'Measurement, Analysis & Improvement' Refer to / taken from Ensuring Compliance: Navigating the EU MDR for Drug-Device Combination Products

This item addresses Measurement, Analysis and Improvement (ISO 13485 §8.5) and requirements for associated statistical analysis (ISO 13485:2016 §7.3.6, §7.3.7, §7.5.6, §8.1 and §8.4)

A. QMS Requirements

1. EU Requirements

EU medicinal product Directive 2001/83/EC has the requirements for Single Integral DDC to comply with **GSPR Annex I of MDR 2017/745** (Article 117). There is therefore no requirement to comply with **EU MDR 2017/745** Article 10 General obligations of a manufacturer:
9 (m) processes for monitoring and measurement of output, data analysis and product improvement.

2. US Requirements

21 CFR Part 4A
Under 21 CFR 820.10 Requirements for a quality management system incorporated from ISO 13485:2016:

- §8.2.5 Monitoring and measurement of Processes
- §7.4.3 Verification of purchased product
- Application of statistical techniques for Design and development verification (§7.3.6) and validation (§7.3.7), Validation of processes for production and service provision (§7.5.6), demonstrate product conformity, ensure QMS conformity and maintain the effectiveness of the quality management system (§8.1) and analysis of data (§8.4)
- 21 CFR 820.35 Control of records - (a) Records of complaints
- §8.2.4 Internal audit

Similarities and Differences
Similarities:
EU MDR2017/745, ICHQ10 and 21 CFR have similar requirements for monitoring and measurement of process and product from both internal and external sources.
Differences
There are no differences.

B. Background on Measurement Analysis and Improvement

Measurement, Analysis, and Improvement are vital for monitoring performance, making data-driven decisions, ensuring continuous improvement, managing risks,

maintaining regulatory compliance, enhancing customer satisfaction, and optimizing resources. These activities collectively help organizations meet regulatory requirements and sustain high-quality standards.

(Text from Section 3: Quality Management Systems (QMS) from an MDR Perspective - Subsection 6: Measurement, Analysis, and Improvement)

The QMS must include processes for monitoring and measuring product performance, analysing data, and implementing improvements.

1) Measurement:

- Performance Metrics: Develop key performance indicators (KPIs) tailored to drug-device combination products. Metrics should include device reliability, drug delivery accuracy, failure rates, and customer complaints.
- Data Collection: Implement comprehensive data collection systems throughout the product lifecycle. This includes manufacturing data, quality control results (including inspections of purchased product and services), clinical performance data, and post-market surveillance.
- In-Process Monitoring: Continuously monitor critical manufacturing processes to ensure they operate within specified limits. Use tools such as Statistical Process Control (SPC) to detect variations and maintain quality consistency.

2) Analysis:

- Data Analysis: Apply statistical methods to analyze performance data and identify trends, anomalies, or areas for improvement. Techniques like root cause analysis help determine underlying issues affecting product performance and contribute to the devices' risk management process.
- Risk Management: Regularly conduct risk assessments to evaluate potential hazards and their impact on the device component. Update risk management plans based on new data and insights.
- Performance Reviews: Hold regular performance reviews to assess the QMS's effectiveness. Evaluate the collected data against predefined objectives and regulatory requirements.

3) Improvement:

- Corrective Actions: Develop and implement corrective actions to address identified issues or non-conformities. Ensure that these actions effectively resolve the problems and prevent recurrence.
- Preventive Actions: Identify potential issues before they occur and implement preventive measures. This proactive approach helps maintain product quality and compliance.

- Improvement: Foster a culture of improvement to ensure and maintain the continued suitability - and even the continuous improvement, adequacy, and effectiveness of the QMS using methodologies like Lean, Six Sigma, and Kaizen. Encourage all levels of the organization to participate in identifying and implementing improvements.
- Management Review: Conduct regular management reviews to evaluate the QMS's performance and improvement efforts. Use these reviews to set new quality objectives and ensure alignment with regulatory changes and business goals.

By integrating these processes into the QMS, manufacturers can ensure their drug-device combination products consistently meet regulatory requirements and deliver safe, effective performance. This comprehensive approach helps maintain compliance, enhance product quality, and improve patient outcomes.

Background on Statistical Techniques
Applying statistical techniques is essential for ensuring product quality, validating processes, managing risks, designing sampling and testing protocols, complying with regulations, making data-driven decisions, and fostering continuous improvement. These practices collectively help meet regulatory requirements and ensure the safety and efficacy of medical devices and drugs.

(Taken from Section 3: Quality Management Systems (QMS) from an MDR Perspective - Subsection 3: Quality Management System (Apply risk-based approach to the control of the appropriate needed processes), Subsection 6: Measurement, Analysis, and Improvement - Section 4: Post-Market Surveillance)

Various sections of ISO 13485:2016 address the application of statistical techniques:

- **§7.3.6 Design and Development (D&D) verification**:
  The organization shall document verification plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.
- §**7.3.7 D&D validation**:
  The organization shall document validation plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size.
- **§7.5.6 Validation of processes for production and service provision**:
  The organization shall validate any processes for production and service provision where the resulting output cannot be or is not verified by subsequent monitoring or measurement and, as a consequence, deficiencies become apparent only after the product is in use or the service has been delivered.

Validation shall demonstrate the ability of these processes to achieve planned results consistently.
The organization shall document procedures for validation of processes, including, as appropriate, statistical techniques with rationale for sample sizes.

- **§8 (Measurement, analysis and improvement) §8.1 General**:
  The organization shall plan and implement the monitoring, measurement, analysis and improvement processes needed to:
  (a) demonstrate conformity of product;
  (b) ensure conformity of the quality management system;
  (c) maintain the effectiveness of the quality management system.
  This shall include determination of appropriate methods, including statistical techniques, and the extent of their use.
- **§8 (Measurement, analysis and improvement) §8.4 Analysis of data**:
  The organization shall document procedures to determine, collect and analyze appropriate data to demonstrate the suitability, adequacy and effectiveness of the quality management system. The procedures shall include determination of appropriate methods, including statistical techniques and the extent of their use.