Quality Oversight in Non-interventional Studies : A Collaboration Project by RQA & JSQA

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- This presentation includes the personal opinions and views of the presenter.
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Agenda

1. Overview of RQA and JSQA Collaboration Project
2. Non-Interventional Studies (NIS)
3. Challenges of NIS in the UK/EU
4. Challenges of NIS in Japan
5. Conclusion

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Overview of RQA and JSQA Collaboration Project

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RQA and JSQA Collaboration Project for NIS

- ✓ Joint initiative between RQA PV Committee and RQA NIS Special Interest Group
- ✓ Collaboration with JSQA focusing on Japanese Post-Marketing Surveillance (PMS) studies
- ✓ Common interest: Quality Assurance (QA) in NIS
- ✓ Project members are discussing, sharing experiences and perspectives, and consolidating insights on QA challenges in NIS

We are also preparing a booklet to share our insights and suggestions for best practices. More details about the booklet will be provided later in this session.

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Why Focus on QA in NIS?

- ✓ Increasing MHRA regulatory inspection findings and critical issues related to NIS
- ✓ Generating reliable real-world evidence for regulatory decision-making
- ✓ Navigating diverse regulatory frameworks and study designs
- ✓ Sharing international experiences and perspectives

This session aims to support global knowledge exchange and serve as a starting point for further discussion on QA in NIS.

Non-Interventional Studies (NIS)

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What is NIS ?

No Universal Definition

- Concepts and criteria vary by region, country, and study design
- Regulatory guidance must be consulted: FDA, EU, EMA, EPHMRA, and ICH

Core Principles of NIS

- Treatment is prescribed in the usual manner, aligned with the product's marketing authorisation
- No protocol-mandated interventions or assessments beyond routine clinical care
- The aim is to advance science, improve disease treatment, and enhance patient outcomes

Evolving Boundaries of Routine Care

- Definition of "routine care" is not fixed and continues to evolve
- Key factor in distinguishing NIS from clinical trials
- Some biomarker/genetic tests may be considered non-interventional if part of routine care

Regulatory Framework for NIS

- NIS requirements are primarily defined at the national level
- No ***single*** EU-wide regulation for all NIS, but ***EMA GVP Module VIII*** provides key guidance for Post-Authorisation Safety Studies (PASS) and safety reporting

Key references:

- ✓ FDA, EMA, PMDA, MHRA and others have issued frameworks and guidance for NIS and Real-World Evidence (RWE)
- ✓ ICH, ISPE, ENCePP, and CIOMS provide methodological and ethical standards
- ✓ Industry codes of practice (EFPIA, ABPI) set additional requirements for study conduct and transparency

Clinical trial regulations and ICH GCP do not directly apply, but some concepts may be adopted as appropriate.

NIS as a Part of the PV System

- ✓ NIS plays a critical role in the ongoing assessment of a medicinal product's benefit-risk profile
- ✓ Integration with core pharmacovigilance (PV) processes is essential
  - Systematic capture, assessment, and reporting of safety data
  - Compliance with regulatory requirements
- ✓ EU GVP Module VIII outlines QA requirements for Non-interventional PASS (NI-PASS)
- ✓ Sponsors need to implement robust QA systems for NIS, ensuring:
  - Scientific validity
  - Data quality
  - Regulatory compliance
  - Integration with overall PV activities
- ✓ QA in NIS supports reliable RWE for regulatory decision-making

Challenges of NIS in the UK(/EU)

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Challenges of NIS in the UK

MHRA's PV inspections include NI-PASS as one of four key arms of their inspection strategy.

- ✓ **Regulatory Compliance**
  - Limited MAH experience with NI-PASS requirements
  - Increased risk of non-compliance
- ✓ **Risk Management Issues**
  - Problems maintaining Reference Safety Information
  - Difficulties with additional risk minimization measures
- ✓ **Quality Management System Gaps**
  - No documented audit strategy
  - Delays in implementing Corrective and Preventive Actions
- ✓ **Data Integrity & PV Integration**
  - Safety data collection and reporting not systematic
  - Weak connection between study conduct and PV system

Challenges of NIS in Japan

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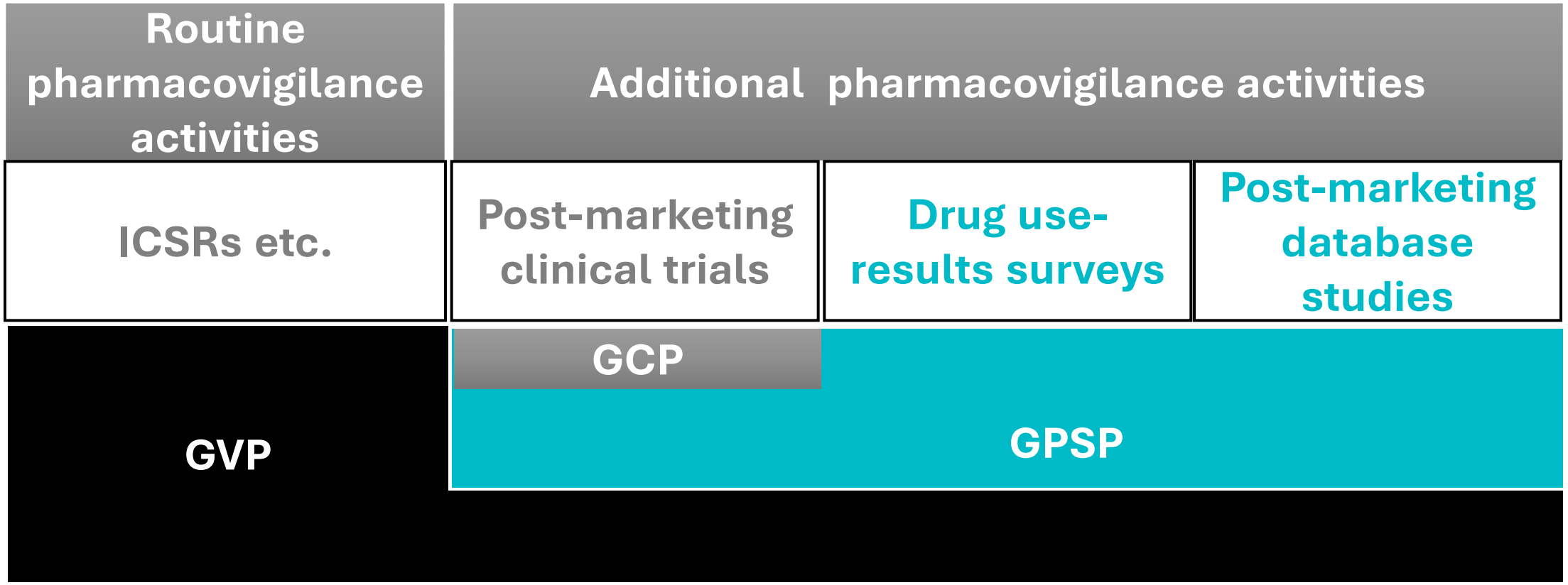
Relationship of GVP and GPSP in Japan



Japan-Specific QA Requirements for NIS

- ✓ ***Good Post-marketing Study Practice (GPSP) ordinance*** sets legally binding standards for *PMS*
- ✓ Mandatory appointment of ***a Post-marketing Study Manager***, independent from sales/marketing
- ✓ Strict protocol development and approval procedures
- ✓ Required ***self-inspections*** and documentation of QA activities
- ✓ Detailed requirements for training of all personnel involved in PMS
- ✓ Strict requirements for record retention and archiving
- ✓ Limitations on outsourcing and clear responsibilities for MAH
- ✓ Regular and final reporting to PMDA, with strict timelines and content requirements

Challenges of NIS in Japan

- ✓ Strict regulatory requirements under **GPSP ordinance**
- ✓ Complex documentation and record-keeping obligations
- ✓ Heavy reporting and compliance requirements to PMDA
- ✓ **Difficulties in harmonizing with global NIS standards**
- ✓ Securing cooperation from medical institutions
- ✓ Adapting risk-based QA approaches to the Japanese context
- ✓ Strict requirements under **GPSP ordinance**, even for secondary data studies

Post-Marketing Database Studies in Japan

- Post-Marketing Database Studies (DB studies) are increasingly recognized as a type of NIS for post-marketing safety surveillance.
- Regulatory changes under *the 2017 MHLW Ministerial Ordinance No. 116* institutionalised DB studies, allowing their use for re-examination and re-evaluation applications since April 2018.
- PMDA actively encourages DB studies to enhance additional safety monitoring of approved drugs.

Challenges of Database Studies in Japan

Risk Perception and QA Oversight

- Secondary use of data is often perceived as low-risk, leading to limited QA involvement globally
- This perception may overlook risks related to data integrity, ethical oversight, and regulatory accountability

Challenges of Database Studies in Japan

Japan-Specific Regulatory and Operational Challenges

- ✓ Strict requirements under GPSP ordinance, regardless of perceived risk level
- ✓ Complex documentation, record-keeping, and reporting obligations to PMDA
- ✓ Limited transparency (e.g., no public registry like EU PAS Register)
- ✓ Limitation to domestic databases; overseas DB use is generally not expected

Data Quality and Access Issues

- ✓ Each medical information database has unique characteristics and limitations
- ✓ Ensuring data quality and reliability (coverage, accuracy, validation)
- ✓ Restricted access due to limited DB options, high costs, and contract challenges

Practical and Strategic Considerations

- ✓ Limited practical experience; best practices are still evolving
- ✓ Securing cooperation from medical institutions
- ✓ Adapting risk-based QA approaches to the Japanese context

Conclusion

- ✓ NIS present complex QA challenges across all regions
- ✓ These challenges include regulatory diversity, integration with PV systems, and evolving study designs
- ✓ Differences between UK/EU and Japan highlight the need for region-sensitive yet globally aligned QA approaches
- ✓ Robust QA systems are essential to ensure scientific validity, data integrity, and regulatory compliance
- ✓ Collaboration and shared learning among QA professionals are key to advancing NIS oversight

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Introducing the NIS QA Booklet

- ✓ Developed by RQA & JSQA project members
- ✓ Practical guidance for QA professionals working with NIS
- ✓ Based on current standards and regulatory frameworks
- ✓ Focused on medicinal drug products (not medical devices)
- ✓ Scheduled for release in Q1 2026

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What's Inside the NIS QA Booklet?

Key Topics Covered:

- ✓ Regional Regulatory Requirements for NIS
- ✓ Key Consideration by NIS Type
- ✓ Interface with Key PV Activities
- ✓ Role & Responsibilities, and Common Operational Model
- ✓ QA Oversight – *Best practices*

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Why You Need This Booklet

– Strengthen Your QA in NIS

Facing challenges in NIS QA?

- Regulatory complexity across regions
- Inspection readiness concerns
- Data transparency and ethics in DB studies

This booklet offers strong support:

- Practical QA guidance based on RQA & JSQA experience
- Risk-proportionate approaches aligned with current standards
- Real-world examples focused on medicinal products

Ideal for:

- QA professionals in NIS
- PV and PMS managers
- Teams preparing for inspections

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Release details coming soon!

Don’t miss out

– get your copy and lead QA in NIS!

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Thank you !

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