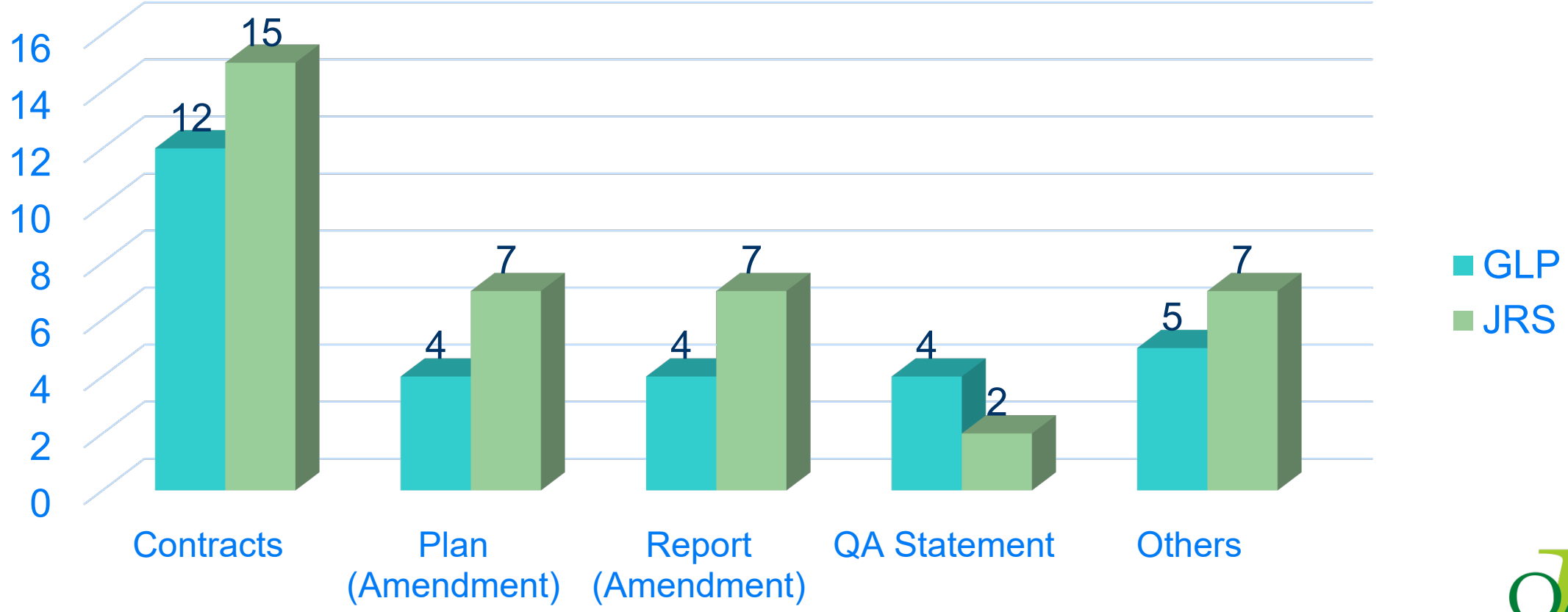


Many facilities have implemented or are in the process of implementing electronic signature systems, more so in JRS facilities than in GLP facilities.

Documents Targeted by Electronic Signature System

What documents are signed by the electronic signature system implemented in your company?



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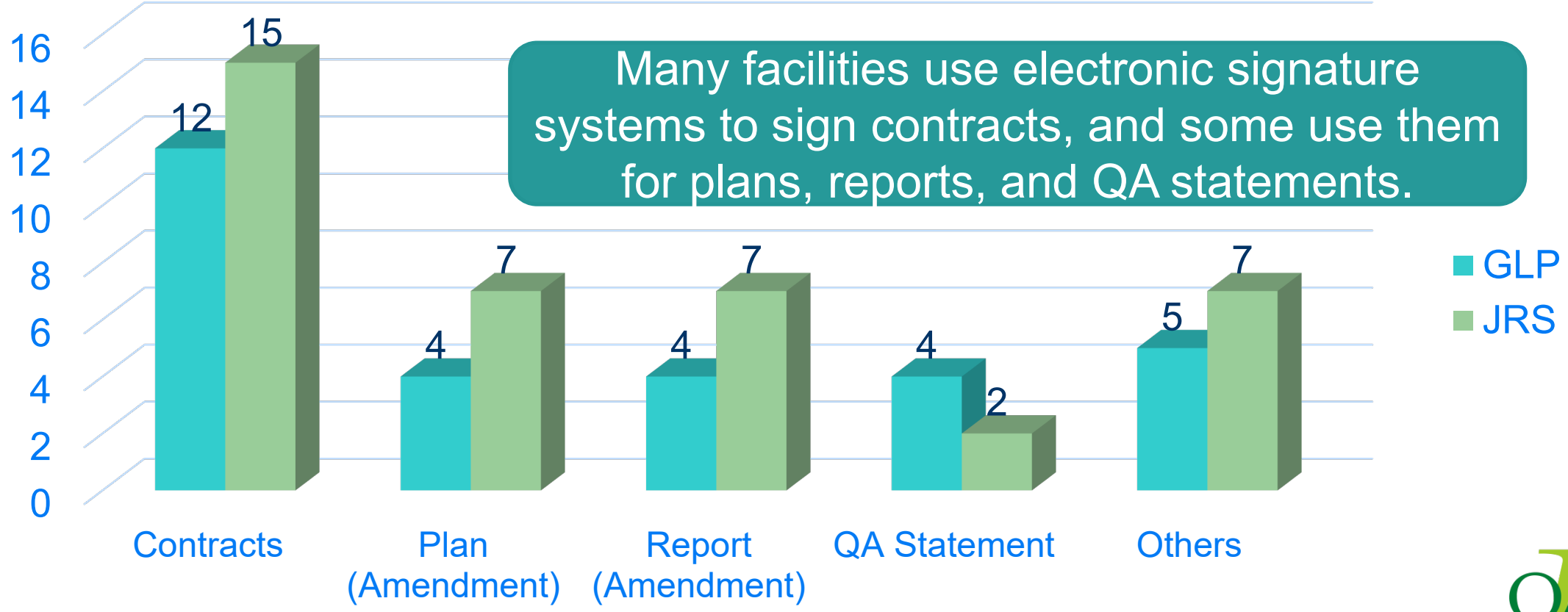


Summary of Survey

The questionnaire survey revealed the following trends in Japanese laboratories:

- One of the criteria for disposal of test and facility data is regulations.
- Most facilities have no trouble storing their original SOPs. Other facilities outsource retention or store electronic records that have been digitized.
- Analytical device data is often stored in the form of printouts.
- A lot of facilities have implemented electronic signature systems for signing contracts and other documents.
- There are no significant differences in data storage methods between GLP and JRS.

POSSIBLE MEASURES TO ADDRESS ISSUES RELATED TO DATA STORAGE

Issues to be Considered

We found some issues based on the survey shown in the previous session and inquiries from KSQA.

The issues include the following:

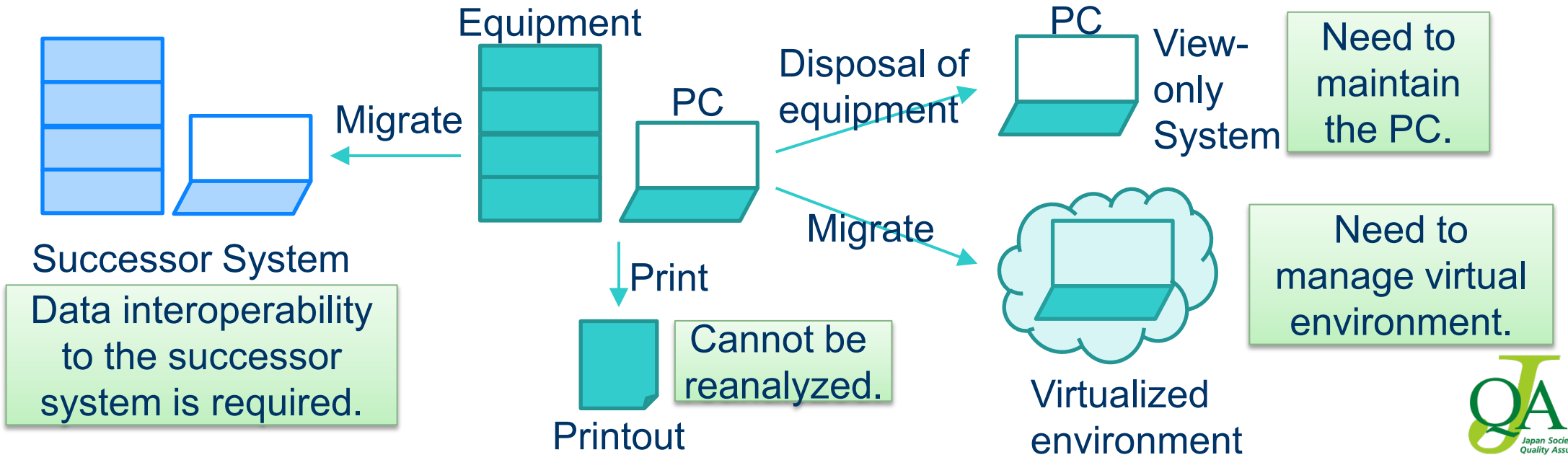
- Data Storage after Legacy System Retirement
- Transfer of Electronic Data Collected by CROs
- Maintain Data after Contracted Storage Period
- Readability Check of Data Stored on External Media
- Storage Period for GLP Data and Non-GLP Data
- Request for Amendment of Final Report to CRO
- Accuracy Check of Digitized Paper Records

We discussed solutions to these issues.

Data Storage after Legacy System Retirement

After retiring the analytical device, it is difficult to handle data that can only be analyzed by the supplied application.

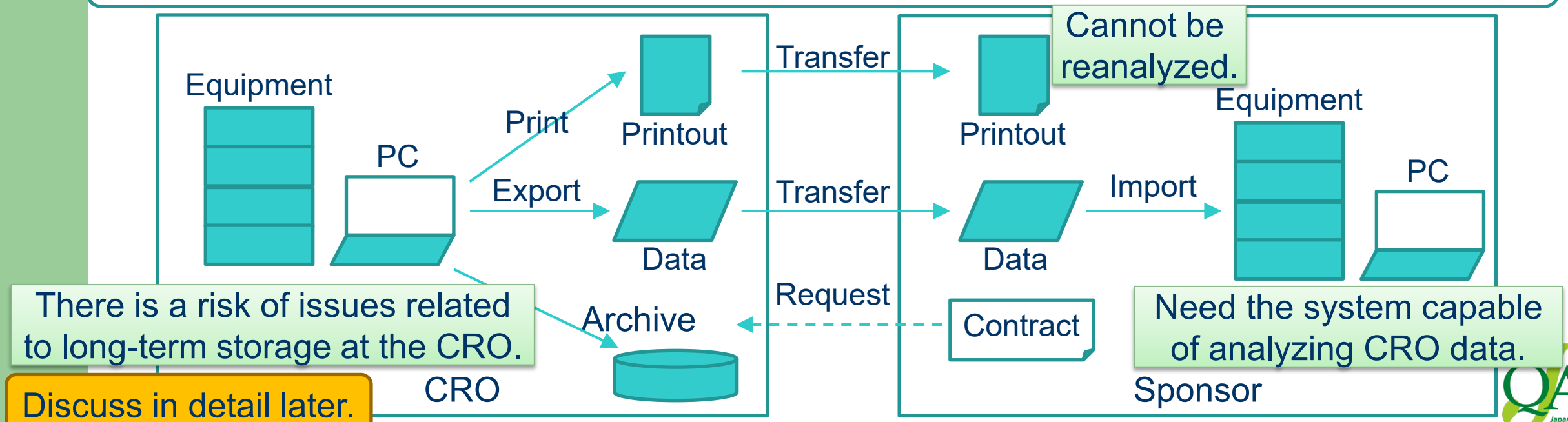
There are various measures, but each has its merits and demerits.



Transfer of Electronic Data Collected by CROs

When archiving electronic data obtained at CROs for long periods, there are difficulties in handling that electronic data.

There are various measures, but each has its merits and demerits.



Discuss in detail later.

Maintain Data after Contracted Storage Period

How should CROs handle outsourced study materials after the end of the pre-contracted retention period?

The GLP Ordinance provides no answer to this issue.

Before outsourcing

The contract should provide for the handling of materials after the retention period, including disposal, return, and continued retention.

After contracted storage period

Retiring the contracting staff	The contact person at the sponsor's company may be an alternative solution.
Bankruptcy of a sponsor	The company that succeeds the sponsor's business may be an alternative solution.

Readability Check of Data Stored on External Media

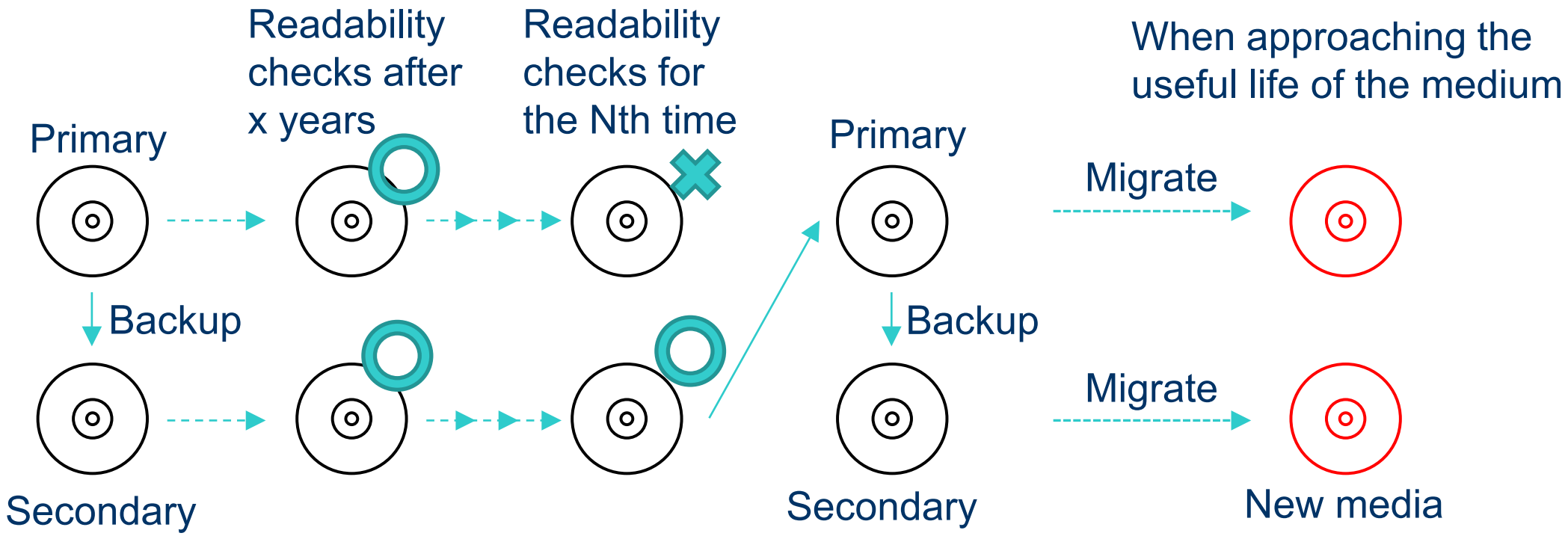
When electronic data is stored on external media such as CDs, or DVDs, there is a risk that the data may become unreadable due to media damage or other problems.

The following steps should be taken:

1. Data should be stored on multiple media to be prepared for media defects.
2. Perform readability checks on a regular basis.
   If a defect is found, copy the data in the remaining media to new media.
3. Migrate data to new media before the media's useful life is exceeded.

The next slide will represent it schematically.

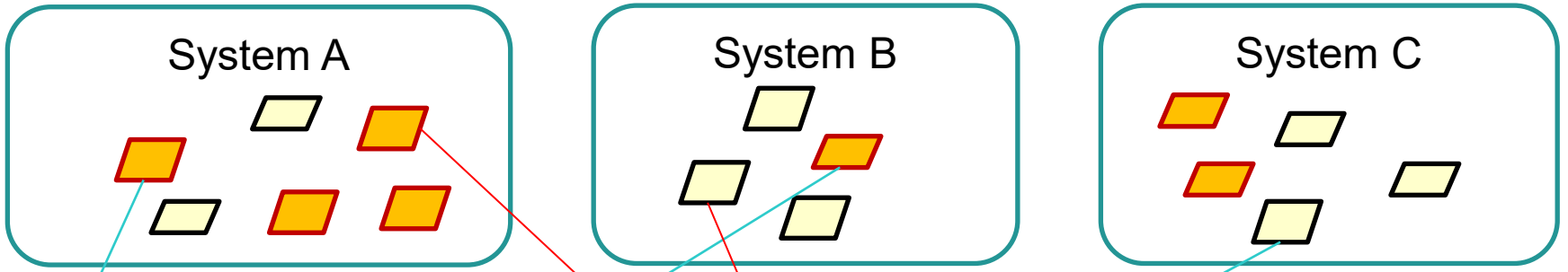
Readability Check of Data Stored on External Media



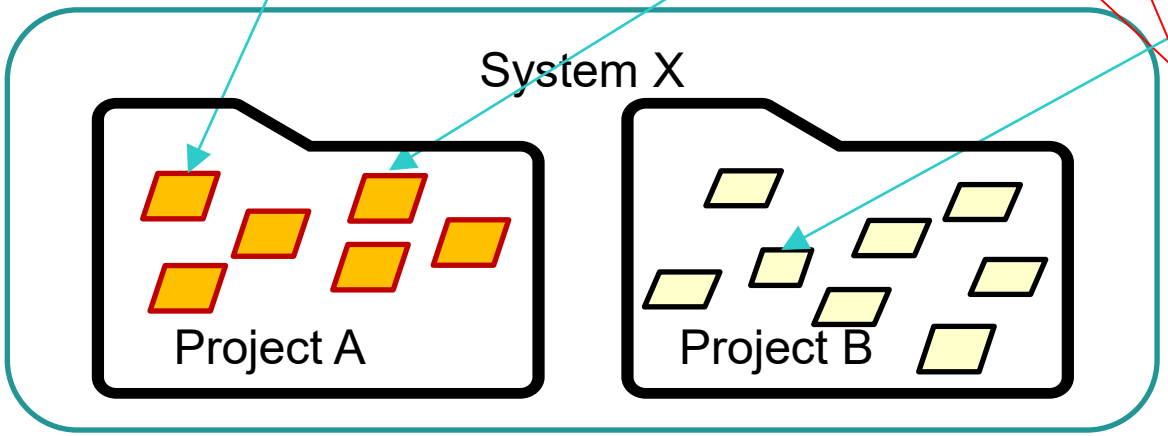
As shown in this figure, there is a lot of work involved in maintaining data in external media. It is recommended that it be stored on a server or a cloud system instead of on external media.

Trouble due to Decentralized Storage of Data

It is difficult to find data stored in multiple and dispersed locations.



Solution 1: Centralized Data



Solution 2: Creating List

Project	File Name	Location
A	Experiment Record	System A
A	HPLC Data	System B
B	Experiment Record	System A

Storage Period for Facility Data and Test Data

Is the retention period for facility data the same as for test data in Japan? If different, how is it set?

A survey conducted in 2015* found the following:

Test data is required to be stored until 5 years after the approval date or completion of the reexamination.

Facility data hesitates to be discarded and is often stored permanently.

This is due to the difficulty in determining whether to dispose of the data.

* Refer to the JSQA deliverable No.15L04.

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Facil

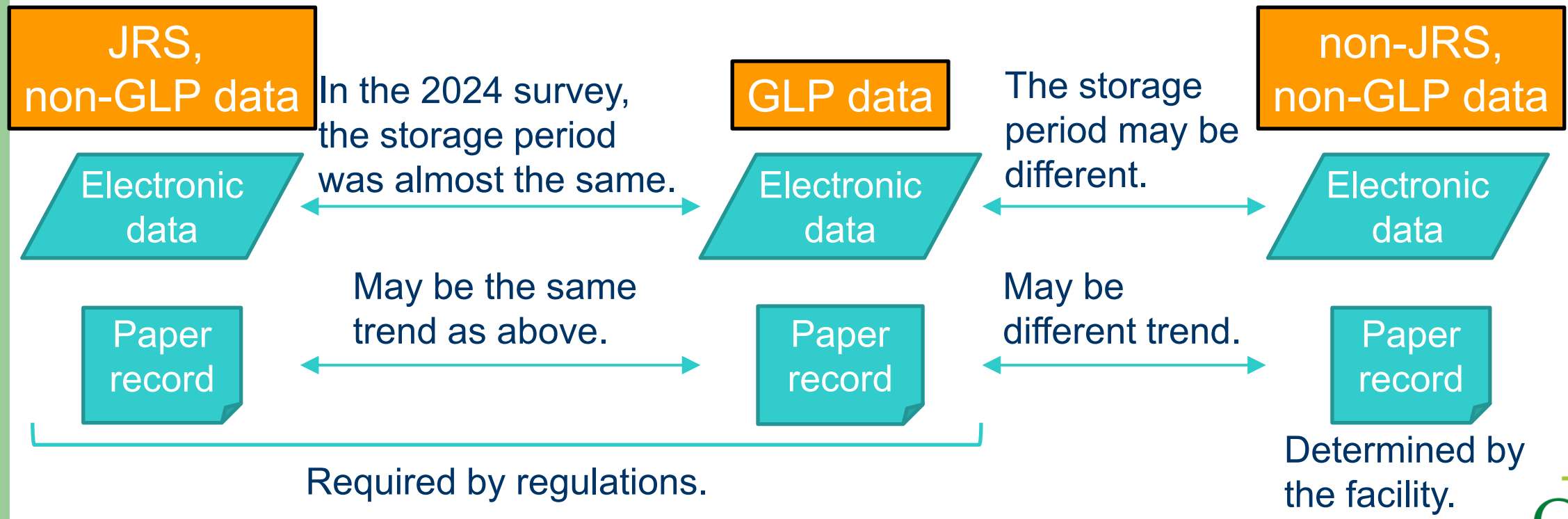
This

This differs from the results of the 2024 survey.
Particularly, in the 2024 survey, some facilities discarded facility data.
This difference may be due to the 2024 survey's focus on electronic data, or it may be due to changes in company policy over time.

* Refe

Storage Period for GLP Data and Non-GLP Data

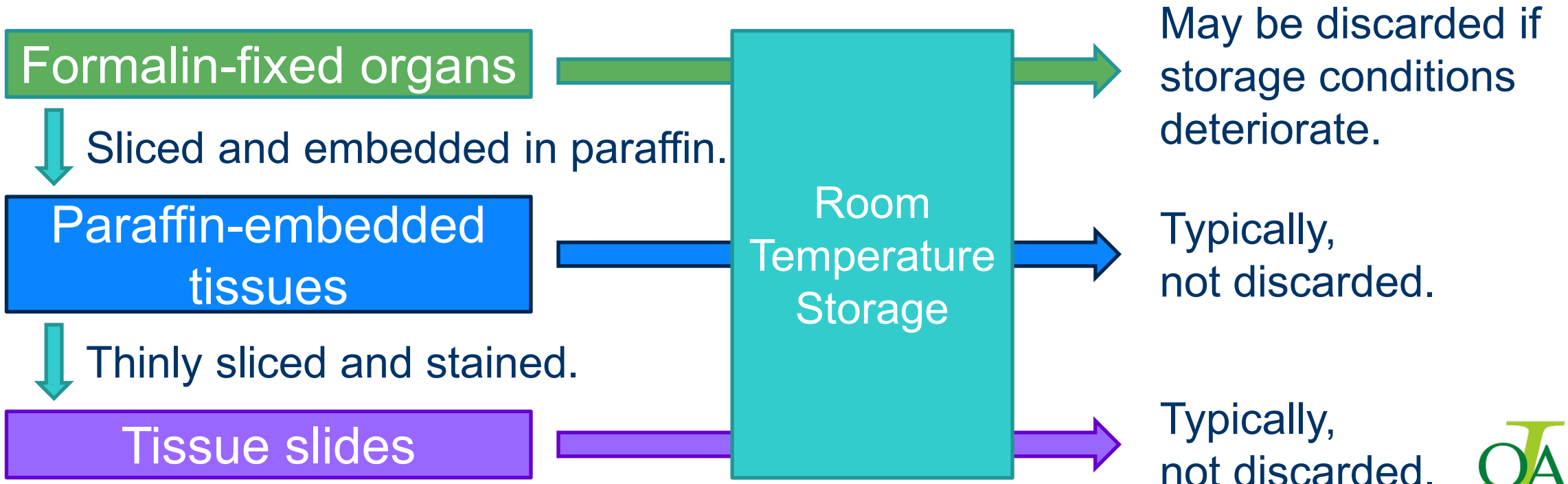
Is there any difference in storage period between GLP and non-GLP data in Japan?



* JRS: Japanese Reliability Standards in Ordinance for of Pharmaceutical and Medical Device Act

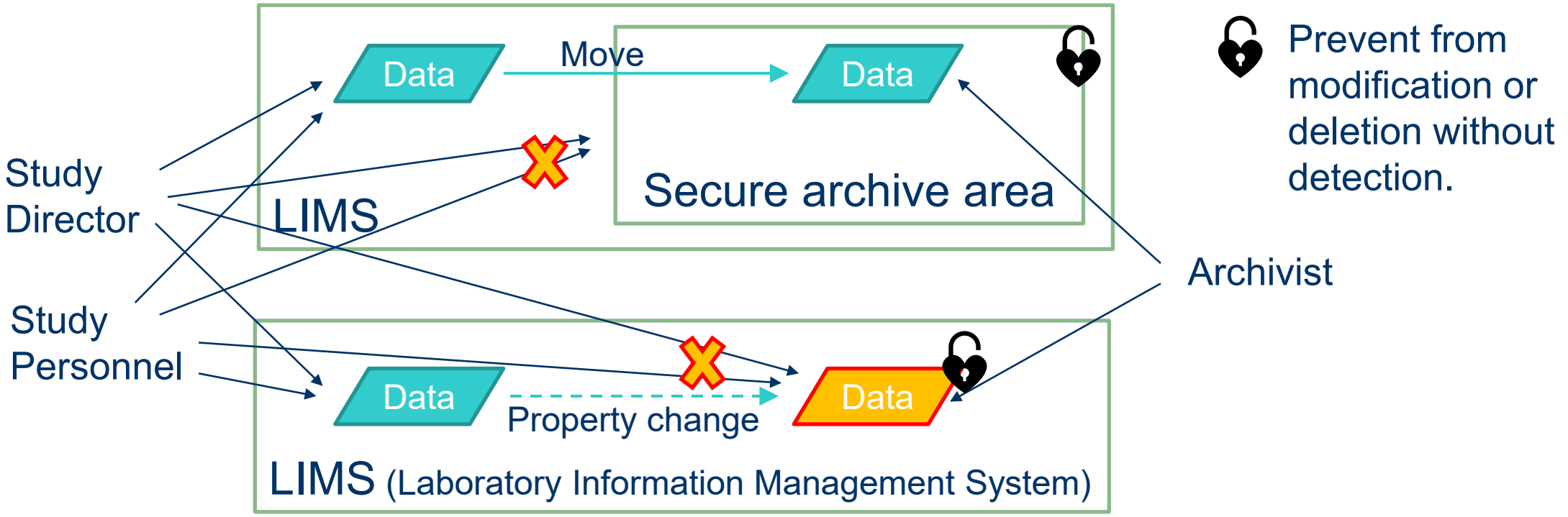
Storage Period of Formalin-Fixed Organs

How to determine the general storage period for formalin-fixed organs, paraffin-embedded tissues, and tissue slides, and how they should be stored.



How to Archive Test Data in LIMS

How should LIMS data be archived at GLP facilities?



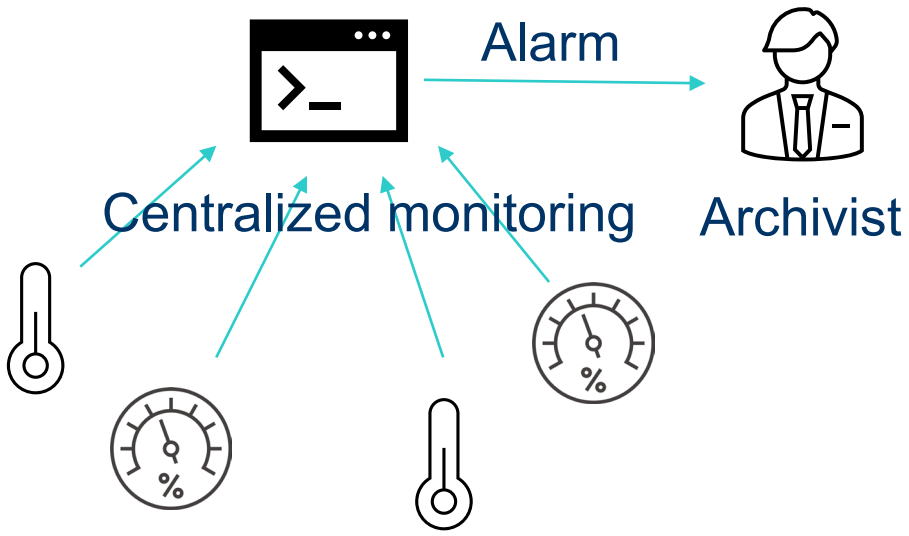
Prevent from modification or deletion without detection.

Refer to “8.3 Defined Archive Area on a Computerised System” in OECD GLP AD No.15 “Establishment and Control of Archives that Operate in Compliance with the Principles of GLP”

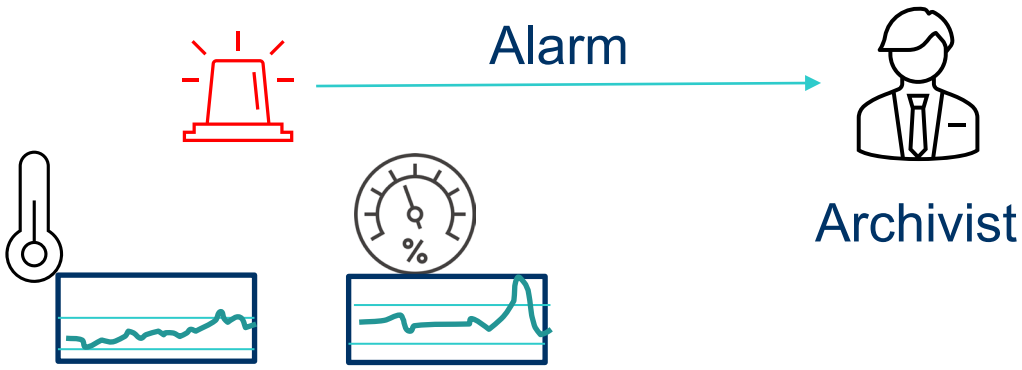
Temperature/Humidity Control in Archival Facilities

How is the temperature and humidity controlled in Japanese laboratories for archiving test-related materials? Are they recorded manually? Or is it centrally monitored?

Many facilities



Some facilities



Recorded in charts and checked periodically (e.g., weekly, monthly).

Electronic Data Storage Environment

What should be the storage environment for electronic data?

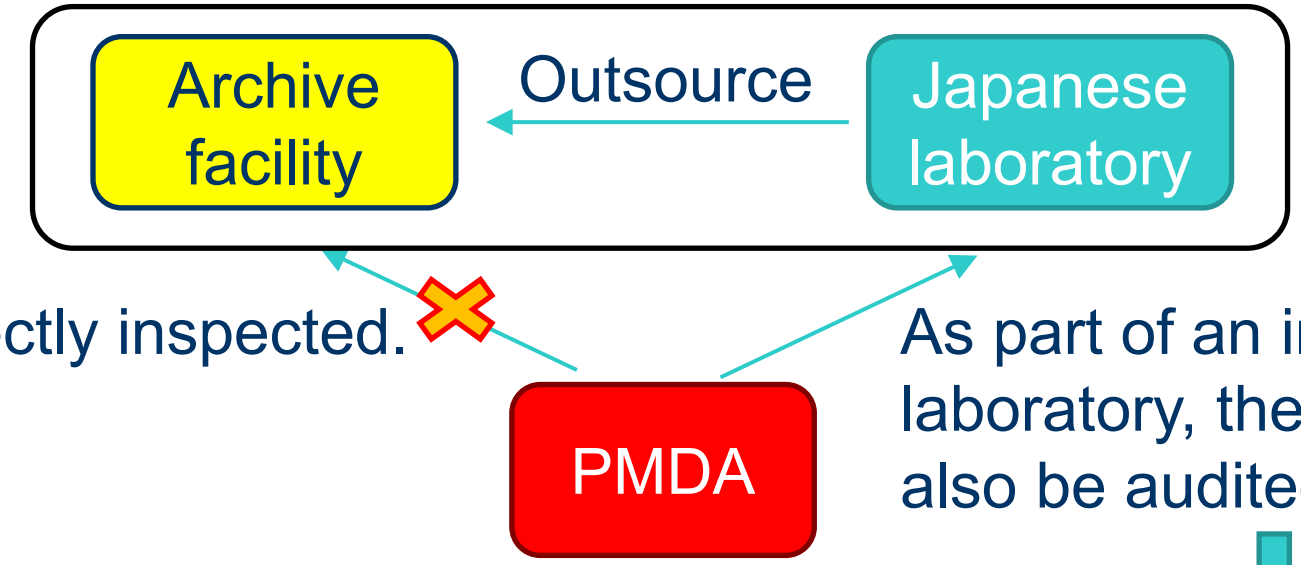
There are no recommended storage conditions in GLP ordinances.

However, the storage environment for electronic data requires stricter management than paper or tissue materials.

- More limited range of temperatures and humidity
- Low dust environment
- The storage structure is fireproof, lockable, free from sunlight, and free from condensation.
- No harmful gases

Outsourcing the Archiving of Materials

Can archiving of materials be outsourced in Japan?
Can outsourced facilities be qualified as GLP facilities?

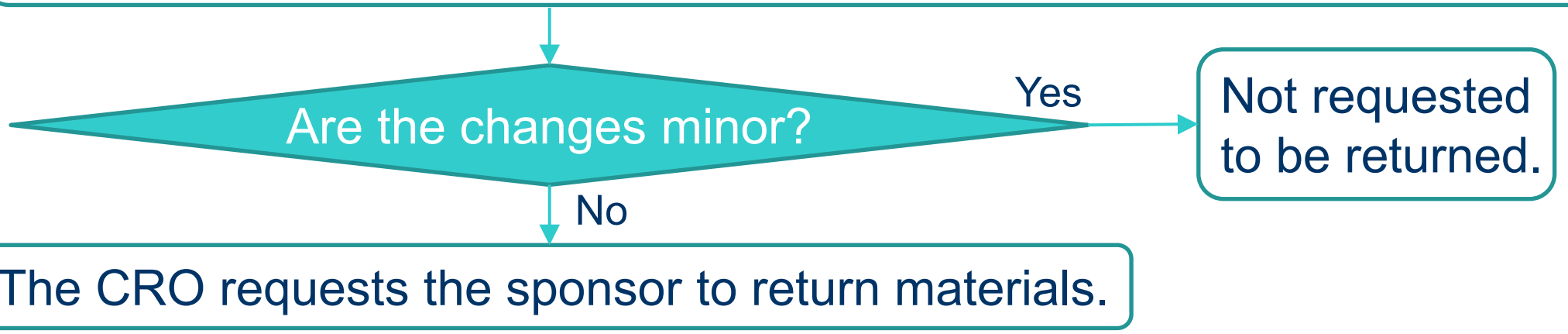


It is unlikely that the archive facility will be the subject of subsequent inspection after the above inspections.

Request for Amendment of Final Report to CRO

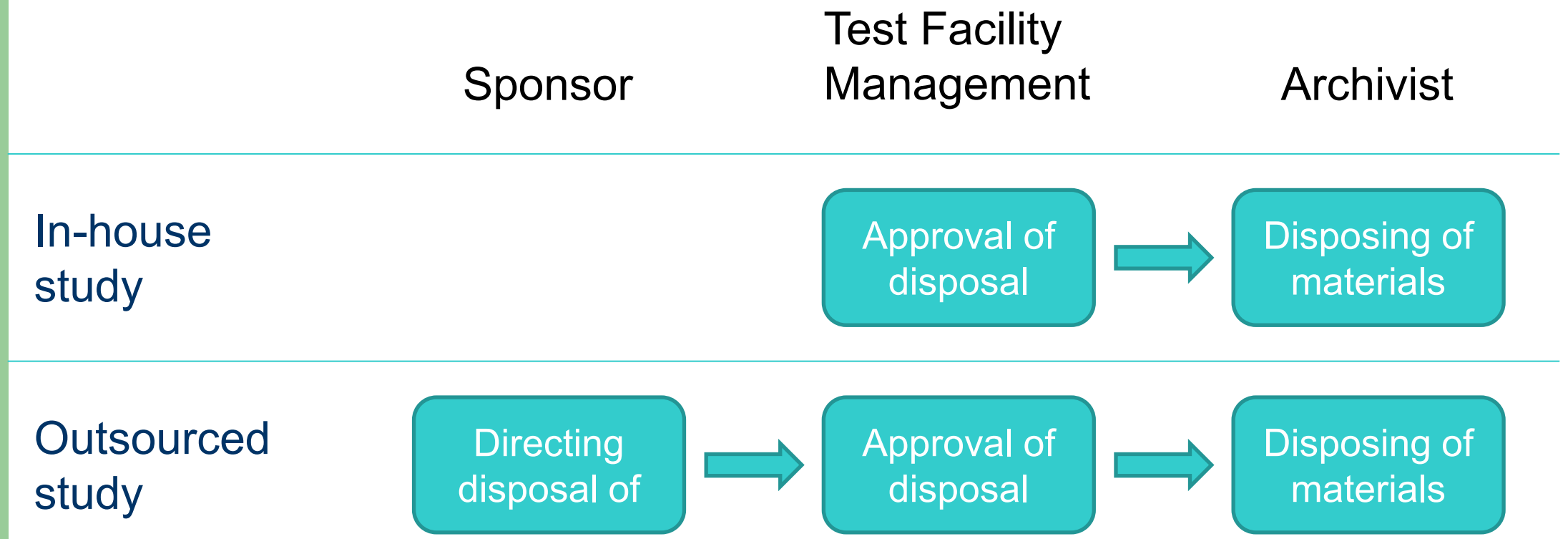
After returning study data to the sponsor, what should the CRO do if the sponsor requests an amendment to the final report for that study?

The sponsor should contact the CRO because the study director needs to prepare the amendment to the final report.



Disposal Procedure after Storage Period

How are they disposed of after the storage period has expired?



Accuracy Check of Digitized Paper Records

When paper records are digitized and saved in PDF or other formats, it is necessary to ensure that the digitized records accurately reflect the contents of the paper records.

The following processes need to be properly executed.

Preparation → Scanning → Identification → Checking Quality → Amendment → Storage

The above approach will be described in the next session.

How to Catalog when Digitizing Paper Records

What level of cataloging should Japanese laboratories use when digitizing paper records?

When

For in-house studies, a list of digitized records needs to be prepared prior to transfer to the archive facility.

For outsourced studies, a list of digitized records needs to be prepared prior to handover of materials to the sponsor.

How

Manually or Created by electronic laboratory notebooks.

Detailed methods will be described in the next session.

Summary

- There are some issues with electronic data, such as the retirement of measuring equipment, returning data to CROs, and long-term storage using electronic media.
  - These issues should be addressed appropriately using the characteristics of electronic data and information technology.
- For other records, various issues have been identified, such as the handling of materials when the entrusted preservation period has expired, differences in the preservation periods for facility data and test data.
  - These issues should be addressed in accordance with regulations, science, and the policies of each facility.

FURTHER CONSIDERATIONS ON STORAGE OF DIGITIZED RECORDS

Further Considerations on Digitized Records

As explained on the previous slide, there are several challenges in digitizing paper records.

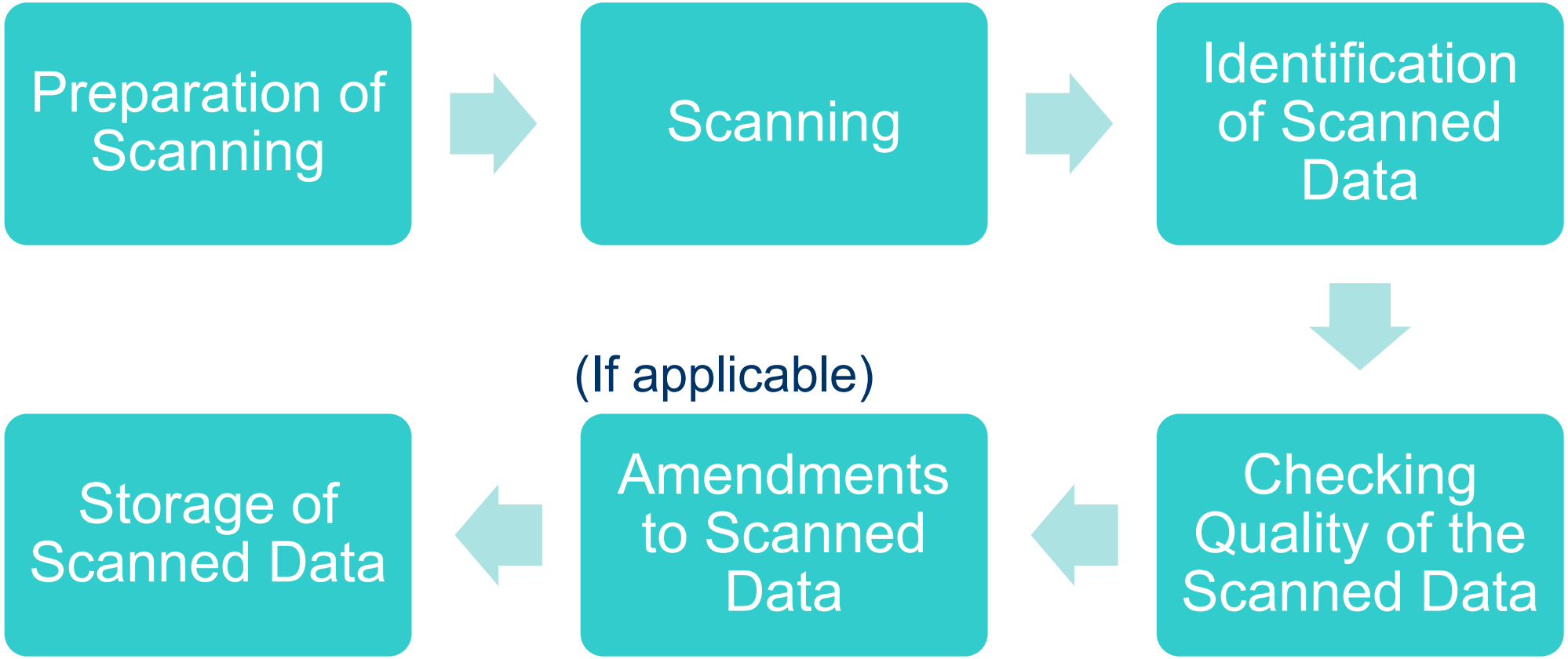
We have discussed the appropriate process for digitizing records.

I'll provide an overview of our discussions.

Background on Discussions

- Recently, pharmaceutical companies have begun requiring CROs and academia contracted for non-clinical studies to digitize study-related materials, but some facilities lack the equipment and procedures for this.
- In July 2023, the PMDA, Japan's regulatory agency, notified us that it will remotely conduct investigations into non-clinical trials (including trials conducted outside of Japan) associated with NDA/BLA. For this purpose, digitization of materials is required.
- Under these circumstances, we have considered how to provide guidance to CROs and academia on the digitization of materials.

Workflow for Digitizing Records



Preparation of Scanning

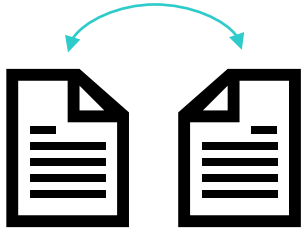
Check for and fix any problems that may adversely affect scanning.

Stapled paper

Folds

Wrinkles

Sticky notes



Double-sided printing

Scanning

Dark fluorescent markers

Scanning

Light-colored text

Confirm the pages to be scanned for later quality checks.

Scanning

Paper records are preferably scanned as soon as possible after the experiment is completed.

This is recommended to reduce opportunities and temptations for falsification/fabrication.

It is recommended that scanning create image files without text.

Optical character recognition is not recommended due to the risk of misidentification.

Scanning (Continued)

The following scanning conditions are recommended.

File format	Resolution	Color mode
PDF or TIFF	> 200 dpi	Black and white in principle, color as needed.

The scanning setting should be adjusted, as needed.

Small text or graphics → May need to increase resolution.

Dark fluorescent markers or light-colored text → May need to adjust density setting.

Double-sided paper → Need to scan both sides.

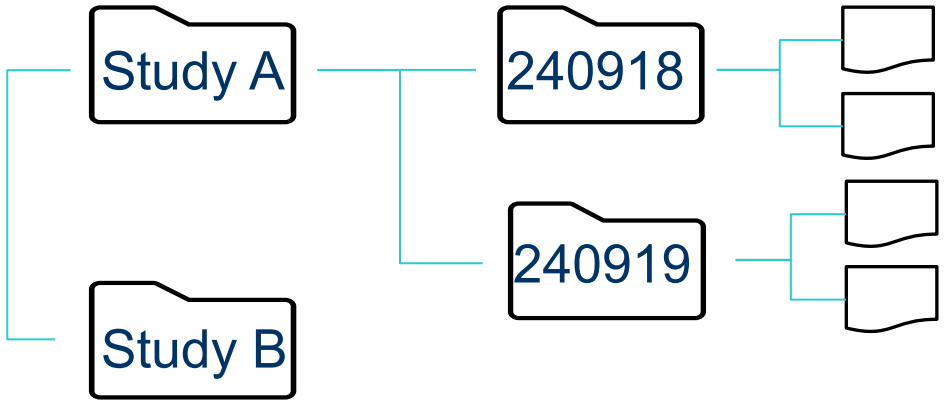
Identification of Scanned Data

The scanned file needs to be identified.
There are two possible methods for identifying the file.

File name may contain background information on the data.

e.g., Study A_20240918_Preparation record for the dosing solution.pdf
Study number　Date　Record type

The folder structure may indicate background information on the data.



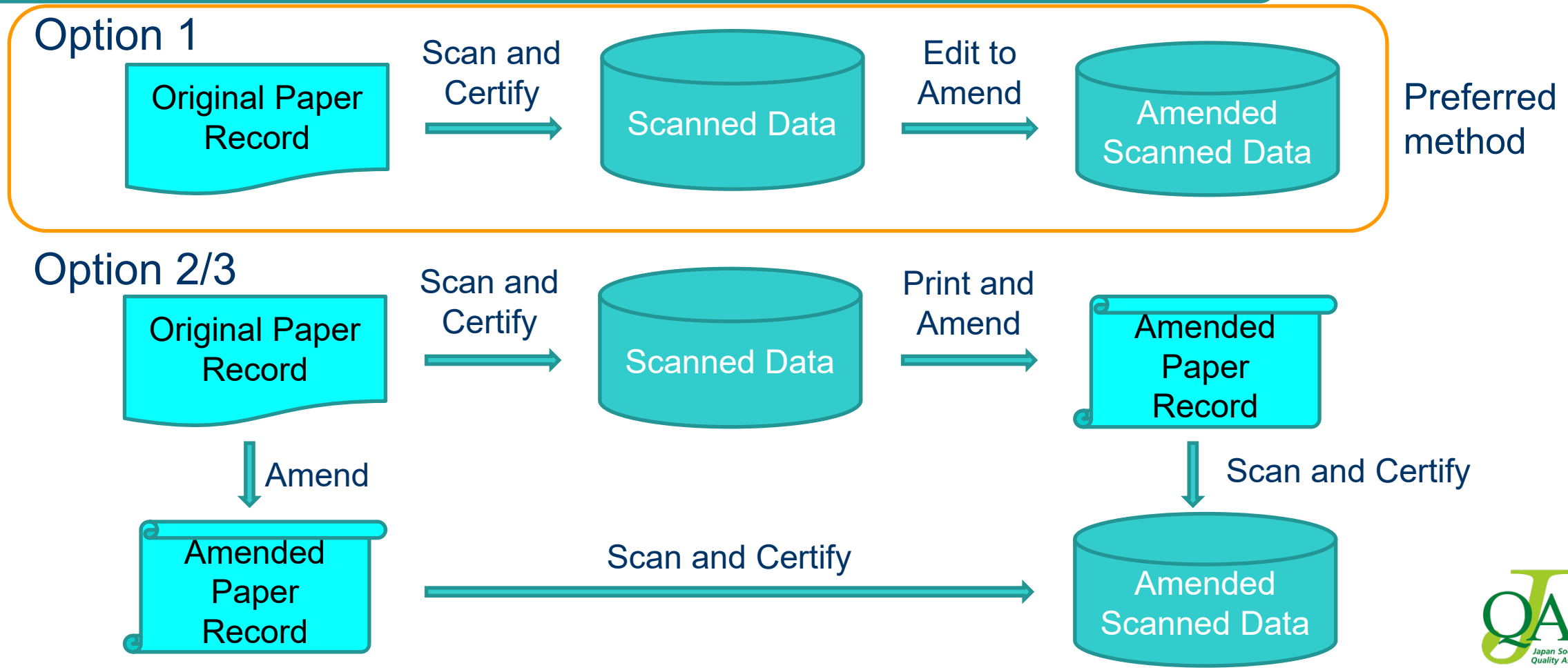
Checking the Quality of Scanned Data

Why?	Confirm equivalence of scanned data and the original paper records.
Who?	While the primary responsibility rests with the person who recorded or scanned it, third-party review can be helpful.
What?	Confirm equivalence based on the following criteria, rescan and reconfirm if there is a problem.

- The scanned data must be legible, including color that has meaning.
- It should be checked whether all the pages to be scanned have been scanned. This includes double-sided printed paper.
- The contents can be predicted from the file name and folder name.

Amendments to Scanned Data

Scanned data can be amended in following three ways:

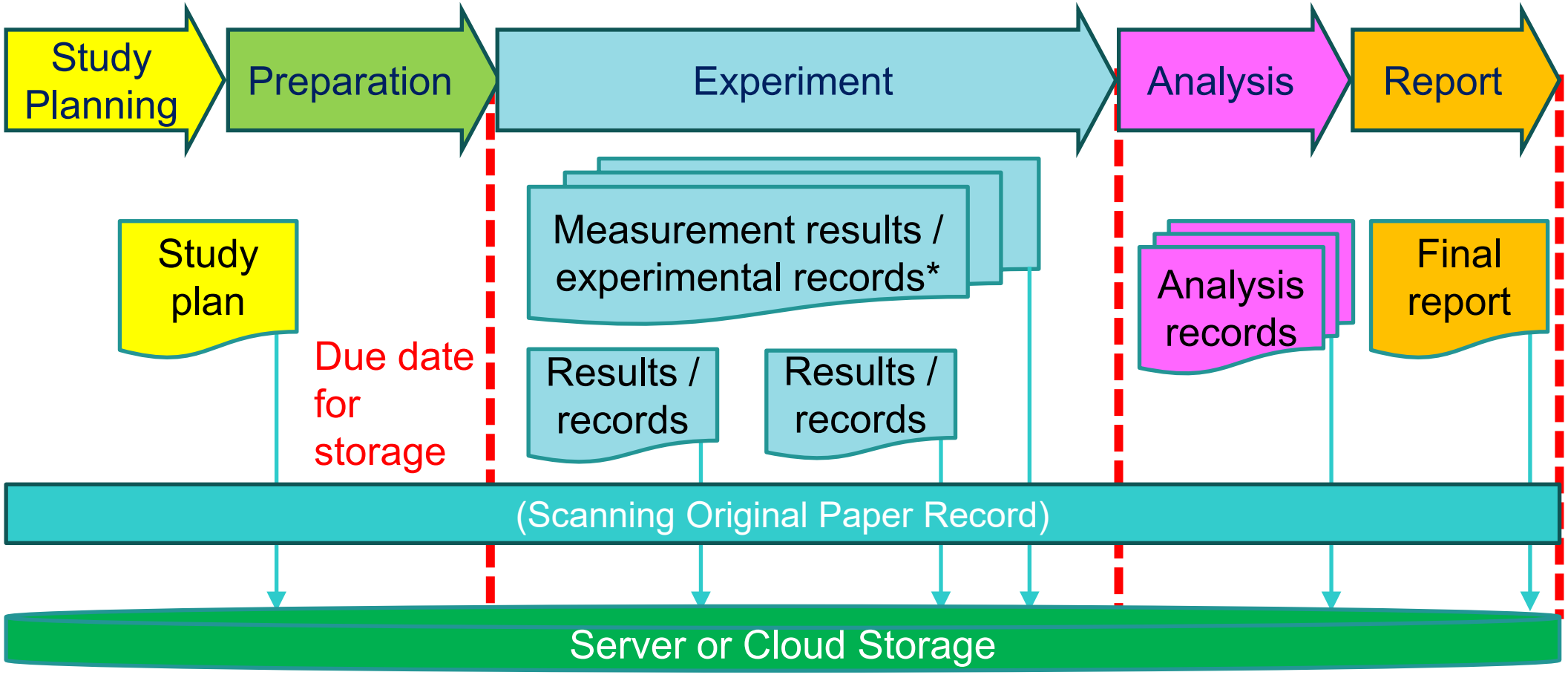


Storage of Scanned Data

Considerations for storage of scanned data include:

- When should the data be saved?
- Where should the data be saved?
- Why should data lists be created?
- What should be included on the list?

Storage Timing of Scanned Data



*: To eliminate the opportunity for tampering/fabrication and to reduce the risk of accidental deletion of files, it is recommended that the files are saved promptly on the experiment date.

Storage Location of Scanned Data

The following requirements are recommended for the storage location of scanned data.

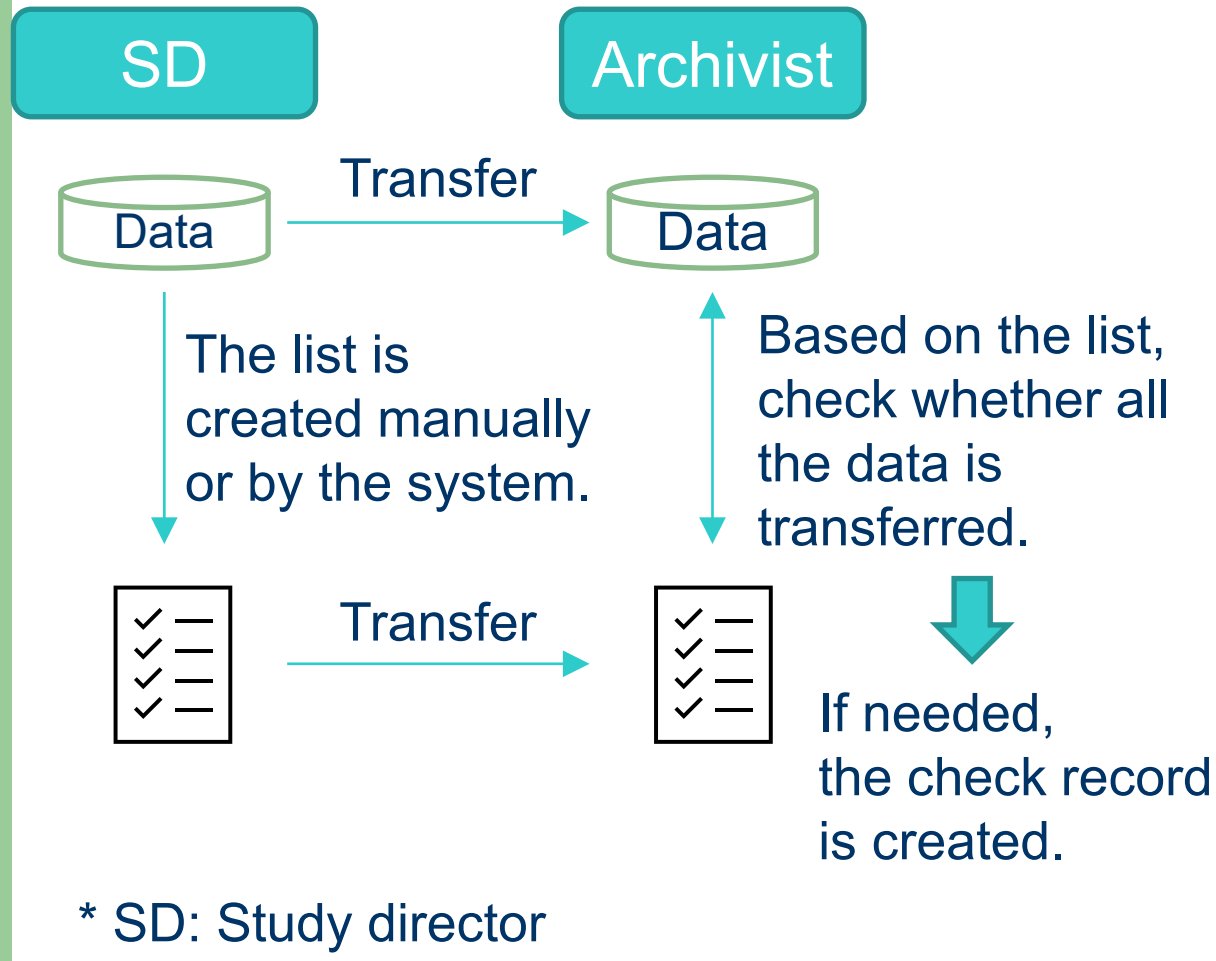
Computerized system should have the following function and/or procedures.

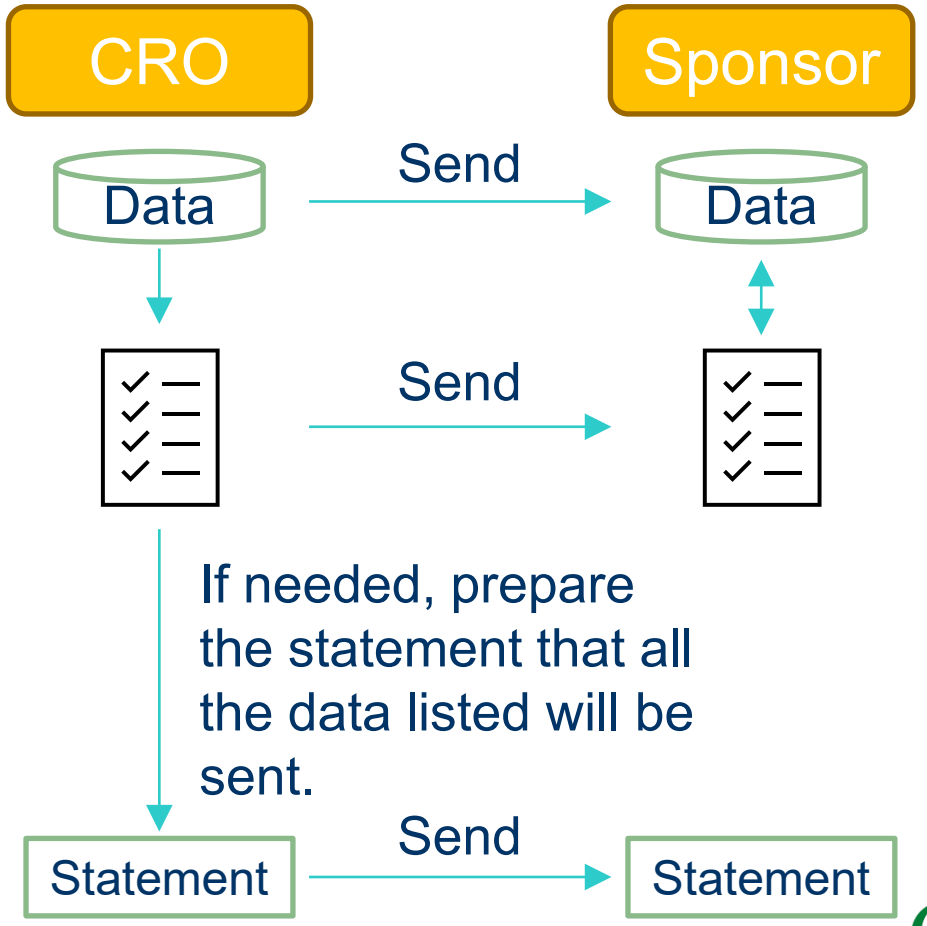
- Account Management
- Data Backup
- Audit Trail or Alternative Procedure

When using cloud services for data storage, the provider should be evaluated.

If outsourcing to a facility that does not meet the above conditions, it is recommended to promptly transfer the scanned data to an appropriate storage provided by the sponsor.

Utilizing Lists of Scanned Data





* SD: Study director

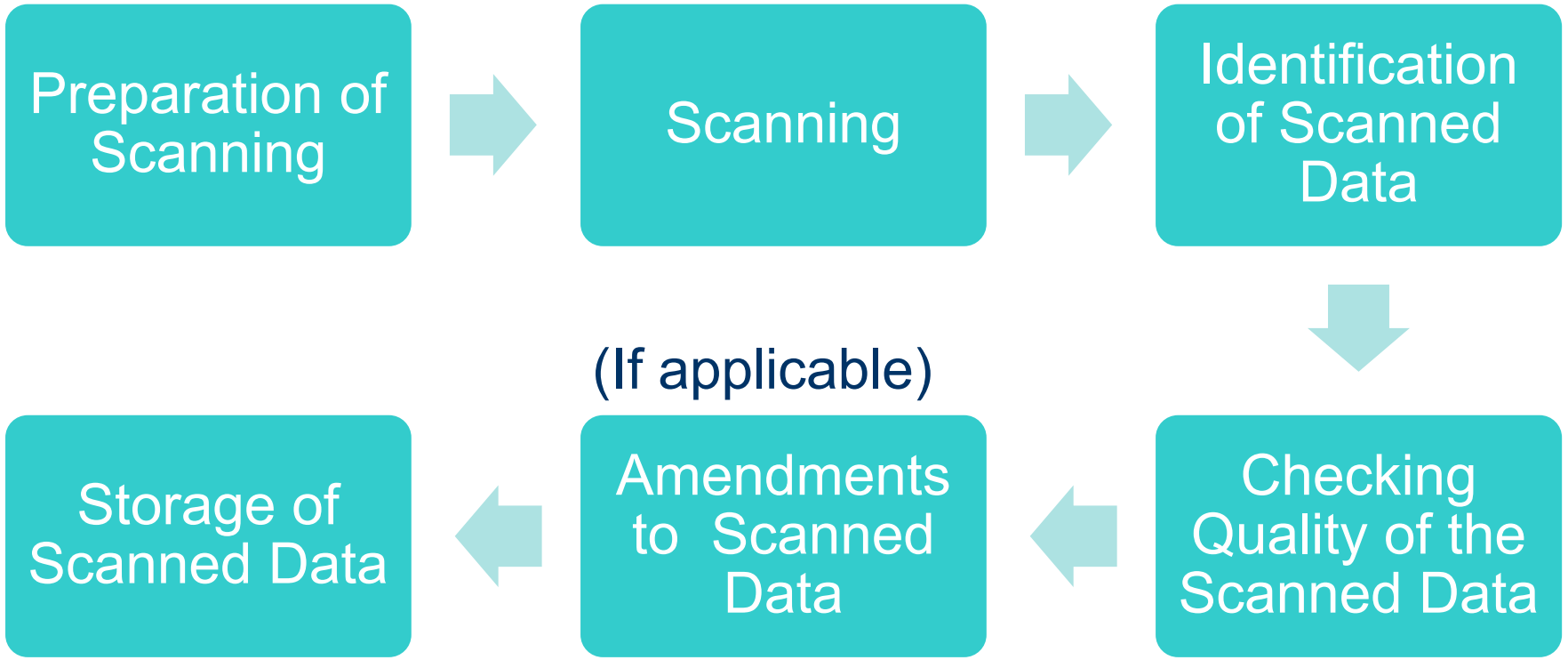
List Items in the Scanned Data

List items may include, but are not limited to:

- File name
- Storage location — It may include the name of the storage system and the folder path.
- File type — Including text, graphic and pdf.
- The last update date and time

Summary

To ensure that the content of the original paper records is properly reflected in the scanned data, all processes related to scanning should be carried out appropriately.



CONCLUSIONS

Conclusions

- In Japan, regulations have been established for non-clinical studies and electronic data.
- A questionnaire survey of non-clinical test facilities in Japan has clarified the current situation regarding electronic data.
- We considered measures to address issues related to data storage at non-clinical test facilities, including GLP facilities.
- We considered measures to ensure that paper records are properly digitized.
- We are confident that this presentation will be useful for your future activities.

Acknowledgements

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Thank you for your attention.
잘 들어 주셔서 감사합니다