Developing and maintaining a quality management system for IVDs

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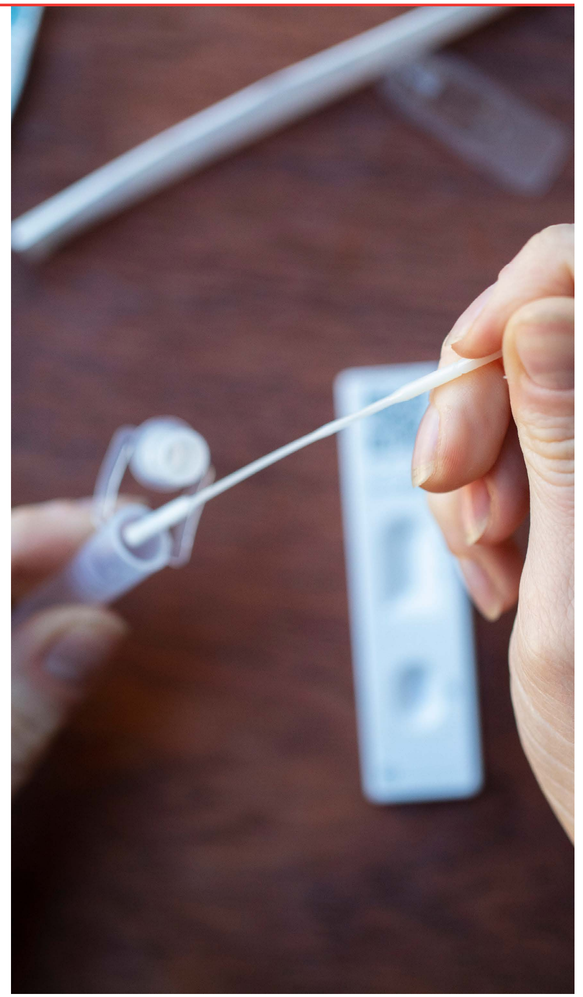
Contents

Introduction

There are many different requirements with which *in vitro* diagnostic manufacturers have to comply in order to place products on the market. At the core of most of these requirements is a fundamental need to have a good quality management system (QMS) in place. This is certainly not a new requirement for companies. Philip B. Crosby said "Quality Management is a systematic way of guaranteeing that organized activities happen the way that they are planned… Quality management is needed because nothing is simple anymore, if indeed it ever was."[1] Although this quote is now nearly 40 years old, it is as true today as it was then. Companies still need a system in place to ensure that activities happen according to plans, especially as the environment continues to get more complicated with increasing regulation, customer expectations and product complexity.

There are several regulations and standards that focus on QMS requirements, but this paper primarily examines the QMS requirements in the new *In Vitro* Diagnostic Device Regulation (IVDR) 2017/746[2] which has entered into force as of 26 May 2017 and will serve as the basis for access to the European market. Complying with the requirements of BS EN ISO 13485:2016, *Medical devices — Quality management systems — Requirements for regulatory purposes* will largely fulfil those requirements established in the IVDR.
The reader is referred to Annex ZB of BS EN ISO 13485:2016 for further details on mapping between the IVDR to ISO 13485:2016 as well as to *ISO 13485:2016 — Medical devices — A practical guide*.[3]

In February 2022, the FDA issued a proposed rule to harmonize the QMS requirements currently established in the Quality System Regulations in 21 Code of Federal Regulations 820 with those of ISO 13485-2016.[4] With the IVDR in the EU, and these announced changes from the FDA, it is a good time to review the fundamental requirements of the QMS to ensure that the manufacturer has the most streamlined approach for easy market access and efficiency in execution.



1 Philip B. Crosby, (1979), *Quality is Free: The Art of Making Quality Certain*, McGraw-Hill, p. 19.

2 *In Vitro* Diagnostic Device Regulation (IVDR) 2017/746 published 5 May 2017 in the Official Journal of the European Union, http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2017.117.01.0176.01.ENG [accessed 17 March 2023].

3 *ISO 13485:2016 — Medical devices — A practical guide*, https://www.iso.org/publication/PUB100422.html [accessed 17 March 2023].

4 https://www.fda.gov/medical-devices/quality-system-qs-regulationmedical-device-good-manufacturing-practices/proposed-rule-quality-system-regulation-amendments-frequently-asked-questions [accessed 17 March 2023].

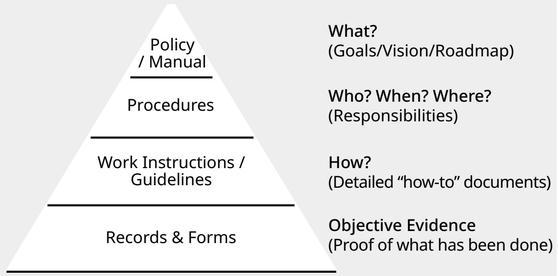
QMS basics

QMS creation

Article 10 (8) of the IVDR establishes a number of requirements and expectations for the QMS of which the most basic is for the manufacturer to establish a QMS. As a reminder, the QMS is made up of all of the processes that are documented and recorded that can support the organization to run efficiently and effectively: A Quality Manual, Quality Policy, Procedures, Work Instructions and Records. The first part of Article 10 (8) addresses the obvious need to have processes that ensure design and production is done such that the device continues to meet the requirements of the regulation throughout its lifetime. This will typically include aspects such as process validation, production process controls and quality controls. For most existing manufacturers, these expectations have not significantly changed since the previous directive, nor from any other standards.

As previously, the QMS should address the risks throughout the lifetime of the device and ensure that adequate controls are in place around identified risks. It should also ensure that adequate and accurate records are produced in order to demonstrate and record that the process and products are operating per expectations.

Figure 1: Documentation Pyramid



QMS Maintenance

While the main requirement of effectively creating, documenting and following a QMS is not substantially different than the previous directive or standards, it is important to note that the IVDR specifically includes the three phrases:

- “maintain”;
- “keep up to date”; and
- “continually improve”.

Since they are generally accepted as synonyms, there must be some significance in the inclusion of both “maintain” and “keep up to date”. This brings to mind the notion of “timeliness” and the idea that the QMS needs to be regularly updated to take into account any sort of changes, whether they are external changes to standards or specifications, internal changes to the organization or products, or the results of a process to continuously review and improve the QMS. Later in the phrase we also find the words “in the most effective manner”, meaning that an overly complicated or complex QMS can be burdensome for the manufacturer to both

implement and maintain, as well as possibly be considered non-compliant.

With this in mind, the IVD manufacturer has to ensure that an adequate process for reviewing, assessing, documenting and integrating design changes, including changes to the raw materials of the product, is in place. While this is evident for most manufacturers, this phrase further includes requirements to take into account changes to harmonized standards or common specifications that were used in the development or production of the device. Additionally, there is an emphasis that these need to be taken into account in a timely manner. To achieve this, the QMS has to then specify not only the harmonized standards and common specifications applicable to a given product, but also have a process in place to be alerted to changes when they happen (timely), to perform an assessment of those changes and to determine how they affect the product and QMS.

A good monitoring process, which is necessary to identify these kinds of changes, will include various activities such as regulatory surveillance, standards monitoring and review of public findings e.g. warning letters, injunctions. There are many options for implementing these processes, ranging from using companies which offer this kind of assessment as a service, participating in external industry working groups, setting alerts on websites for key words or subscribing to various newsletters on key topics. People need to have this activity identified as part of their job responsibilities, with adequate time allocated to the process. When changes are identified, a formal assessment should be done to determine what actions will be put into place to account for the new or modified requirements. This documented assessment should include those responsible for performing the assessment (job title, profile or qualifications), as well as those in management who are making or approving the final decision. It is also important to document when a change is determined to *not* require changes to the QMS to demonstrate that adequate due diligence was done. In the case that changes are extensive, the manufacturer should document the plan for implementing the changes, indicating the expected timelines, along with an explanation of needed tasks. This will provide a means to justify gaps between current standards and those referenced in the QMS if necessary and will ensure alignment within the organization on the expected outcomes.

Scope

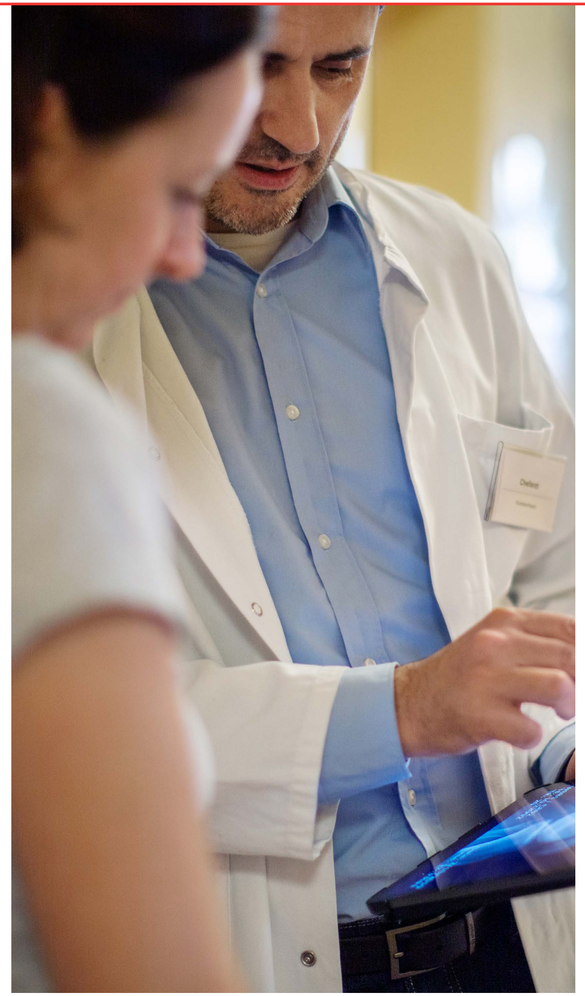
The QMS covers “all parts and elements” of a manufacturer’s organization, and not only those that are directly related to product realization. This includes any and all processes around product realization, including planning, design, development, production and service provision as well as all supporting functions that contribute to these missions, including meeting regulatory requirements. With this in mind, the manufacturer needs to evaluate the whole organization, to ensure that all processes and procedures that can impact quality are well documented in the QMS. Some areas, such as Human Resources, will become more critical to the QMS elements than in the past. Notably, the QMS governs the structure of the organization with an emphasis on the key responsibilities, and, in particular management responsibilities. The Quality Manual and organization charts can be used to fulfil this requirement. The manufacturer should pay special attention to job descriptions or other documents that define the responsibilities of employees.

These job descriptions, and other role documentation, are often the basis for developing training and competency. Job descriptions can be the cornerstone of demonstrating that a specific role is fulfilled within the QMS and that the individuals performing the function are adequately qualified to complete the tasks. The responsibilities for monitoring and implementing the QMS should be clearly defined.

Roles & responsibilities

Person responsible for regulatory compliance (PRRC)

One of the new key areas of responsibilities that needs to be defined is the person or persons responsible for regulatory compliance defined in Article 15 of the IVDR. If more than one person will maintain this role (to help the manufacturer meet the accessibility requirement) the divisions of responsibility will need to be documented in writing, such as in job descriptions, objectives, performance related criteria, etc. As the qualification requirement for this role should be fulfilled by a) a diploma, certificate or other evidence of qualification and at least one year of professional experience in regulatory affairs or in quality management systems; or b) four years of professional experience as stated above, it is important to ensure that objective evidence is maintained within the records associated to the person(s) named. The experience requirements are specific to *in vitro* medical devices, and experience in other types of medical devices/QMS is likely to be considered inadequate.



Beyond the role description and list of respective responsibilities, the manufacturer should be ready to demonstrate through records that the person responsible for regulatory compliance has indeed been acting in the expected capacity. This includes covering the conformity of devices being manufactured and released, the technical documentation and EU declaration of conformity, post-market surveillance obligations, reporting obligations and the specific classes of performance studies involving interventional devices or risk to patients. It should not be interpreted or expected that the PRRC is reviewing or approving each of these documents themself, as this responsibility can be delegated through procedure.

Objective evidence of PRRC involvement can include, but is not limited to:

- approving procedures that cover these areas;
- approving reports dealing with these items; or
- participation in management reviews where these topics are covered.

Finally, specific attention is drawn to Article 15 (5) which states that the PRRC “shall suffer no disadvantage within the manufacturer’s organization in relation to the proper fulfilment of his or her duties…”.
It could be helpful for this to be reflected in the relevant job descriptions or contracts.

Economic operators

In addition to the person responsible for regulatory compliance, the IVDR has defined a number of responsibilities for various economic operators (importers, distributors and authorized representatives). The manufacturer needs to ensure that these various responsibilities, and the oversight of them, are documented as part of the QMS. The authorized representative must accept, in writing, the designation of responsibility, and other economic operators will find that they have responsibilities to verify various aspects of product compliance. It is advisable to review the roles and responsibilities among various economic operators, ensuring that each party is prepared to fulfil the IVDR, as well as ensuring access to the necessary records. Manufacturers should review contracts with their various economic operators and verify that these agreements are clearly documented in writing, including all new responsibilities.

Management responsibilities

The regulation also clearly requires that the management of resources necessary to implement and to carry out the procedures and policies be defined within the QMS. To conform to these expectations, the QMS has to include adequate provisions to review the allocation of resources to key processes as well as management reviews which are aimed at identifying whether a process is under-resourced. For example, corrective actions that are systematically late could be indicative of an inadequate provision of resources.

Management of resources also includes the selection and control of suppliers and sub-contractors, with emphasis on critical suppliers in accordance with risk. Any processes that are assured through suppliers and sub-contractors need to have adequate provision defined to demonstrate that these are under control. This should include selection and/or qualification criteria, as well as a process for monitoring performance/output. For critical or high risk suppliers, a regular audit program is also advisable. As with other clauses, the key is to scale the actions commensurate with the risk.

Strategy for regulatory compliance

Another one of the elements to be defined within the QMS is a strategy for regulatory compliance, including compliance with conformity assessment procedures and procedures for management of modifications to the devices covered by the system. The requirements under the IVDR are much more detailed than under the IVDD. To comply with these expectations, the manufacturer will need to include new processes in the QMS for device classification under the new IVDR rules, intended purpose and the definition of intended use. The new device classification, as shown in Figure 2, will determine the different types of documentation required for each device.

Figure 2: IVD Classifications

Class	Risk Profile
A	Low individual risk and low risk to public health
B	Moderate individual risk and/or low risk to public health
C	High individual risk and/or medium risk to public health
D	High individual risk and high risk for public health

The QMS needs to ensure that all required documentation and evidence will be produced in order to support the intended conformity assessment, and subsequently maintained. This should identify not only what is required for a given type of product, but also who is responsible for executing the activities necessary for registration. This is particularly key when managing shared (or partially outsourced) development and manufacturing. The change management system used subsequently needs to include adequate provisions to ensure that not only are changes managed in a controlled fashion (and adequately assessed prior to implementation) but that they are also adequately reviewed to ensure that if the change has a material impact to the registration, this is also taken into account and any notification or re-registration is performed prior to placing the modified device on the market. The manufacturer can consider developing different strategies by product class or family, product risk or business unit if the devices vary significantly.

Risk management

Risk management, based on the type of device as well as its inherent risks, is also embedded within the IVDR with the expectation that this is taken into account while structuring the QMS. For manufacturers that have more than one type of device, or devices which range across multiple classifications, this means that it is necessary to also reflect on which parts of the QMS can be scaled based on the device risk. This requires a deep understanding of both the devices and the QMS. Whenever a process has different requirements based on device classification, this should be noted and clearly expressed. A process can have specific activities or outputs that are required for Class C and D products but are not required for Class B and A.

Throughout the regulation, there is emphasis on the integration of risk management, and much of this is based on the classification of the device. Manufacturers need to always have this risk-based approach in mind when implementing the QMS, ensuring that controls and checks put into place are appropriately scaled to the risk, since a one-size-fits-all approach will not meet the expectations of efficiency and effectiveness.

As a company portfolio changes, through development or acquisition, it should be reviewed to ensure that any adaptations based on the risk of new products are taken into account.

Some specific requirements are set out in Section 3 of Annex I of the IVDR. This includes a documented process to ensure that each device has an adequate risk management plan, and that the process is continuous throughout the life cycle of the device so that the device remains safe and effective for its intended use. The reader will find that Section 3 of Annex I is substantially similar to *BS EN ISO 14971:2019, Medical devices – Application of risk management to medical devices*, with respect to the expectations of risk management. General requirements include the identification of risks, including foreseeable misuse, mitigation of those risks with preference for design reduction to eliminate the risk as far as possible and communication of any residual risks to the user. Overall, the risk has to be reduced to demonstrate that the benefits of the product outweigh any remaining risk. From a QMS perspective, the key is ensuring that risk management is a living activity throughout the product life cycle and not something done only during product conception. Manufacturers can consider using a process map or similar methodology to demonstrate all of the points where risk management is incorporated.

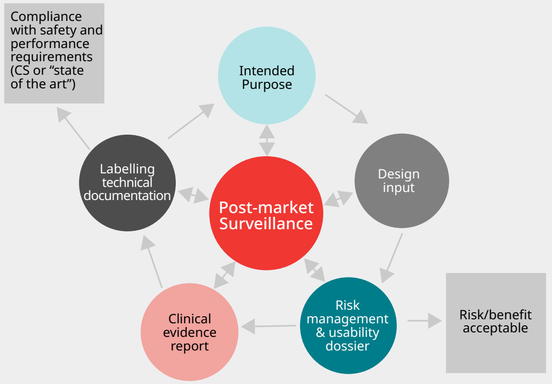
The QMS is required to identify applicable general safety and performance requirements for the products in the manufacturer’s portfolio and explore options to address those requirements. Although this is complementary to risk management activities, the IVDR specifically segregates this as a specific requirement as it goes beyond those requirements as an output of risk management. Annex I, Chapter II of the IVDR describes other aspects of this category with specific expectations for different types of devices. In order to fulfil the requirement, the QMS has to adequately identify these general requirements in each product development, where applicable, and incorporate the means to address these requirements. The QMS should provide processes to evaluate or establish these requirements from one product to the next (for example, the compliance with known standards) and provide, when possible, standardized response(s) to common requirements. The manufacturer can find value in developing an input document by product family or business unit where products share substantial similarities. Alternatively, a generic, and more encompassing list, could be presented for all products allowing each development team to select only what is applicable. The approach will depend largely on the manufacturer’s portfolio.

Performance evaluation and post-market surveillance

Performance evaluation, in accordance with Article 56 and Annex XIII of the IVDR, including the new post-market performance follow-up (PMPF) plan has to be defined within the QMS. This is another area that will have variation based on the classification of the device and should be adapted accordingly. The QMS process therefore needs to be sufficiently descriptive while allowing the necessary variation to accommodate a manufacturer's different types of devices. The PMPF will be a key element in the post-market surveillance activities. The plan can be a stand-alone document, or if it is sufficiently homogenous across a product family, can be part of the QMS as either a procedure or a template to be completed for each product. If it is intended to be a procedure, the scope of the procedure will need to be sufficiently clear to identify it as the plan. The introduction of the plan is a key indicator that the IVDR is shifting from reactive PMS (relying only on vigilance activities) to something more proactive.

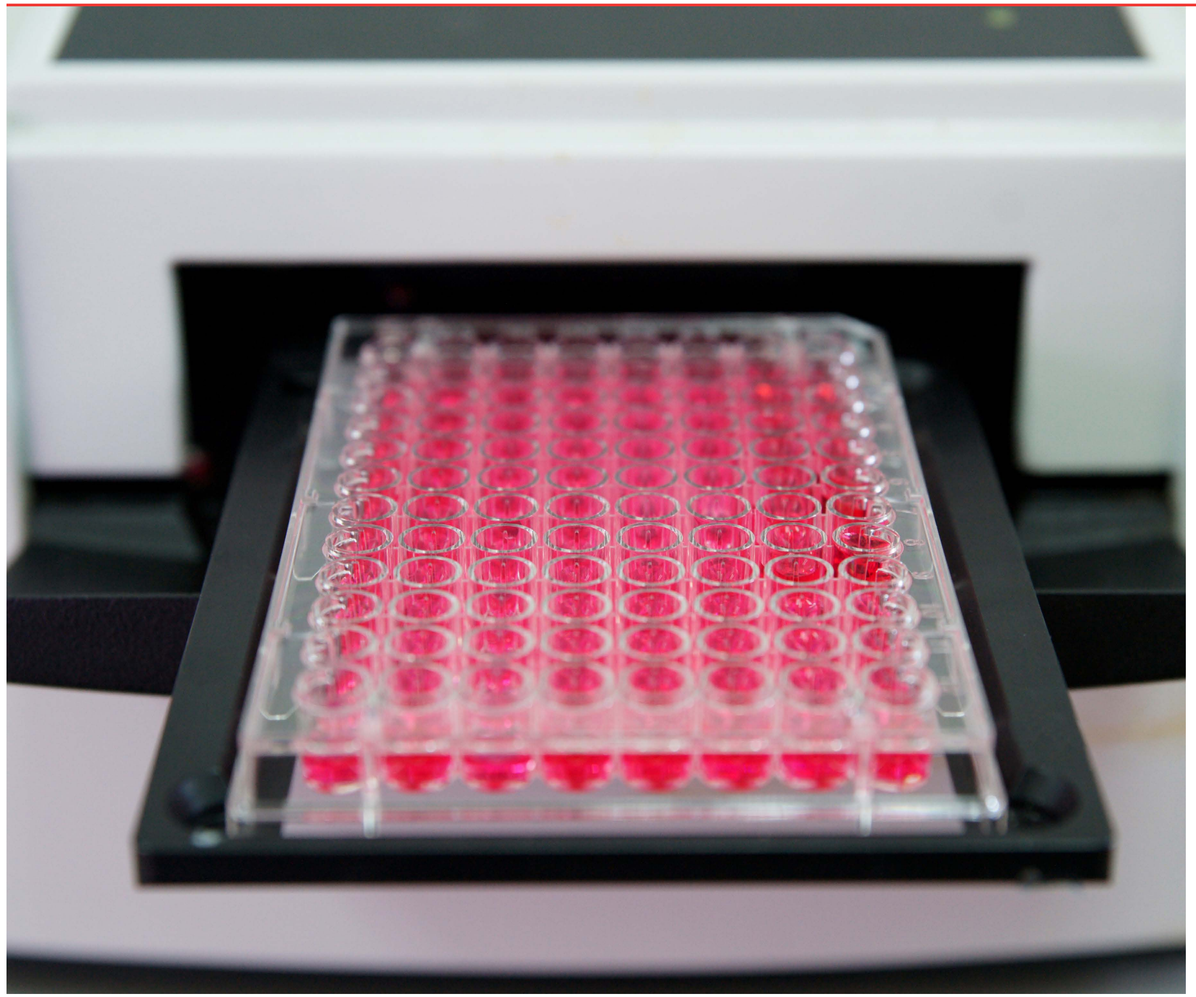
Post-market surveillance activities need to be established, implemented, and maintained in accordance with Article 78, and, as stated in the IVDR, this has to be an integral part of the QMS. Although the details of the post-market surveillance activities are not the subject of this paper, it is necessary to note that a number of links between this process and other areas of the QMS have been prescribed in the regulation, including risk management, performance evaluation, updates to the technical documentation, Corrective and Preventive Actions (CAPA), adverse event reporting and process/product monitoring. For IVDs in Classes C and D, the manufacturer is required to prepare a Periodic Safety Update Report (PSUR). Ultimately, the manufacturer needs to demonstrate that the product is compliant with all safety and performance requirements, using as reference any Common Specifications (CS) that exist or "state of the art" comparisons.

Figure 3: Post-market surveillance throughout the product life cycle



The manufacturer needs to take into account these links (as inputs, outputs or connections) to the various processes in order to ensure that they are adequately interfaced and effectively associated. A key aspect of this will be in ensuring that common terminology and references are used throughout the various files in order to maintain traceability. A common source of error can be a disconnect between early product development, before the name of the final product has been established, and the final marketed name of the product. Manufacturers must ensure that these are adequately connected, if not fully updated, in order to maintain the connection throughout the life cycle of the device.

Unique Device Identification (UDI)



Another new element in the IVDR is the implementation of Unique Device Identification for the EU. The UDI rule implemented by the IVDR is substantially similar to the US rule, but there are several differences which will require manufacturers who already have a system in place to make some modifications. As the requirement to add an UDI to each product is becoming more widespread, manufacturers need to set up a process to deal with the variations across both regions and risk classification.

From the QMS standpoint, it is important to put into place procedures and policies that cover controlling the issuance of the UDI code, verifying the quality of the printed AIDC symbols (e.g. barcodes) on labels, data management and record retention. While an issuing agency will provide the initial number range and standards for assigning the UDI number, it is up to the manufacturer to ensure that the numbers are assigned appropriately, not reused or reissued, and the appropriate records are maintained throughout the manufacturing and distribution of the device. As a large data set of information on the product will need to be synchronized with various databases such as EUDAMED (European Database on Medical Devices) and the GUDID (Global Unique Device Identifier Database in the US). There also needs to be governance around the creation, submission and maintenance of these data.
The manufacturer should clearly identify the data owners and the source of the data (creating a single source of truth for data that will be used by multiple parts of the organization), and document those responsibilities. Both the data and the UDI number will need to be incorporated into the change management process to ensure that modifications which impact the identification include the modification of the UDI and that changes of data are appropriately synchronized to the required database(s). Finally, the UDI will need to be included in post-market activities such as complaint records, medical device reporting and field actions.

Communication

The IVDR also requires the QMS to address handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders. Communication in this case has several aspects to be taken into account. The manufacturer should consider a number of factors, including the following.

- Who will receive communication (receivers) including all stakeholders?
- Who will be responsible for the communication?
- When will the communication take place?
- What will the communication contain?
- How will the communication will take place?

As communication is bi-directional, we need to consider both the recipient of the communication and the person responsible for the communication. While some recipients are evident, such as the customers or the notified body, other stakeholders need to be identified. Once all stakeholders are appropriately identified, the remainder of the communication plan can be elaborated. As roles and responsibilities have been previously discussed, it is important to identify who has the authority to communicate on behalf of the organization for each of these cases.

Considering “when” communication will take place often takes the form of deadlines for specific events, and can be dictated by regulatory constraints: for example, responding to a customer complaint within a certain number of days or filing a report with applicable authorities following a reportable event. Timing needs to be compliant, but also realistic for the overall process. The manufacturer should evaluate the full process and consider possible bottlenecks or areas where there could be delay in relaying information.

Both the content and form of the communication will need to be considered. While examining what is allowed in terms of communication, it is also important to reflect on what is not allowed. For example, a salesperson cannot communicate to a client a potential product use that is not officially documented in the approval and instructions for use. The method of communication can be supported by tools, such as a customer relationship management (CRM) tool, or be more classical methods such as telephone, email, or face-to-face visits.

When communication is done outside of a tool that maintains records, the manufacturer should evaluate if any policies for documenting the communication are required.

It is important to note that the communication plan does not necessarily need to be a stand-alone procedure, but rather may be considered as a section of each process where communication is deemed likely. The manufacturer can embed communication planning into each applicable procedure. It is also recommended to include communication aspects in job descriptions and associated training.

Vigilance activities

One area where clear communication will be of major importance is in the reporting of serious incidents and field safety corrective actions in the context of vigilance. The IVDR is clear that this process has to be adequately addressed in a manufacturer's QMS. Here it is important to note, in particular, the key deadlines, responsibilities and how reconciliation will be managed. While it is often challenging to obtain a full reconciliation of responses, manufacturers need to show their due diligence in the process with adequate attempts, using different means, to obtain a response from the customer when necessary.

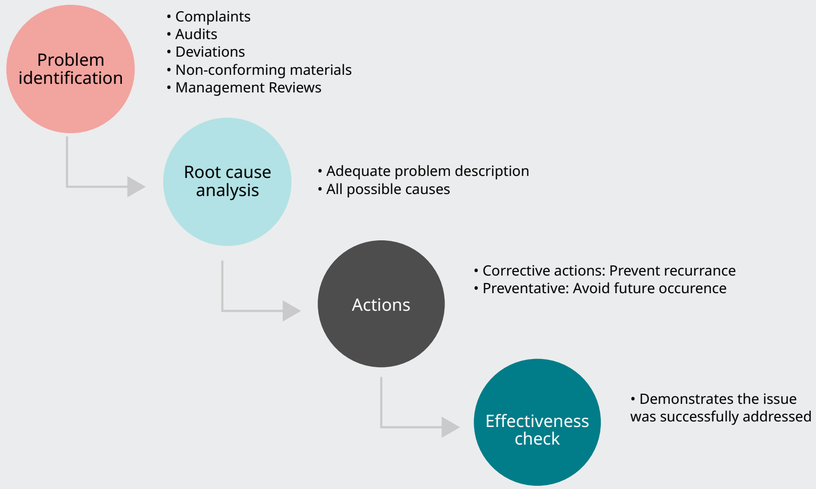
Although many large manufacturers can manage the process of local contacts in different countries through subsidiaries or distributors, it is critical to remember that the manufacturer remains responsible for the overall process. In cases where these activities are not performed by a corporate entity, ensure that these activities are included in relevant contracts or agreements and that adequate monitoring of these steps is in place. Verify not only the timeliness of the information, but also completeness. Ensure that in cases where reconciliation of responses cannot be fully attained there are adequate records demonstrating how and when contact was attempted. Finally, ensure that adequate training and records of the training are in place.

Continuous improvement activities

Corrective and preventive actions (CAPA)

While most organizations or manufacturers already have established processes for the management of corrective and preventive actions (CAPA), this is a good opportunity to review it. Key elements to consider in this process are inputs, root cause analysis, timeliness and effectiveness check. Inputs to the CAPA system can originate in many different places including, but not limited to, the complaint system, internal or external audits, internal events such as deviations or non-conforming materials/products – and management reviews. Each issue that is entered into the system needs to have an adequate problem description (what, where, when, how, how much, who) focused on facts that are verifiable. The process then needs to include a method for root cause analysis to ensure that the true cause of the event(s) is identified so that the following action(s) can adequately address the issue. Ensure that the process differentiates among corrections, which eliminate the detected nonconformity; corrective actions, which will prevent recurrence; and preventative actions, which prevent future occurrence.

Figure 4: High level CAPA process



A good CAPA system will be managed in a timely manner. Timelines given should be appropriate to the issue, commensurate with the risk and attainable. Different CAPAs can require different lengths of time to implement depending on the complexity and the risk of the issue. While it is a good idea to establish a standard for timelines, it is also wise to ensure that the standards accommodate more complex or long-term issue correction. As a final step of the process, an effectiveness check of the actions needs to be included. The period for the effectiveness check should be established based on the issue itself. It should be long enough to objectively demonstrate that there has not been an additional occurrence of the issue. If an effectiveness check fails, and particularly if there are routine failures of the effectiveness check, it can be a sign that the root cause analysis was not adequately performed or that not all root causes were identified. The reason that the action was not effective should be analysed and documented.

While the CAPA system is part of a manufacturer's efforts toward continuous improvement, something that is mentioned multiple times in the IVDR for both products and processes, it is not alone sufficient to demonstrate continuous improvement as an ongoing activity. Another such continuous improvement requirement found in the list of items to include in the QMS is that the manufacturer has processes for the monitoring and measurement of output, data analysis and product improvement. This should include a system of Key Performance Indicators (KPIs) or metrics to monitor the health and effectiveness of the QMS as well as product performance. Some basic indicators for the QMS itself can be deviations from the QMS (indicating that a process is difficult to follow), internal or external findings for noncompliance to a specific portion of the QMS, or parts of the QMS routinely identified in the root cause analysis for any types of failures. Product indicators tend to be more evident in items like complaints, recalls, scraps or rework.

Key Performance Indicators

As organizations or manufacturers generate more and more data, it is important that the indicators chosen are representative and useful in driving the desired changes. Measuring too many data points will lead to an overload of data, which is not exploitable, as well as significant time and energy in trying to gather and process this data. Measuring too few data points can result in inadequate information to monitor the process or product. Finally, be sure that what is being measured is clear. For timeliness measures, ensure that everyone is aligned on the starting and ending point of the measurement and that it includes enough of the process to be meaningful. For long processes, or processes which involve multiple departments or entities, it is often useful to have an overall timeliness measurement as well as some “sub-process” measurements specific to departments.

Defined KPIs drive the desired results. Avoid metrics that drive behaviours that are not desirable. For example, if only the timeliness of effectiveness checks are measured, it could drive employees to close the effectiveness check only based on the calendar and not based on when enough data are available to adequately resolve the problem. This can, in itself, lead to additional recurrences of avoidable problems. Similarly, the data analysis needs to be meaningful and representative. A organization or manufacturer could use as an indicator the number of complaints which, in itself, is quite important. However, as the sales volume increases, the number of complaints can also increase. This is not necessarily indicative of a problem as long as the ratio of complaints to sales remains consistant. Just as the QMS should cover all parts of the organization, so too should the data analysis. Data should also be collected externally as well, as noted in the post-market surveillance requirements. When considering each key process, include KPI requirements; indicate the kind of data that should be collected, how it should be used and the target results.

Gathering and analysing data alone is not adequate. Manufacturers need to demonstrate that they are implementing actions based on this data. Management reviews, which should be held at least annually but can be needed more often depending on the manufacturer’s situation, should be using the data collected to monitor the overall health of the QMS and the products. The data reviewed, as well as discussions on the data trends, should be documented. Appropriate actions should be implemented in accordance with the data observed. If a CAPA or product improvement is initiated as a result of one of the trends, ensure that the associated records indicate the data that were at the origin of the initiative to demonstrate that the data are being used. Much as CAPAs are required to have an effectiveness check, there should also be routine monitoring to ensure that product improvements that were made did have the desired results on the data. The UDI can be used, in case of significant change, to compare data trends before and after the improvement process, effectively demonstrating that there is an effective process for product improvement based on product data and feedback. If data are presented that is routinely non-actionable, then it is a good indication that the data are either not necessary or not measuring the right output. Reconsider collecting any data which are not routinely used to make decisions and remember to update the metrics accordingly when changes to either product or process are introduced.

Taking action

During the conformity assessment, not only will the manufacturer be required to submit the documentation on the QMS itself in addition to the technical documentation, but they will also be required to submit a description of the procedures and how those fulfil the regulation. Note that the conformity assessment process varies by risk classification and Class A devices do not require a conformity assessment by a notified body.

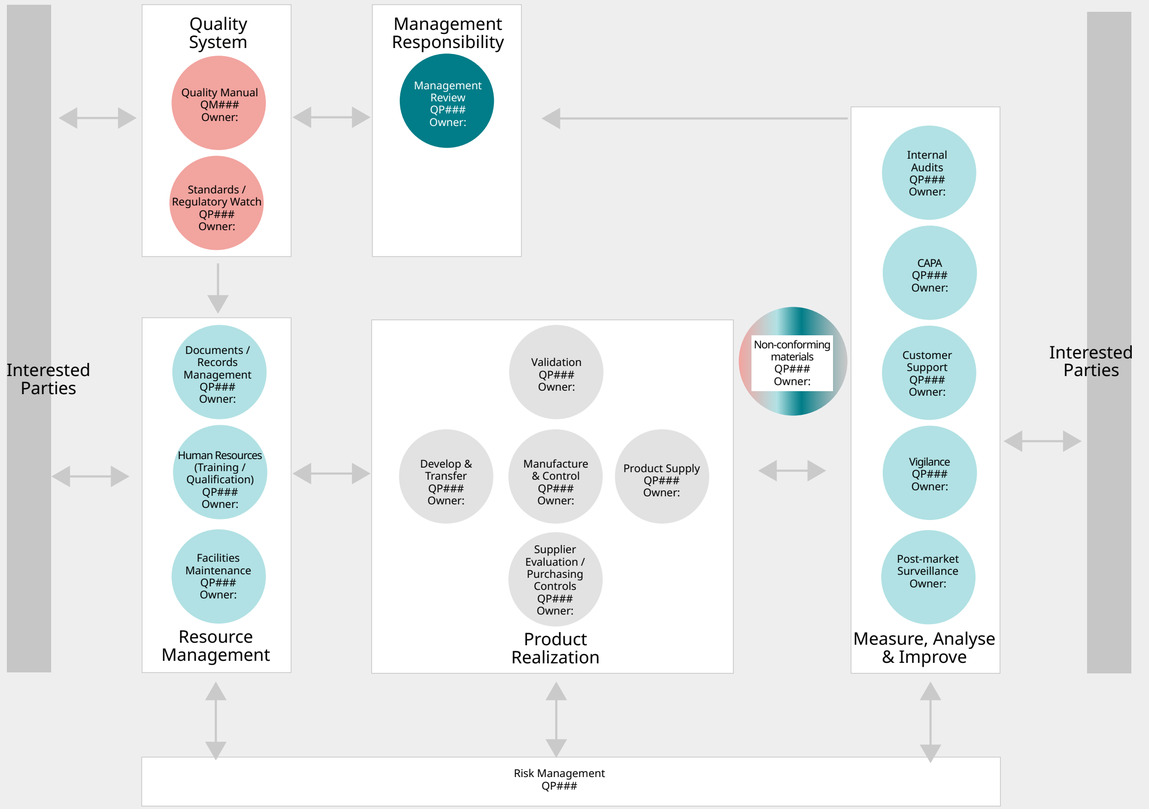
Conformity assessments

As part of Annex IX, Conformity Assessment, the following documentation, among others, is specifically required to be submitted to the notified body with respect to the QMS:

- the documentation on the manufacturer's quality management system;
- a documented description of the procedures in place to fulfil the obligations arising from the quality management system and required under this regulation and the undertaking by the manufacturer in question to apply those procedures; and
- a description of the procedures in place to ensure that the quality management system remains adequate and effective, and the undertaking by the manufacturer to apply those procedures.

With these requirements in mind, it is in the manufacturer's interest to prepare an overview of the QMS demonstrating how the QMS maps to the regulation and fulfils the outlined requirements. Some possible presentations for this information can include process maps documenting the end-to-end process employed by the organization with relevant procedures named or a traceability matrix identifying the key requirements of the IVDR with their deliverables and relevant procedures noted.

Figure 5: Example process map



In the third bullet point (see above), we find again the requirement to have a procedure to ensure that the QMS remains adequate and effective. This is explicit in requiring that there is a process by which the QMS will continue to evolve and adapt to changing circumstances, internal and external, that require continued growth. The emphasis, once again, is not in having a perfect QMS, but rather one that is able to continue to improve and grow over time.

The last part of both the second and third bullet points is also quite important to note: “the undertaking by the manufacturer to apply those procedures”. It is critical to demonstrate not only that adequate procedures are in place, but that those procedures are applied. Manufacturers need to keep in mind this requirement as the procedures are authored. What type of documentation can be provided as objective evidence that the procedure is being applied? Meeting minutes, reports and other concrete documentation that are a natural by-product of the process can all be effective in meeting the requirements for objective evidence necessary. It is useful to define these records in building each process.

Transitioning from IVDD to IVDR

Transitioning from IVDD to IVDR

The transition period for the IVDR has now begun. The initial timeline for date of application, on 26 May 2022 (after which, no new IVDD certificates can be issued), has been *partially* extended to allow manufacturers to continue to sell “legacy” devices already placed on the EU market for up to an additional 5 years, depending on the risk class, as long as no significant changes are made to the device design or intended purpose. Any new devices placed on the market will need to conform to the revised rules of the IVDR. However, all devices, including legacy devices, must immediately conform to post-market surveillance, vigilance, registration of economic operators and of devices from the original date of application (i.e. 26 May 2022). It is also important to note that the Mutual Recognition Agreements between the EU and Switzerland and the UK have been impacted. The QMS will need to be updated to reflect these changes as well, including, but not limited to, references to the appropriate regulations (e.g. in Switzerland the Ordinance on In Vitro Diagnostic Medical Devices or IvDO) and the UK Conformity Assessment mark, appropriate Authorized Representatives, and other related changes.

Manufactures who already have a QMS in place have to make a decision on how to handle this extended transition. During the next few years, they will need to begin to submit new products under the new regulation and therefore under a fully updated QMS, taking into account all of the requirements discussed above. At the same time, they will need to determine whether the updates to the QMS will apply to all existing products or only to those registered under the new IVDR. While some clauses, such as communication plans or updated responsibilities, can take effect immediately, other parts of the QMS could need to be applied in a product by product approach, such as UDI changes, while others, such as those for post-market surveillance, must take effect immediately for all products. There are different options to consider when taking this into account.

One option is to see this as an opportunity to create a new, parallel QMS that is optimized for the new IVDR with a defined progression from the old to the new system. This parallel QMS system has the advantage of allowing each file to refer to the appropriate procedures, as well as making very clear that the new system is in place. For organizations with a long history, and a complicated QMS, this could be the opportunity to dramatically simplify the structure of the QMS, ensuring a higher efficiency, rather than adding on to existing layers. However, it does involve significant overhead and management to create and later abolish the old procedures. It may also create confusion for employees faced with two sets of processes.

Another option is to update existing QMS documents to meet new requirements. This would likely be the preferred option for organizations who do not have a tremendous gap between their existing QMS and the new requirements found in the IVDR. The disadvantage of this approach is having parts of the QMS in effect that cannot be applied to all products at the same time and, in some cases, several options within a procedure to clarify devices that are pre- or post-transition.

With either approach, a transition needs to be documented to determine what is applicable, at what moment, and to which products. This progression can be defined within the procedures themselves, for example as part of the scope indicating that the procedure or record only applies to products registered under the IVDR, or it can be defined in a separate project plan which clarifies which procedures are immediately applicable and which become applicable only upon product registration. Whichever approach is used, it is critical that everyone using the procedures understands how and when to apply new aspects of the QMS. Training to the new requirements will be imperative. Finally, it is important to remember that this change to the QMS is likely to be considered “substantial” and should be clearly communicated with the notified body as well as following the established Change Control process.

QMS simplicity

All of the expectations listed above could result in a significant number of documents (procedures, forms, records) which will, in the long run, make it difficult to maintain the QMS in line with expectations. It is necessary to structure the QMS in such a way that it maintains its usefulness, flexibility and clarity while fulfilling all of the requirements. An overly complex QMS will result in non-conformities because the procedures conflict or the team is not able to remember and implement all of the documents in the quality system. To overcome this, a manufacturer can apply several tools to help structure their QMS. Creating process maps to highlight interfaces, key actors and the associated requirements will facilitate the creation of the documented procedures. Building trace matrices, either manually or using an electronic system containing the procedures, regulations, and claimed standards, will help ensure that everything is covered and can highlight redundancy that can be removed. Not only can these be used as tools to help facilitate the review by the notified body, potentially shortening the review period and reducing the number of questions, but they can also be a valuable internal tool to help maintain the QMS.

Having an embedded traceability provides a point for verification prior to making changes to the QMS. With the built-in traceability, the manufacturer can check that the intent of the regulation is still fulfilled prior to implementing changes, avoiding removing something that is required by the regulation.

Figure 6: Example document traceability matrix

Document Map	QMS				
ISO 13485:2016	4.1.1	4.1.2	4.1.3	4.1.4	4.1.5
IVDR	10.8	10.8	10.8	10.8	10.8
Quality manual QM###	X	X	X	X	X
Standard & Reg Watch QP###	X			X	
Document Records Management QP###	X		X	X	
Risk Management QP###		X		X	

Conclusion

In spite of all of the regulations and requirements, it is important to focus on the end goal of the QMS, which is to have a method in place that allows the manufacturer to deliver a safe and reliable product to customers that meets their needs on-time, every time. Throughout the implementation and maintenance of the QMS, it is important to ensure that the goals remain aligned with those of the business. The IVDR is an opportunity to take an objective look at the QMS to ensure that it meets the business goals while delivering all of the elements necessary for compliance. In particular, under the IVDR, the QMS needs to contain at least:

- a strategy for regulatory compliance
- identification of applicable general safety and performance requirements
- management responsibility
- resource management, including selection and control of suppliers and sub-contractors
- risk management
- performance evaluation, including PMPF
- product realization, including planning, design, development, production and service provision
- verification of the UDI assignments
- setting-up, implementation and maintenance of a post-market surveillance system
- handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders
- processes for reporting of serious incidents and field safety corrective actions in the context of vigilance
- management of corrective and preventive actions and verification of their effectiveness
- processes for the monitoring and measurement of output, data analysis and product improvement.

Remember, the QMS is in place to support the business to achieve its goals and not as an entity on its own.

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