Data Integrity: Current Management Status by Japanese Regulatory Authorities

Japan Society of Quality Assurance（JSQA）
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Agenda

- **Trends in Data Integrity (DI) regulations in Japan**
  - Requirements from the Pharmaceuticals and Medical Devices Agency (PMDA)
  - Responses by GLP test facilities
- **JSQA initiatives**
  - Establishment of discussion forums with PMDA
  - DI education seminars
  - Studies and initiatives on risk assessment for data integrity

TRENDS IN DI REGULATIONS IN JAPAN

PMDA Requirements for DI Compliance

- Three requirements for GLP facilities (from 2025/10/1):
  - Transition to DI-compliant equipment
  - Automated recording of weighing values
  - Management of blank worksheets

From April 2028, insufficient compliance will be considered a GLP deviation and corrective action will be required.

Reference: PMDA GLP Training Materials in 2025.10.1
https://www.pmda.go.jp/review-services/symposia/0191.html

Transition to DI-Compliant Equipment

- GLP test facilities are expected to replace equipment with audit trail functionality within three years.
- Serious DI violations involving electronic data were found during GLP inspections in Japan in the past 1–2 years. PMDA takes this very seriously.
- PMDA emphasizes management via audit trails. However, if audit trails cannot be implemented, alternative methods are permitted.

Discussions between the PMDA and industry groups

- Since 2024, industry groups and PMDA have repeatedly discussed responses to equipment without audit trails, as well as the cost and management impact on facilities.

Industry Groupe

Japan Society of Quality Assurance (JSQA)

Japan Pharmaceutical Manufacturers Association (JPMA)

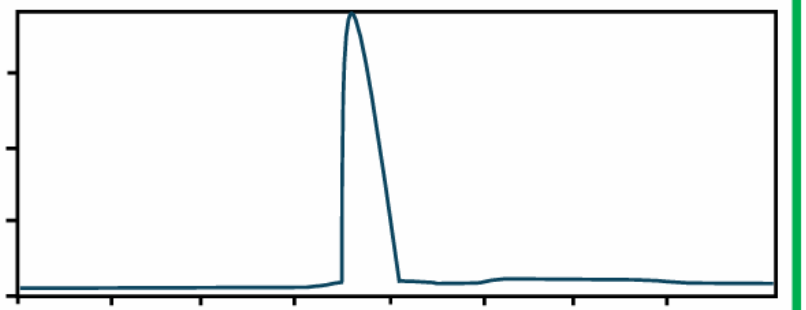
Japan Association of Contract Research Organizations (JACL)

Japan Federation of Medical Devices Associations (JFMDA)

A major incident of data integrity violation involving electronic data

HPLC chromatogram

サンプル名：tox study_01
サンプルID：A-1
バイアル番号：A-1
注入量：15 ml
分析日時：2025/10/25 19:52:44　分析者：abc def
解析日時：2025/10/25 20:47:35　解析者：ghi jkl



ピーク	化合物名	保持時間	面積	高さ	濃度	濃度単位	.....
1	-	7.441	61103	1765	0	μg/ml	.....
2	-	8.515	1713599	51066	0	μg/ml	.....
合計	-	-	1774702	-	-	-	.....

- The raw data was defined as the printout of the measurement results on paper.
- The operator (who committed the misconduct) performed multiple measurements on the same sample and printed out all the measurement results.
- **The operator selected the most favorable result** from multiple measurements and fabricated data by **physically cutting and pasting** parts of the information using scissors and glue
- In the figure on the left, the information in **the red box** and the information in **the green box** were originally separate data sets.

Reference: PMDA GLP Training Materials in 2025.10.1
https://www.pmda.go.jp/review-services/symposia/0191.html

Measures for equipment without audit trail functionality

If raw data can only be retained on paper:

- Ensure at least two people verify and sign the raw data

If raw data can be retained electronically but lacks an audit trail:

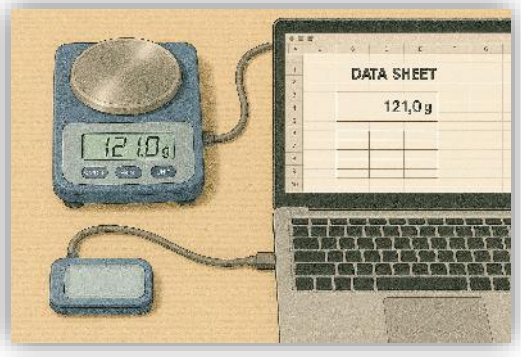
- Apply strict access controls
- Prevent easy deletion or modification
- Record and retain user, operation times, data size, and save times

Automated Recording of Weighing Values

Electronic balances and pH meters should not have values transcribed by hand, but should be automatically recorded via printer or PC/network.

Not acceptable

OK



This prevents transcription errors and intentional data changes, ensuring objectivity

Discussions between the PMDA and industry groups

Q : OECD AD No.22 does not require printouts for balance weights. What is the basis for this requirement?

A : Sections 6.2 and 6.7 of No.22 apply. Not all records can be automated, but risks should be minimized.

6.2. Generation, capture or recording of raw data

Data recorded manually may require independent verification based on a data integrity risk assessment or by other requirements.

6.7. Transcription

Transcriptions should be avoided as they increase the risks of errors and inconsistencies.

Discussions between the PMDA and industry groups

Q : Additionally, problems may arise regarding the storage and management of printed materials, such as accidentally discarding documents or mixing up different printouts.

A : Printed outputs from electronic balances should be properly managed to ensure objective verification. PMDA emphasize the importance of traceability and data integrity.

Management of Blank Worksheets

Control the use of blank worksheets for handwritten data and work records

Minimize the risk of falsification, such as rewriting or replacing records.

Specific Countermeasures

- Third parties not directly involved in using blank formats should manage issuance.
  - Methods include stamps, punches, signatures, and tracking the number of sheets issued/used
- Use notebook-style worksheets or electronic document management systems with audit trails.

Discussion with PMDA on Blank Sheets

Q : Who should manage blank sheets in GLP facilities? FM or QA?

A : Should be someone not involved in the study

Q : What records should be managed? Common or study-specific?

A : Facilities should decide based on risk analysis

Discussion with PMDA on Blank Sheets

Q : Are requirements consistent across OECD countries?

A : The approach is the same among OECD members and the US

※ However, JSQA found differences :

US : Not specifically required

EU : More strictly required

Korea : What is the situation?

JSQA recognizes differences in management methods by country

Other PMDA Responses

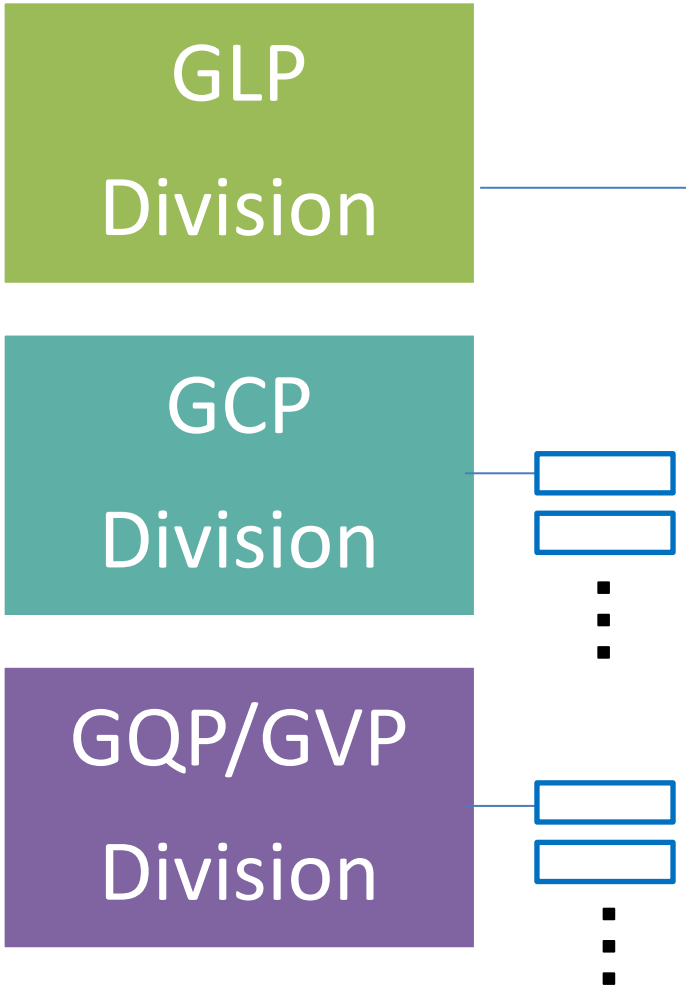
- No special requirements for non-GLP studies (e.g., pharmacological or medical device performance studies).
- No special DI requirements for studies conducted in overseas OECD MAD countries and submitted to Japan.

Summary

- In Japan, replacement to DI-compliant equipment, automated recording of weighing values, and management of blank worksheets are mandatory.
- Facilities have three years to implement, and many are struggling to comply.
- PMDA’s policies reflect major incidents and OECD No.22 interpretation, which may be unique to Japan.
- For overseas applications to Japan, PMDA’s stance should be understood, though no special DI requirements are imposed.

JSQA INITIATIVES FOR DATA INTEGRITY

JSQA Organization Chart



Sub Groupe

GLP :
- Domestic and international GLP operations
- Communication with monitoring authorities

Non-GLP :
- CMC, pharmacology, pharmacokinetics

Computerized system :
- CSV, Cloud computing, AI
- Collaboration with SQA(Computer Validation Initiative Committee)

GLP basics for beginners :
- Understand GLP requirements,

Academia collaboration :
- Quality of study data in university labs.

Members: 916
Corporate entities: 360 companies

JSQA Initiatives on DI

- Establishment of discussion forums with PMDA
- DI education seminars
- Research activities on DI

Discussion with Monitoring Authorities

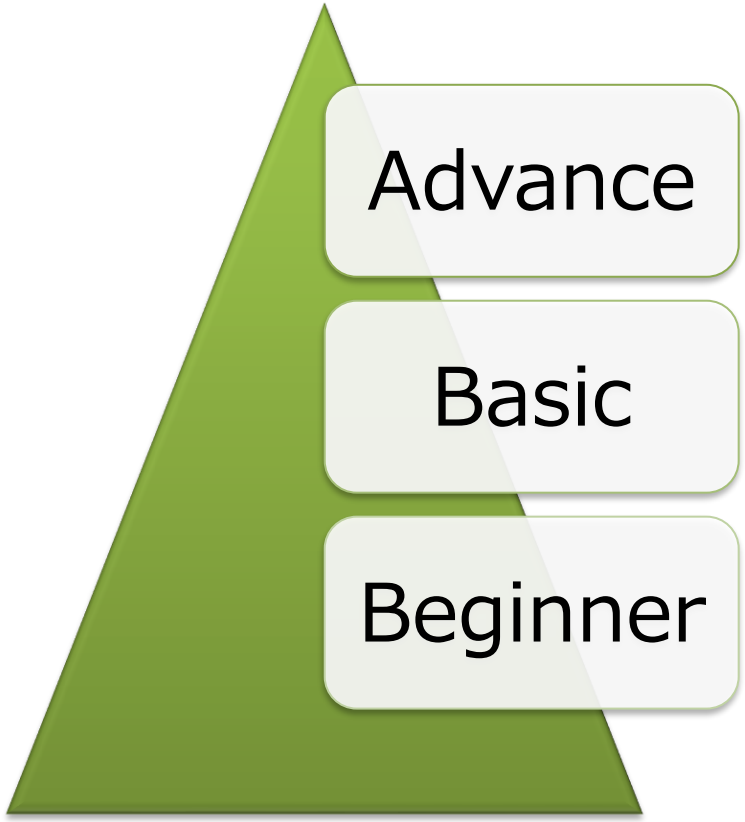
- Biannual meetings with PMDA and industry groups
  - Pharmaceutical Manufacturers Association, Medical Device Association, Safety Research Association, JSQA)
- Current Topics:
  - DI, cloud computing, long-term readability of electronic data, requirements for reference standards (OECD No.17)

Other Fields

- Pesticide GLP
  - JSQA also holds biannual meetings with FAMIC (Food and Agricultural Materials Inspection Center).
  - FAMIC and PMDA exchange information and have a close relationship.
- Chemicals, Environmental substances, veterinary drugs:
  - Different ministries oversee these areas, but all follow pharmaceutical GLP principles, including data integrity.

Planning of Education Seminars

- JSQA's education system



Workshop-style sessions

On-site lectures

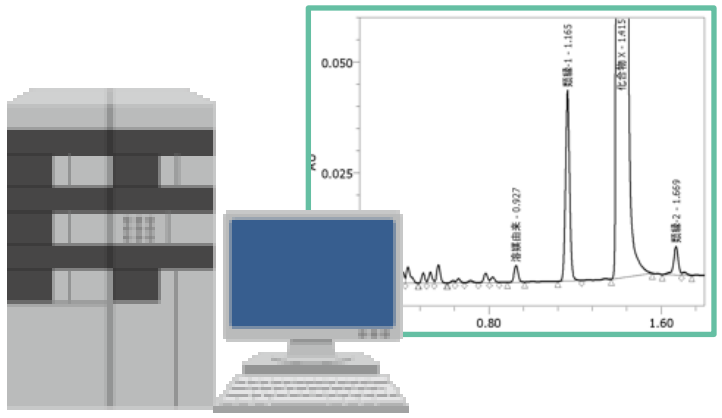
On-demand lecture videos

For details:
https://jsqa.com/wp3/wp-content/uploads/2024/10/Education-system-chart_20240927.pdf

Advanced GLP Seminar for DI

Example Scenario for Exercises

- Scenario: Continue using an HPLC system in use for 10 years; conduct DI risk analysis



System specs:

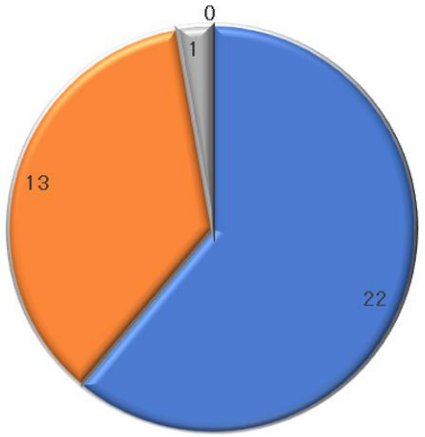
- Standalone
- local storage, flat file format
- data/methods printed on paper,
- DI functions (audit trail, e-signature, individual ID, permissions, backup, archive)

Risk Assessment Training Exercise

Seminar Scene and Worksheet Example

Process Step	Potential Failure Mode	Effect of Failure	Cause	Current Controls	Occurrence	Severity	Detection	RPN	Recommended Action

Groups of 5–6 extract risks from the scenario and evaluate using FMEA



High participant satisfaction

- **Very satisfied**
- **Satisfied**
- **Somewhat dissatisfied**
- **dissatisfied**

Research Activities on DI

JSQA publishes results of working groups every two years (members only)

- 2023: Interpretation of OECD GLP DI guidance and creation of educational materials
- 2023: DI compliance for computerized system introduction
- 2025: Long-term readability of analytical instrument data
- 2025: Practical DI risk analysis
- 2025: Roadmap for DI compliance
- 2025: DI questionnaire survey for MOU organizations

DI Questionnaire Survey

- Sent to MOU organizations from 10/2 to 11/21; responses being collected
- Results and analysis will be fed back to each organization
- Questions:
  - Does the equipment used in the GLP study have audit trail functionality?
  - Is there an SOP that describes how QA personnel should inspect audit trails?
  - Who controls blank forms?

Developement of DI Master Plan

DI Master Plan

overall plan for organizational DI initiatives

Contents
- Purpose
- Background
- Scope,
- Policy
- Schedule
- Roles and responsibilities
- Risk management
- Improvement plan
- Education
- Document management

Assessment Tools

Data Integrity Compliance Assessment Sheet

Data Integrity Laboratory Equipment and System Assessment Sheet

Training Tools

Training Materials for Management

Training Materials for Operational Staff

Summary

JSQA Initiatives on Data Integrity (DI)

- Regular dialogue with GLP authorities
  → Exchange opinions to stay aligned with regulatory expectations.
- Accurate understanding of trends
  → Reflect latest requirements in member companies' practices.
- Training & research activities
  → Provide learning opportunities and strengthen QA systems.

Results of JSQA's internal DI questionnaire in 2024

ADDITIONAL INFORMATION

Questionnaire Results
“Implementation status of audit trails”

JSQA members with GLP facilities: 46 companies

Equipment	Completed	1-3 years	Within 5 years	Not feasible	Not planned
Electronic thermometer-hygrometer	33%	2%	7%	35%	23%
Infrared spectrophotometer	19%	4%	15%	56%	7%
Blood testing	57%	4%	4%	22%	13%
Blood biochemical analyzer	57%	4%	4%	26%	9%
Urine qualitative testing device	47%	0%	12%	35%	6%
Infrared spectrophotometer	29%	0%	14%	50%	7%
Plate reader	30%	15%	11%	37%	7%
Electrocardiograph (ECG)	23%	0%	8%	69%	0%
Telemetry system	56%	0%	11%	33%	0%
Respiratory and pulmonary function	33%	0%	11%	56%	0%
Fully automated patch-clamp system	67%	0%	0%	33%	0%
HPLC	34%	16%	16%	29%	5%
LC/MS/MS	42%	16%	10%	29%	3%
Flow cytometer	18%	6%	12%	59%	6%
Endotoxin testing device	75%	0%	25%	0%	0%

Questionnaire Results
“Methods of recording measurement values”

JSQA members with GLP facilities: 46 companies

Ownership of Equipment and Methods for Recording Measurements
(Multiple Answers Allowed)

Equipment	Equipment owned	Automatic recording via printer or PC	Manual transcription of displayed values
Electronic balance	46	91%	41%
pH meter	43	53%	56%
Colony Counter	22	86%	27%
Thermometer	16	25%	88%
Spectrophotometer	26	92%	23%

- Some facilities adopt both automated and manual recording methods.
- LIMS-connected balances and manual reading coexist in certain sites.
- Thermometers generally lack printer connectivity

Questionnaire Results
“Challenges in managing blank worksheets”

JSQA members with GLP facilities: 46 companies

Study-specific worksheets

Status	Responses
Managed	7
Under consideration	31
No plan to implement	8

facility-shared worksheets

Status	Responses
Managed	3
Under consideration	32
No plan to implement	11

If GLP requires management of blank worksheets, what would be the main challenges? (multiple answers allowed):

	Responses
None	5
Heavy workload	38
High system cost	21
Unclear scope	19
Others	8

Acknowledgment

Thank you very much for the opportunity to present at the KSQA Conference.

I am grateful for the valuable exchange of opinions through this presentation on the current status of data integrity in Japan.

I hope this exchange will contribute to the further development of quality assurance activities in both countries.

KSQA Korean Society of Quality Assurance 한국신뢰성보증연구협동조합

一般社団法人 日本QA研究会 Japan Society of Quality Assurance