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Society of Quality Assurance
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Spotlight on Quality Assurance: The Future is Bright

Implementation and Challenges of PV-QMS in Japan

Japan Society of Quality Assurance (JSQA)
Post-marketing Division
Subcommittee 1 (GVP)
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Disclaimer

- This presentation focuses on the work conducted by the groups within the Subcommittee 1, the Post-marketing Division of JSQA.

- However, the views and opinions expressed in part of this presentation are those of the author.

Activity of Groups within Subcommittee 1

- Setting of a mission in each group (A, B, C) every two years
- On-site or remote meeting once every month from 1:30pm to 5:00pm for 3.5 hours
- Consultation for problems or challenges and discussion about making deliverables in the meeting
- A survey by using questionnaires may be performed to monitor the situation of the JSQA member companies.
- Completed deliverables will be disclosed on the JSQA website to the JSQA members.

Missions of Subcommittee 1, Post-marketing Division (2024-2025)

- **Group A（PV-QMS）：**

This group will examine the optimal state of PV-QMS in Japan and suggest a mechanism for real-time, continuous improvement of the quality and compliance of PV operations.

- **Group B（PV Audit）：**

Japanese companies have accumulated experiences in global PV audits and inspections. By collecting and organizing the latest information, this group will suggest points to prepare for and pay attention to global PV audits and inspections.

- **Group C（Self-inspection）：**

This group focuses on self-inspection conducted under the Japanese GVP regulation and will explore and propose effective and efficient techniques for self-inspections.

Agenda

- Background and Implementation Status of PV-QMS in Japan
- Japanese Pharmaceutical Regulations and Self-Inspection
- Challenges of Japanese PV-QMS
- Recent Topics in the Japanese Pharmaceuticals
- Conclusion

Background of Implementation of PV-QMS in Japan

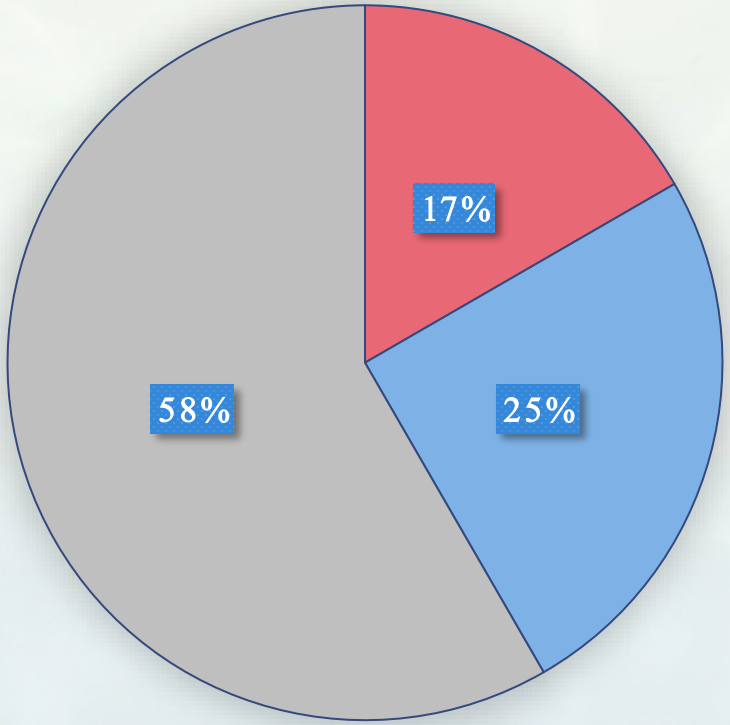
- Until now, as a method of monitoring the quality of PV operations in Japan, “self-inspections” have been carried out by the PV divisions themselves, as required by the Japanese GVP regulations.
- However, with the globalization of PV business in recent years, there are increasing opportunities to be audited and audit based on Pharmacovigilance Agreement exchanged with License Partners (LPs).
- At this time, many LPs conduct “PV audits” using the EU-GVP guidelines as audit references and then focus on the implementation of PV-QMS within the LP’s PV system.

Implementation Ratio of PV-QMS in Japan

＜Survey by the JSQA Member Companies＞

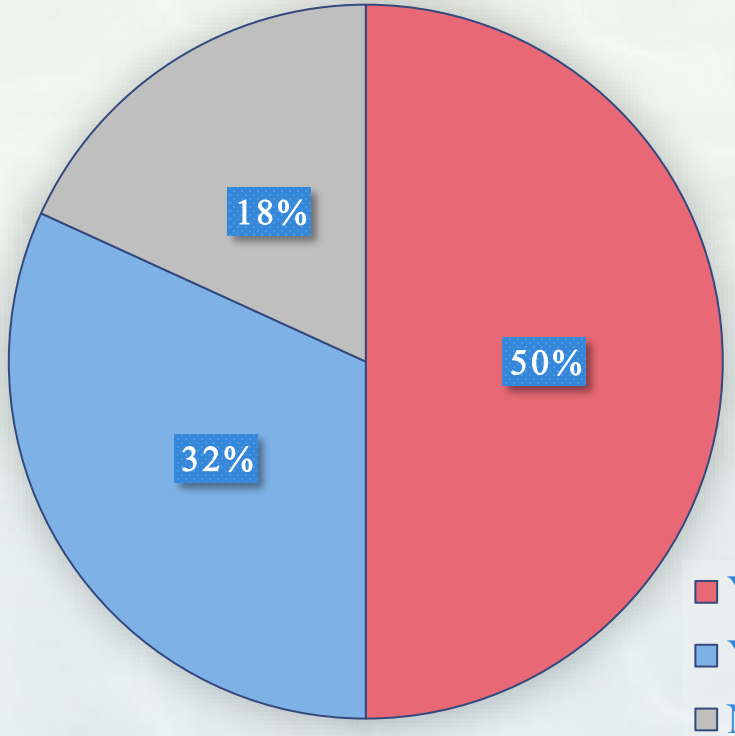
Does your company have PV-QMS at the level required by the EU-GVP?

2019



Ca. 40%

2023



Ca. 80%

Reason for Implementing PV-QMS

＜Survey by the JSQA Member Companies＞

Please select the reason. (Multiple selections allowed)

Objectives of PV-QMS

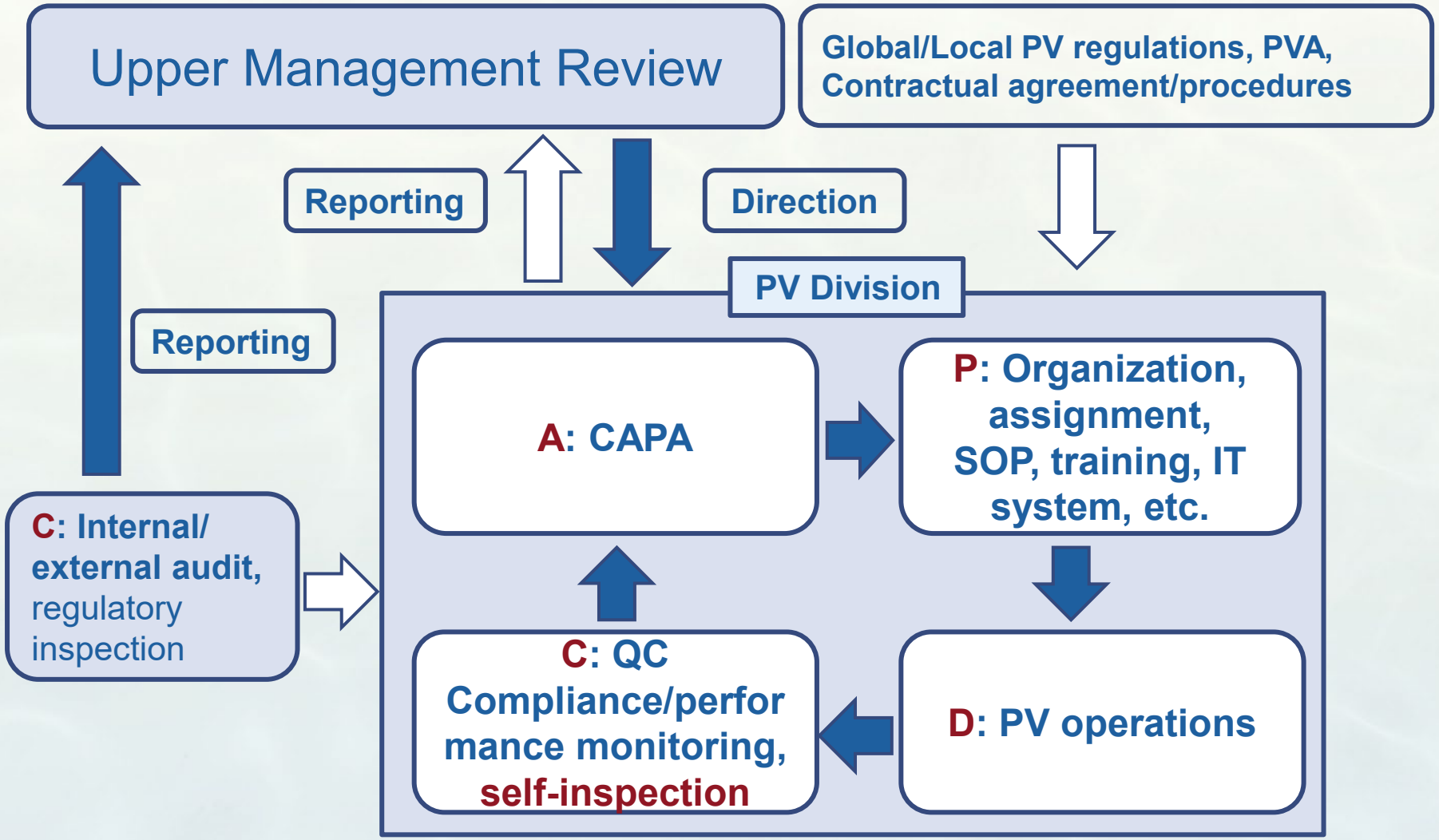
Basically, Japanese PV-QMS follows the EU-GVP guideline.

The objectives of PV-QMS are:

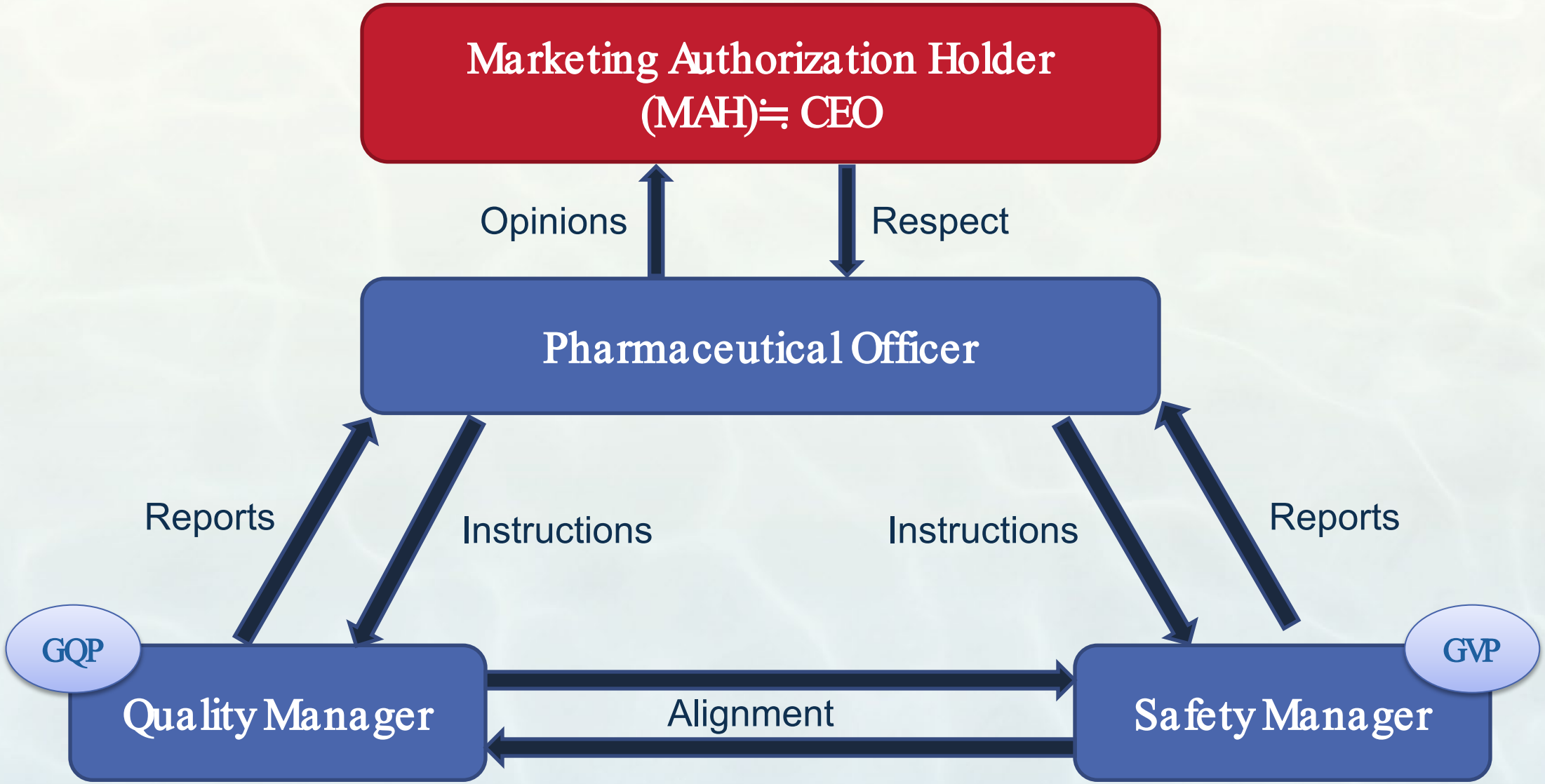
- Complying with the legal requirements for pharmacovigilance tasks and responsibilities
- Preventing harm from adverse reactions in humans
- Promoting the safe and effective use of medicinal products
- Contributing to the protection of patients' and public health.

(Ref. EU GVP Module I.B.4)

Schema of PV-QMS



Organization of Marketing Authorization Holders in Japan



Japanese Pharmaceutical Regulations

- *Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960)*
  (https://www.japaneselawtranslation.go.jp/ja/laws/view/3213/je) (English)

- *Order for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Order of the Ministry of Health, Labour and Welfare No. 1 of 1961)*
  (https://www.japaneselawtranslation.go.jp/ja/laws/view/3215) (English)

- *Good Vigilance Practice* (GVP) Ordinance
  (https://elaws.e-gov.go.jp/document?lawid=416M60000100135) (Japanese)

- *Good Post-marketing Study Practice (GPSP) Ordinance*
  (https://elaws.e-gov.go.jp/document?lawid=416M60000100171_20220520_504M60000100084) (Japanese)

Contents of GVP Ordinance

- Responsibilities of Pharmaceutical Officer (delegate of MAH)
- Organization and staff
- Standard operating procedure (SOP)
- Responsibilities of Safety Manager (≒QPPV)
- Collection of safety information
- Review of safety information and development of safety measures
- Implementation of safety measures
- Risk management plan (RMP)
- Early post-marketing phase vigilance (EPPV)
- Self-inspection
- Training of PV staff
- Record retention

Self-Inspection Stipulated by the GVP Ordinance

Article 11: The MAH should conduct regular self-inspections of post-marketing safety management activities by designated individuals, based on procedures and documents related to post-marketing safety management.

2. If the designated individual is the Safety Manager, the MAH should ensure that the Safety Manager creates and retains records of the self-inspections mentioned in the preceding paragraph.

3. If the designated individual mentioned in paragraph 1 is someone other than the Safety Manager, the MAH should ensure that this individual creates records of the self-inspections mentioned in paragraph 1, reports them to the Safety Manager in writing, and ensures that the Safety Manager retains them.

Self-Inspection Stipulated by the GVP Ordinance

4. The MAH should require the Safety Manager to report the results of the self-inspections to the MAH and the Pharmaceutical Officer in writing and should retain copies of such reports.

5. The MAH should enable the Pharmaceutical Officer to examine the necessity for improvement in post-marketing safety management based on the results of the self-inspections mentioned in paragraph 1. If there is a need for improvement, the MAH should ensure that appropriate measures are taken and records are created.

6. The MAH require the Safety Manager to retain records of the preceding paragraph.

General Workflow of Self-inspection

Differences between the EU-GVP and the Japanese GVP

QMS Processes	EU-GVP Guideline	GVP Ordinance
1. Organisation	Qualified Person for Pharmacovigilance (QPPV)	Pharmaceutical Officer (GVP/GQP), Safety management supervisor (GVP)
2. SOP management	Yes	Yes
3. Training & Assignment	Yes	Yes
4. Deviation & CAPA	Yes	No
5. Audit	Yes	No (Self-inspection?)
6. Compliance/performance monitoring	Yes	No
7. Record management	Yes	Yes (Archiving)
8. Service provider management	Yes	Yes
9. Business continuity plan	Yes	No
10. Regulatory intelligence	Yes	No
11. Computer system management	Yes	No
12. Management review	Yes	No

Challenges of Japanese PV-QMS

- There is less concept of QMS in the Japanese pharmaceutical regulations.
- Some procedures are influenced by the nature of the Japanese pharmaceutical regulations.
- Consistency of global/local PV operations and related global/local SOP descriptions and their management.
- Organizations and SOPs that are optimized in accordance with the Japanese regulations are instead disturbing adaptation to global standards.

Scandals in Japanese Pharmaceutical Companies in Recent Years

- Delay in reporting adverse reactions to regulatory authorities
- Discrepancies between approval documents and actual manufacturing methods
- Contamination of different products
- Falsification of test data
- Shortage of medicines due to repeated recalls　　etc…

Government Actions in Recent Years

- Require the responsible officer (ex.MAH) to be present during on-site inspections

  ⇒ Legal compliance education for responsible officer

  ⇒ Management Review & Quality Culture

- Recommendation to create deviation procedures (Local Government)

  ⇒ CAPA Management

- Explanation of the significance of implementing PV-QMS (Opinions of local government officials at lectures)

  ⇒ PDCA cycle

Conclusion

- The implementation of PV-QMS in Japan has dramatically progressed over the past few years.
- PV-QMS is a very fundamental and important function to be implemented in Japanese PV system.
- Although the Japanese PV-QMS has several regulatory challenges, it’s not only essential for globalization, but also effective in improving quality issues that have occurred in Japan in recent years.

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Thank you for your time!

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