NEWS on diagnostics

2023 Volume 2

In this issue....

Welcome to this second issue of News on Diagnostics for 2023. Managing risk is essential in IVD manufacturing. Part of ISO 13485 requires a 'feedback loop' for monitoring and mitigating risk is added to the overall manufacturing process.

We have several services and product attributes that can help to support this activity.

What is risk?

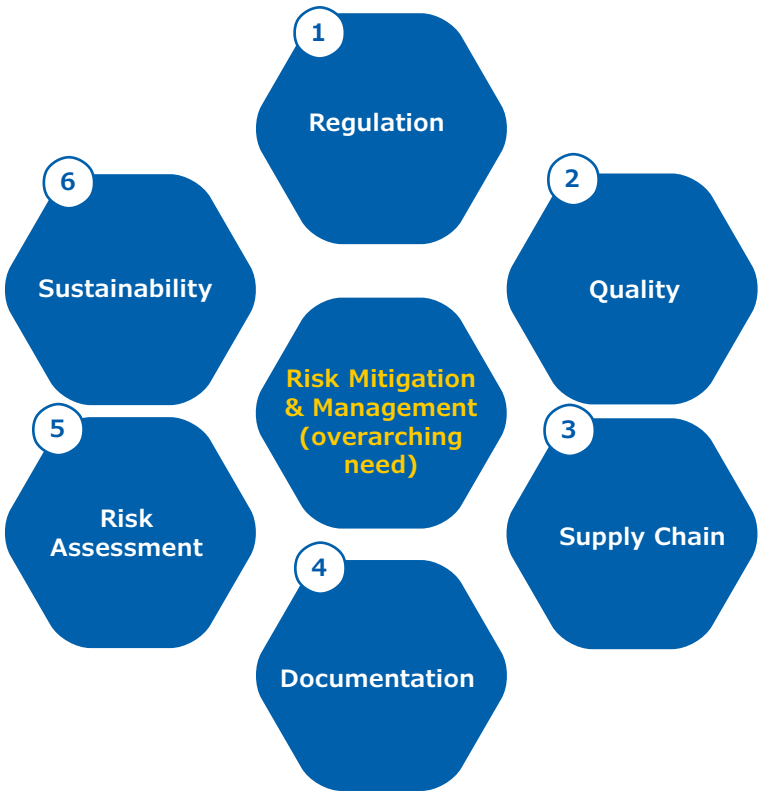
The term risk, as defined in ISO 13485, refers to the combination of the probability of occurrence of harm and the severity of that harm. The scope of ISO 13485 includes not only safety, but all product and applicable regulatory requirements. Therefore, risks related to product performance and regulatory compliance also need to be considered.

Risk management is defined as a systematic application of management policies, procedures, and practices to the tasks of analysing, evaluating, controlling, and monitoring risk.

What does IVDR say about risk?

The IVDR requires that a benefit/risk analysis be performed for all risks and the overall residual risk. Therefore, a benefit/risk analysis must be included in any technical file submission regardless of the risk acceptability. IVDR states that manufacturers must have a risk management system that is compliant with the General Safety and Performance requirements of Annex I of the EU regulation.

Elements of a robust Risk Mitigation & Management program



1. Regulation

Changes within IVDR included:

1. IVD Device Classification
2. Technical File Structure
3. Additional Post Market Surveillance
4. Additional Clinical Evidence Requirement
5. Performance Evaluation & PMPF (Post-Market Performance Follow-up)
6. Increased Responsibility for and scrutiny of Notified bodies
7. Additional requirements for economic operators

This is a number of complex and in-depth changes, in a relatively short timescale.

Please note – Merck (as a raw material supplier) limited/no influence on items 1, 4 & 6

What does Merck offer that supports you to be IVDR compliant?

Robust Quality Program (M-Clarity™ Program) [2, 3, 5, 7]

Products MQ200-MQ400 are typically suitable for Dx manufacturing, as determined by customer processes. There is an option in M-Clarity™ Program customer workshops, to personalise this information to a particular application.

Quality Agreements[5, 7]

IVDR suggests a fully transparent quality and supply agreement for IVD manufacturing grade products will support economic operators in fulfilling their obligations (application Critical Raw Materials).

Change Notification[3, 5, 7]

Changes to the way a product is made/supply chain changes etc. help an IVD manufacturer to assess and mitigate risks associated with products/services they use from us. IVDR demands a risk-based approach to manufacturing.

Risk Mitigation/Risk Assessment Workshops[3, 5, 7]

Application & customer specific information, designed to support you in choosing the right product for each stage in your application.

2. Quality

At the core of maintaining our high quality and regulatory standards is a robust Quality Management System, where all relevant quality and regulatory processes are described. Inspections from authorities, customer and internal audits, customer feedback, along with targeted quality improvement plans provide the input for maintaining these highest standards, as well as for continuously improving our systems, processes and products. This results in an active involvement and ownership of employees across all functions and lives the model that Quality is embedded in everything we do.

Our Quality Standards

ISO 9001:2015 is the foundation of our Quality Management System for our products and services. Our ISO 9001 Quality Self-Assessment provides in-depth information about our Life Science Quality Management System. The table of content of this document is aligned to « Contents of ISO 9001:2015 Quality Management Systems ». The company profile is aligned to « RX-360 Supplier Assessment Questionnaire, Module 1 ».

The majority of our Life Science sites are certified to the ISO 9001:2015 standard.

Overview of our ISO certified Life Science sites and download our ISO certificates.

Sites that manufacture medical devices are additionally certified to ISO 13485.

To cover higher requirements, we follow additional Quality standards, for example Good Manufacturing Practice (GMP) regulations:

- U.S. Food and Drug Administration – Code of Federal Regulations Title 21
- European Medicines Agency – Eudralex Volume 4
- ICH Quality Guidelines

3. Maintaining Supply Chain Excellence

Close collaboration with integrated supply chain operations

- Utilising both short- and long-term planning to prevent backorders, and support future capacity decisions
- Promoting business continuity planning and supply security
- Life Cycle Management (support margin, growth opportunity & costs)

Supplier quality management

- Ensuring the Supplier Quality Management procedure complies to our corporate standards
- Training, assessing, monitoring & assisting Life Science sites
- Maintaining the Supplier Quality Management program

Supplier assessments & audits

Categorisation of Supplier	Assessment Frequency	Method of Assessment
Critical	Chemicals: Once every 3 years Non-chemicals:Once every 2 years	On-site Audits
Essential	Once every 3 years	Questionnaire & Audit as determined by Risk Assessment
Non-critical	N/A	As determined by site level procedure

4. Documentation

Quality agreement

Quality Assurance Agreements are legally binding contracts negotiated between Merck and you, our customers. Having executed a QAA for products used in regulated environments, you can be sure to comply with applicable regulatory and legal requirements.

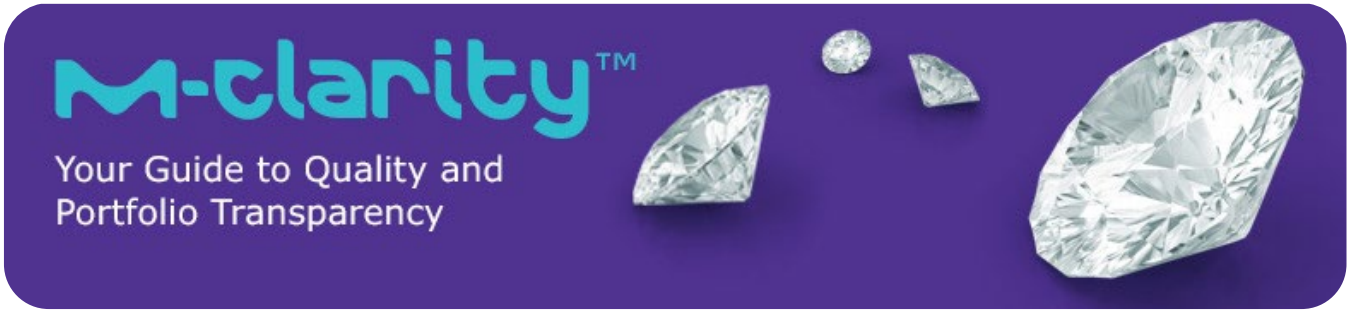
Due to the extended requirements and support levels that need to be in place, QAAs are available for products with MQ segment of MQ300 and above.

The term of a QAA is five years. An expiry notice will be received two months in advance, to allow time to prepare for a renewal.

Customer Change Notification

To ensure that we provide the most-up-to-date product information, we have a best-in-class Change Notification Program based on a validated Change Control process and on our M-Clarity™ Program to inform customers about important changes that could impact their R&D or process development programs

Find out more, including the notifiable events at **SigmaAldrich.com/m-clarity**



5. Risk Assessment

Development and manufacture of IVD products is a complex process involving multiple suppliers and raw materials. Minimising disruptions of any kind is vital to supply chain management.

Proprietary assessment of our current supply chain is carried out at the product level within several key parameters. The risk assessment is targeted at general disruption of supply of the current product, ideally a product in development.

Our Supply Chain Risk Assessment Program

This proprietary program helps you to clearly understand these potential risks for critical raw materials and provides recommendations to proactively take the necessary steps to mitigate risk.

How the program works:

IDENTIFY: You compile a list of highly critical materials that we supply to you.

MANAGE: We analyse supply chain risk potential for each material along key risk categories

MITIGATE: We provide a composite supply chain risk score report accompanied by customised risk mitigation recommendations.

Find out more about how Merck can support your Risk Mitigation processes at **SigmaAldrich.com/risk-mitigation**

6. Sustainability

Working and manufacturing in a 'greener' manner, isn't just about finding alternatives to banned or restricted chemicals. It also refers to sustainability in terms of reduced packaging, waste minimisation and inventory management.

We think responsibly and act in terms of generations instead of quarters, believing in the long-term impact on our clients and products. This spirit underpins our sustainable success. We take an active role in shaping the future through our products and technologies, enabling brilliant people to solve global challenges.

We focus our strengths on those areas where we can have the greatest impact and continuously seek to hone our competitive edge while working to sustainably secure our future.

We demonstrate our commitment to responsibility through extensive programs in three main areas:

- Greener Products and Solutions
- Sustainable Operations
- Employee and Community Engagement

Find out more at **SigmaAldrich.com/ssbi**

DID YOU KNOW...?

Tomorrow's digital laboratory management…Today IS possible!

The LANEXO™ System is an integrated inventory, safety and compliance management system for chemicals, reagents and other consumables in the laboratory.

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