



Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

Title: Quality Management System –Medical Devices–
Guidance on the Corrective Action and Preventive
Action and Related QMS processes

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Preface

The document herein was produced by the Global Harmonization Task Force, a voluntary group of representatives from medical device regulatory agencies and the regulated industry. This document was developed with participation from AHWP regulatory and industry representatives.

The document is intended to provide non-binding guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Introduction

This guidance document is intended for medical device manufacturers and regulatory authorities. It is intended for educational purposes and is not intended to be used to assess or audit compliance with regulatory requirements. It is expected that the reader is familiar with regulatory Quality Management System (QMS) requirements within the medical devices sector.

For the purposes of this document it is assumed that the medical device manufacturer has a QMS which requires the manufacturer to have documented processes to ensure that medical devices placed on the market are safe and effective. For example ISO13485 Medical Devices – Quality Management Systems – Requirements for regulatory purposes, Japanese Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and in vitro Diagnostics (MHLW¹ Ministerial Ordinance No. 169), the FDA² Quality System Regulation 21 CFR Part 820 or the respective quality system requirements of the European medical Device Directives.

For this purpose the manufacturer will establish processes and define appropriate controls for measurement and analysis to identify nonconformities and potential nonconformities. Also, the manufacturer should establish processes defining when and how corrections, corrective actions, or preventive actions should be undertaken. These actions should be commensurate with the significance or risk of the nonconformity or potential nonconformity.

The terms risk, risk management and related terminology utilized within this document are in accordance with ISO 14971 “Medical Devices-Application of Risk Management to Medical Devices.”

The acronym “CAPA” will not be used in this document because the concept of corrective action and preventive action has been incorrectly interpreted to assume that a preventive action is required for every corrective action.

¹ Japanese Ministry of Health Labor and Welfare

² US Food and Drug Administration

This document will discuss the escalation process from different “reactive” sources which will be corrective in nature and other “proactive” sources which will be preventive in nature. The manufacturer is required to account for both types of data sources whether they are of a corrective or preventive nature.

Regardless of the nature of the data source, if there is a decision to escalate the information to further evaluation and investigation, the steps of investigation, identification of root causes and actions needed, verification, implementation, and effectiveness checks will be similar.

This guidance document will describe measurement, analysis and improvement as complete and integrated processes.

1.0 Scope

This document provides guidance for establishing adequate processes for measurement, analysis and improvement within the QMS as related to correction and/or corrective action for nonconformities or preventive action for potential nonconformities of systems, processes or products.

2.0 Definitions

The references to clauses in this section refer to ISO 9000:2005.

2.1 Correction

Action to eliminate a detected nonconformity (3.6.2)

Note 1 A correction can be made in conjunction with corrective action (3.6.5)

Note 2 Corrections can be, for example, rework (3.6.7) or re-grade (3.6.8)

2.2 Corrective action

Action to eliminate the cause of a detected nonconformity (3.6.2) or other undesirable situation

Note 1 There can be more than one cause for nonconformity

Note 2 Corrective action is taken to prevent recurrence whereas preventive action (3.6.4) is taken to prevent occurrence

Note 3 There is a distinction between correction (3.6.6) and corrective action

2.3 Data Sources

The processes within a Quality Management System that provide quality information that could be used to identify nonconformities, or potential nonconformities

2.4 Concession

Permission to use or release a product that does not conform to specified requirements (3.6.11).

2.5 Preventive action

Action to eliminate the cause of a potential nonconformity (3.6.2) or other undesirable situation

Note 1 There can be more than one cause for nonconformity

Note 2 Preventive action is taken to prevent occurrence whereas corrective action (3.6.5) is taken to prevent recurrence

2.6 Nonconformity

Non fulfillment of a requirement (3.1.2)

2.7 Verification

Confirmation through provision of objective evidence (3.8.1) that specified requirements (3.1.2) have been fulfilled

Note 1 The term “verified” is used to designate the corresponding status.

Note 2 Confirmation can comprise activities such as:

- performing alternative calculations,
- comparing a new design specification (3.7.3) with a similar proven design specification, undertaking tests (3.8.3), performing demonstrations, and reviewing and approving documents prior to issue.

2.8 Validation

Confirmation through provision of objective evidence (3.8.1) that the requirements for a specific intended use or application have been fulfilled

Note 1 The term “validated” is used to designate the corresponding status.

Note 2 The use conditions for validation can be real or simulated.

3.0 Overview

The manufacturer is responsible for the implementation and maintenance of a QMS which enables their organization to provide safe and effective medical devices meeting customer and regulatory requirements.

A nonconformity as defined in 2.6 is a non fulfillment of a requirement. It is important to understand that requirements may relate to product, process or the QMS.

When a nonconformity is identified, the manufacturer will determine the significance, the associated risk and the potential for recurrence.

Once these have been determined the manufacturer may decide the nonconformity has little associated risk or is unlikely to recur. In such cases the manufacturer may decide only to carry out a correction.

Should the nonconformity recur within the QMS, during manufacture or after the medical device has been delivered to a customer, it is an indication that improvement action(s) may be needed. In either case the QMS requires that a corrective action should be carried out with the aim to prevent recurrence. The corrective action may be as simple as retraining, or as complex as redesigning the manufacturing process.

The manufacturer may encounter situations that have not actually caused a nonconformity, but may do so in the future. Such situations may call for preventive action. For example, production or acceptance testing trend data indicates that control limits are being approached and revision of product or production (process, equipment or facilities) requirements may be necessary. These revisions could constitute a preventive action. Preventive action would not include planned process adjustments intended to return process performance to nominal values from the edges of the process control range.

Actions taken to eliminate observed nonconformities within the scope of a single QMS (regardless of whether the actions are taken at more than one site or facility operating within that QMS) would be considered corrective actions. However, similar actions applied within another QMS (regardless of whether it is the same site, facility, or organization) that has not yet experienced these nonconformities, would be considered preventive actions.

Figure 1 illustrates typical Phases to be considered when planning, implementing and maintaining effective processes for measurement, analysis, improvement and providing input to management. See Annex A for a list of possible activities corresponding to the phases in Figure 1.

As a check on the effectiveness of the processes defined, management should regularly review the outputs of processes and make adjustments as needed.

Documented procedures, requirements and records should be maintained by the manufacturer to ensure and demonstrate the effective planning, operation and control of the processes. Documented evidence of decisions and actions taken will be a part of the QMS.

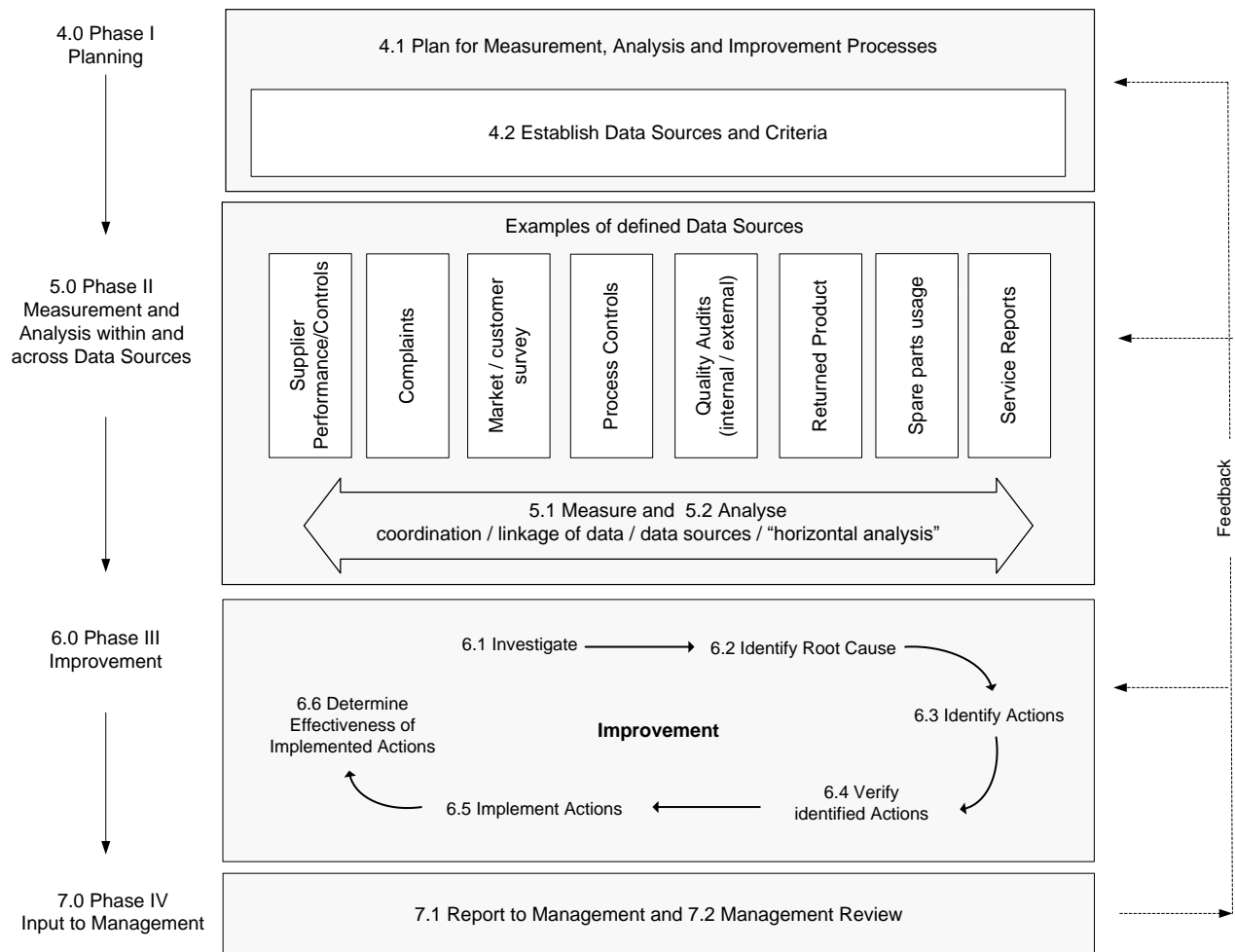


Figure 1: Processes for measurement, analysis and improvement

4.0 Phase I: Planning

Planning involves specifying processes and associated resources in order to meet specific objectives. Factors to consider during the planning phase should be aligned with the manufacturer's overall business planning and include the device's intended use, markets and users, as well as regulatory requirements.

The involvement of management at appropriate levels (e.g. review, approval) in actions taken in response to nonconformities or potential nonconformities should be established. Management should ensure that measurement criteria are defined for identified data sources and communicated across the organization.

4.1 Plan for Measurement, Analysis and Improvement Processes

Factors to consider during this planning phase should be aligned with the manufacturer's overall business planning and as a minimum include the type of device being manufactured, intended markets and users, and regulatory requirements. As part of planning, management should review the processes critical to the operations with regard to quality and regulatory requirements and select relevant data sources to measure, analyze and facilitate improvement as necessary.

In the process of planning measurement and analysis, a manufacturer needs to take into account data sources, the measurement of the data elements within each data source, the frequency of monitoring, and the analysis to be performed within a data source, or across data sources.

The measurement of data elements should be done in a way that ensures the manufacturer is effective in managing the operations and maintain an effective QMS. Each of the data elements should be planned and established with specific requirements for measurement that are monitored routinely.

The scope of the QMS and the scope of the measurement, analysis and improvement processes will provide the boundaries as to whether the data source is reactive/corrective or proactive/preventive.

The planning phase should ensure the following:

- Identification of relevant internal and external data sources that are indicators of process and product performance.
- Provision for adequate resources and establish responsibilities and authorities to enable the necessary actions. Resources may include technical experts, testing laboratories, data management, infrastructure, training, etc.
- Definition of requirements for each identified data source, including limits, acceptance criteria, escalation criteria and mechanisms for reporting of nonconformities or potential nonconformities.
- Analysis of data elements within data sources.
- Coordination and analysis of data across data sources.

For each data element individual criteria should be defined; however, criteria may be defined for a combination of data elements. Criteria should be quantitative whenever possible in order to maximize consistency and reproducibility for subsequent analysis. If the criteria and data are qualitative, subjectivity should be eliminated or minimized.

Acceptance criteria should be based on system, product and process specifications or requirements which are typically identified during design and development activities. This includes the design of the Quality Management System, development and maintenance of assembly processes, delivery processes, servicing and installation processes.

Escalation criteria used for the purpose of initiating the improvement process (see 6.0) may often be called action levels, trigger points, thresholds, etc. These escalation criteria should be proceduralized and would likely include certain generic action levels as well as specific action levels resulting from risk management activities. In particular, criteria should be established for imme-

diate escalation. For example, an incident alleging a death or serious injury should be escalated to the improvement phase (see 6.0) for immediate action.

For new technology and existing technologies with new intended uses/applications, initial escalation criteria may be difficult to define for the monitoring process. Therefore a manufacturer should plan for resources to analyze information in order to confirm initial assumptions and establish or revise escalation criteria.

Planning should provide for confirmation that the defined limits, acceptance criteria, escalation criteria and mechanisms for reporting of nonconformities or potential nonconformities for the original data sources and data elements are still appropriate. Where new data sources need to be established, confirm that they have been identified and their criteria defined.

4.2 Establish Data Sources and Criteria

The manufacturer should identify and document relevant data sources and their data elements, both internal and external to the organization. Data elements provide information regarding nonconformities, potential nonconformities and the effectiveness of the established processes within the data sources.

Examples of data sources can be, but are not restricted to:

- Regulatory Requirements
- Management Review
- Supplier (performance/controls)
- Complaint Handling
- Adverse Event Reporting
- Process Controls
- Finished Product
- Quality Audits (internal/external)
- Product Recall
- Spare Parts Usage
- Service Reports
- Returned Product
- Market/Customer Surveys
- Scientific Literature
- Media Sources
- Product Realization (design, purchasing, production and service and customer information)
- Risk Management

For further examples of data elements see Annex B.

When an issue is identified in one of the data sources, it is also important that the manufacturer identify and review related information from other data sources across the organization. Furthermore a review of information from external data sources should also be considered. The aggregation of information from more than the original data source may lead to more comprehen-

sive knowledge. With this knowledge base a manufacturer will be positioned to better determine appropriate action.

5.0 Phase II: Measurement and Analysis within and across Data Sources

Once data sources, data elements and acceptance criteria have been specified, as part of the planning process, the manufacturer is required to perform measurement, monitoring and analysis processes to determine conformity or nonconformity.

Software used in measurement, monitoring and analysis, whether purchased (Off-The-Shelf) or custom developed, should be validated for its intended use.

For example, a customer survey conducted by the marketing department, indicated that there was a general dissatisfaction with the packaging of product X. When investigated further (within and across other data sources) and reviewed with other data from complaints, returned product and service reports, it became evident that there was a potential for misuse, unsafe use, or damage to the device as a result of the current packaging design. As the result of this analysis, escalation to Phase III (see 6.0) for preventive action may be appropriate.

5.1 Measure

For the purpose of this guidance, measurement is a set of operations to determine a value of a data element (i.e. quantity, quality).

Data collected from the measurement of product, process and QMS are acquired throughout the life-cycle of the product. The manufacturer should define for example frequency of the measurement, precision and accuracy of the data. The manufacturer should also ensure that the data collected is current and relevant.

Measurement data should be retained as a quality record. The manufacturer should maintain the data in a form that is retrievable, suitable for analysis and meets both QMS and regulatory requirements.

Monitoring is the systematic and regular collection of a measurement. The manufacturer should define during the planning phase what, when and how data should be monitored. The data should be defined such that it can be analyzed for further action. The monitoring of data may be continuous or periodic, depending on the type of data source and elements. The monitoring processes should be periodically reviewed for their continued suitability.

5.2 Analyze

For the purpose of this guidance, analysis is a systematic review and evaluation of data from measurements to derive a conclusion.

The manufacturer should have documented procedures for the analysis of data against the established criteria (see 4.1). Analysis is performed to identify nonconformity or potential nonconformity or identify areas where further investigation should be initiated. In addition analysis is used to demonstrate the suitability and effectiveness of product, process and QMS. Analysis can be performed utilizing analytical tools, a team of experts, process owners or independent reviewers. The results of the analysis should be documented.

After it is determined what will be measured, statistical techniques should be identified to help understand variability and thereby help the manufacturer to maintain or improve effectiveness and efficiency. These techniques also facilitate better use of available data to assist in decision making. Statistical techniques assist in identifying, measuring, analyzing, interpreting and modeling variability.

For the analysis of nonconformity, appropriate statistical and non-statistical techniques can be applied. Examples for statistical techniques are:

- Statistical Process Control (SPC) charts
- Pareto analysis
- Data trending
- Linear and non-linear regression analysis
- Experimental design (DOE – Design of Experiments) and analysis of variance
- Graphical methods (histograms, scatter plots, etc.)

Non-statistical techniques are for example:

- Management reviews
- Results from quality meetings
- Safety committees (internal/external)
- Failure Mode and Effect Analysis (FMEA)
- Fault Tree Analysis (FTA)

Analysis will likely occur at several different points (time and/or organizational level). For example, a certain amount of analysis and possible failure investigation (where there is evidence of a nonconformity) will occur for each data source.

In addition to the analysis within the data sources there should also be a level of analysis across data sources to determine the extent and significance of nonconformity or potential nonconformity. The linkage of data from different data sources will be referred to as “horizontal analysis”.

The horizontal analysis may:

- determine that the action proposed from the data source analysis is appropriate without further progress into Phase III (see 6.0); or,
- provide additional information warranting progress into Phase III (see 6.0), regardless of whether the data source analysis escalated the nonconformity or potential nonconformity.

The outcome of measurement and analysis leads to different scenarios as shown in Figure 2.

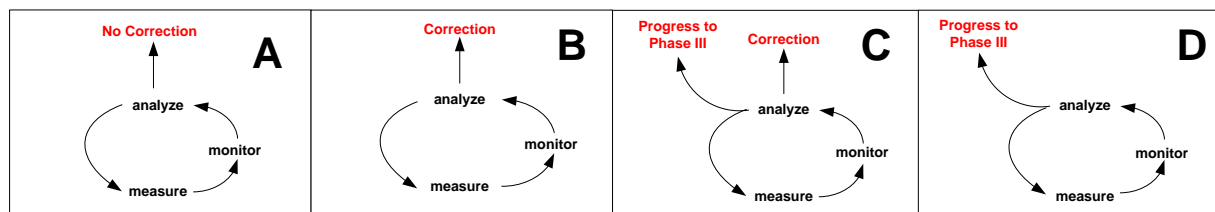


Figure 2: Outcomes of measurement and analysis

The following tables provide more details to support the use of Figure 2. Each scenario is described with an example showing the different outcome of measurement and analysis.

Basic Example	The documentation requirements in a research design and development procedure were not followed. The missing documentation involves changing to a different supplier of an electronic board. The requirement is to document the supplier name and supplier number in the research report.
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Scenario A	No correction required, continue measurement and monitoring The decision is made not to take any correction nor escalate the handling of the nonconformity to Phase III (see 6.0).	
Example	Nonconformity	The supplier number was not included in the research report. (however, the supplier name is documented).
	Key Results of Measurement and Analysis	Analysis indicates that the procedure is adequate and well known to the users of the research procedure. Following a review of the issue this appears to be a one time oversight. The intent of the requirement is for convenience only.
	Conclusion	No initial correction - It is not necessary to update the research report, as the supplier is documented by name, hence traceability is maintained. Do not escalate to Phase III.

Scenario B	Correction required, continue measurement and monitoring The decision is made to perform a correction but not to escalate the handling of the nonconformity to Phase III (see 6.0).	
Example	Nonconformity	The supplier name and number was not included in the research report.
	Key Results of Measurement and Analysis	Analysis indicates that the procedure is adequate and well known to the users of the research procedure. Following a review of the issue this appears to be a one time oversight. The intent of the requirement is to ensure traceability to the supplier and this could be lost if the research report is not updated.
	Conclusion	Take an initial correction to update the research report with the supplier name and number. Do not escalate to Phase III.

Scenario C	Correction and escalation to further investigation under the improvement phase. The decision is made to perform an initial correction. However, there is a need for escalation to Phase III (see 6.0) to further investigate as a result of the analysis performed in order to determine the appropriate corrective action.	
Example	Nonconformity	The supplier name and number was not included in the research report.
	Key Results of Measurement and Analysis	Analysis indicates that the procedure may not be adequate and it is not well known to the users of the research procedure. The issue has been identified in multiple reports. In some cases, traceability to the supplier could be established via other means, and in other cases it could not.
	Conclusion	Take an initial correction to update the research report with the supplier name and number (in the cases where the supplier could be identified). Escalate to Phase III for corrective action.

Scenario D	Escalation for further investigation under the improvement phase. The decision is made that there is not enough information at this time to determine the required action. Therefore the investigation is escalated to Phase III.	
Example	Nonconformity	The supplier name and number was not included in the research report.
	Key Results of Measurement and Analysis	Analysis indicates that the procedure may not be adequate and it is not well known to the users of the research procedure. The issue has been identified in multiple reports. Traceability to the supplier could not be established via other means in any of the cases.
	Conclusion	No initial correction - The supplier is not known so an initial correction cannot be taken at this time. Escalate to Phase III for corrective action.

Documented procedures should clearly delineate and define when escalation to Phase III is required.

Typically manufacturers have organizational groups or processes surrounding some of their main data sources (e.g. complaint handling, handling of nonconformities, material review boards, change management process). Within these groups or processes certain activities described in Figure 2 can be implemented without escalation.

There may be predefined events that due to the significance of the risk will be escalated to Phase III without any delay that can not be justified. In the event a potential nonconformity is identified, it may be escalated into Phase III (see 6.0) for consideration of actions to prevent the occurrence of the potential nonconformity.

When no correction or only corrections within these groups or processes are taken, there needs to be data source monitoring and analysis (e.g. trending) to determine if escalation to Phase III may be necessary from accumulated information. Whenever an issue is escalated to Phase III, any information gained within the defined activities of these groups or processes should be an input to the Phase III activities such as Investigation (see 6.1) or Identified Actions (see 6.3).

6.0 Phase III: Improvement

The improvement phase of a corrective action process or preventive action process is designed to eliminate or mitigate a nonconformity or potential nonconformity.

The improvement activities are dependant on the specific nonconformity or potential nonconformity. Any previous data from Phase II should be utilized as input to the Phase III process.

The improvement phase and the activities described in Figure 3 needs to be documented. Improvement generally involves the following activities that the manufacturer would take sequentially or sometimes simultaneously:

- A thorough investigation of the reported nonconformity
- An in-depth root cause analysis
- Identification of appropriate actions
- Verification of identified actions
- Implementation of actions
- Effectiveness check of implemented actions

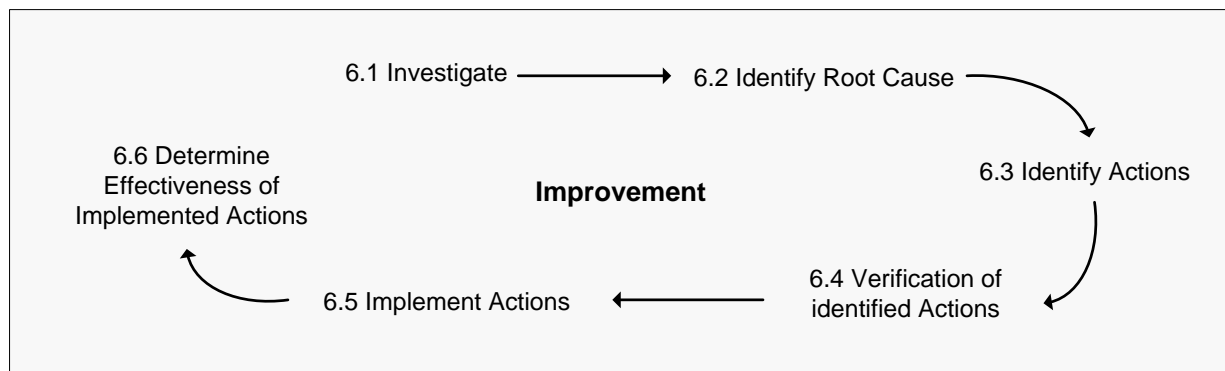


Figure 3: Phase III – Improvement

6.1 Investigate

The purpose of investigation is to determine the root cause of existing or potential non – conformities, whenever possible, and to provide recommendations of solutions. The magnitude/scope of the investigation should be commensurate with the determined risk of the nonconformity.

Good practice shows that a documented plan should be in place prior to conducting the investigation (see Annex D for examples). The plan should include:

- Description of the nonconformity expressed as a problem statement
- Scope of the investigation
- Investigation team and their responsibilities
- Description of activities to be performed
- Resources
- Methods and tools
- Timeframe

From the information obtained throughout the process the problem statement should be reviewed and refined as appropriate.

The investigation should:

- Determine the extent of the nonconformity or potential nonconformity
- Acknowledge that there are likely to be several causes of an event; hence, the investigation should not cease prematurely
- Require that symptoms be distinguished from root causes and advocate the treatment of root causes rather than just the symptoms
- Require that an end point be defined for the investigation. An overly exhaustive investigation may unduly delay the correction of non-conformity or unnecessarily incur additional cost. (For example, if removal of the causes identified so far will correct 80% of the effects then it is likely that the significant causes have been identified (Pareto rule))
- Take into account the output of relevant risk management activities
- Agree on the form of evidence. For example, evidence should support:
 - the seriousness of the event
 - the likelihood of occurrence of the event
 - the significance of the consequences flowing from the event

The investigation should include the collection of data to facilitate analysis and should build upon any analysis, evaluation and investigation that were previously performed (see 5.0). This will require the investigator to identify, define and further document the observed effects/non-conformity, or already determined causes, to ensure that the investigator understands the context and extent of the investigation. It may be necessary to:

- Review and clarify the information provided
- Review any additional information available from an horizontal analysis
- Consider whether this is a systemic issue/non-systemic issue
- Gather additional evidence, if required
- Interview process owners/operators or other parties involved
- Review documents
- Inspect facilities, or the environment of the event

Previous investigations should be reviewed in order to determine if the event is a new problem or the recurrence of a previous problem where, for example, an ineffective solution was implemented. The following questions will assist in making the determination:

- Is the nonconformity from a single data source?
- Does the current nonconformity correlate with nonconformities from other data sources?
- Are multiple data sources identifying the same nonconformity?
- Do other nonconformities have an effect on the problem investigated here?

Many of the tools used in investigations rely upon a cause and effect relationship between an event and a symptom of that event. To ensure that causes are identified, not symptoms, the following should be considered:

- There must be a clear description of a cause and its effect. The link between the cause and the undesirable outcome needs to be described.
- Each description of a cause must also describe the combined conditions that contribute to the undesired effect

A failure to act is only considered a cause if there was a pre-existing requirement to act. The requirement to act may arise from a procedure, or may also arise from regulations, standards or guidelines for practice, or other reasonably expected actions.

Some of the more common tools and techniques include:

- Cause and effect diagrams
- 5 Why's analysis
- Pareto charting
- Fishbone/Ishikawa cause and effect diagrams
- Change analysis
- Risk analysis techniques
- Is/Is Not

The outcome of an investigation should include:

- Clearly defined problem statement
- What information was gathered, reviewed and/or evaluated
- Results of the reviews/evaluations of the information
- Identification of cause(s) or contributing factors
- Solutions to address the cause(s) or contributing factor(s)

6.2 Identify Root Cause

Causes or contributing factors of detected nonconformity or potential nonconformity should promptly be identified so that corrective action can be taken to prevent recurrence, or preventive action taken to prevent occurrence. The process to identify the root cause should start with the output(s) of the investigation (see 6.1).

When assessing relevant data, the following should be considered:

- Systematic generation of cause and effect conclusions supported by documented evidence
- Evaluate significant or underlying causes and their relationship to the problem
- Ensure that causes are identified, not the symptoms
- Check for more than one root cause (above processes if necessary)

Causes or contributing factors of nonconformities or potential nonconformities may include the following:

- Failure of, or malfunction of, incoming materials, processes, tools, equipment or facilities in which products are processed, stored or handled, including the equipment and systems therein
- Inadequate or non-existent procedures and documentation
- Non-compliance with procedures
- Inadequate process control
- Inadequate scheduling
- Lack of training
- Inadequate working conditions
- Inadequate resources (human or material)
- (Inherent) process variability

For further details on aspects to be considered when doing the root cause analysis see Annex C.

The output of the root cause analysis should be a clear statement of the most fundamental cause(s) resulting in the nonconformity (see Annex D for examples).

6.3 Identify Actions

When the root cause(s) has been determined, the manufacturer should identify and document the necessary corrections and/or corrective actions or preventive actions. These actions should be reviewed to ensure that all necessary actions are identified. The review may benefit from a cross functional approach. Where applicable, product disposition decisions should also be documented.

The following outcomes are possible and should be documented:

- **No further action necessary**
(provided that no safety issue exists and regulatory requirements are met)
 - With continuous monitoring
 - Acceptance under concession and continuance of monitoring
- **Correction**
It may be necessary to take initial corrections (e.g. containment, stop of shipment/supply, issuance of advisory notice) in order to address an immediate risk or safety issue. This may be necessary before investigation has been completed and root cause has been determined. However, after investigation and root cause determination, additional and/or possibly different corrections may become necessary.
- **Corrective action**
Corrective action should address systemic problems. For example, changing the procedure and training of personnel to the revised procedure may not, by itself, be appropriate or sufficient to address the systemic cause(s).
- **Preventive action**
By its very nature preventive action can not follow a nonconformity.

As a result of this step, a list of action items should be documented. These may include:

- A detailed description of the implementation
- Review regulatory requirements (e.g. submissions, licensing, certifications)
- Roles and responsibilities for execution of action items
- Identification of the necessary resources (e.g. IT, infrastructure, work environment)
- Verification and/or validation protocols of the action(s) with acceptance criteria
- Implementation schedule, including timelines
- Method or data for the determination of effectiveness with acceptance criteria
- Identify the starting point of monitoring, and end point of correction and/or corrective action or preventive action as described above

6.4 Verify Identified Actions

Before the implementation of action(s), a manufacturer should verify the identified action(s) and approve their implementation. In addition validation may be required where process validation or re-validation may be necessary, or where user needs or intended uses are changed and design validation will be required.

Verification activities are to ensure that all the elements of the proposed action (documentation, training etc) will satisfy the requirements of the proposed action. These activities should be performed by persons who are knowledgeable in the design or use of the product or process that is the subject of corrective or preventive action. Verification of a preventive action can be accomplished by introducing the conditions that would induce a nonconformity and confirming that the nonconformity does not occur.

Validation activities generate data and information that confirm the likelihood of the effectiveness of the corrective action to eliminate the nonconformity or proposed nonconformity.

Examples of items to be considered when planning the verification/validation activities include:

- Does the action(s) eliminate the identified root cause(s)?
- Does the action(s) cover all affected products/processes?
- Does the action(s) adversely affect the final products?
- Is it possible to finalize the actions timely in planned schedule (resources, materials/kits, logistics, communications, etc.)?
- Is the execution of the action commensurate with the degree of risk previously established?
- Are new risks or nonconformities derived from the action?

6.5 Implement Actions

The following items that may be considered at implementation should be documented:

- Parties involved
- Materials
- Processes
- Training
- Communications
- Tools
- Timelines for the implementation of the approved action

Verify that the implementation has been completed.

6.6 Determine Effectiveness of Implemented Actions

The manufacturer should gather data over a period of time related to the effectiveness of the implemented action (see Annex D for examples).

Management should ensure and be involved in a review and confirmation that actions taken were effective and did not introduce new issues or concerns. The following questions should be considered at appropriate times throughout the process and be revisited in the final review:

- Has the problem been comprehensively identified?
- Has the extent of the problem been identified (e.g. range of affected devices, patient outcome, process, production lines, operator)?
- Have the root cause/contributing factors of the problem been identified and addressed?
- Has the improvement action(s) been defined, planned, documented, verified and implemented?

If the manufacturer finds the actions are not effective, the manufacturer should re-initiate Phase III activities (see 6.0). If the manufacturer finds the actions create a new issue or a new nonconformity then the manufacturer needs to initiate Phase II (see 5.0) activities.

7.0 Phase IV: Input to Management

Management at different levels in the organization should be involved in each improvement action either through approval of the improvement steps or reporting.

The Management Review is the overall mechanism for management to ensure that the Quality Management System as a whole is effective.

7.1 Report to Management

The manufacturer should have a mechanism/procedure that expeditiously raises safety related issues or other high risk issues to management. These issues can be identified in the data sources, the improvement phase (see 6.0), or originate from other sources external to the Quality Management System. In addition to this expeditious escalation mechanism, the manufacturer should define management and personnel responsibilities (i.e. process owner) for the measurement, analysis and improvement processes, to ensure that the processes and the actions being implemented are effective. For this purpose there needs to be a mechanism for management at different levels to stay informed of the information or data from:

- The measurement and analysis activities from the individual data sources
- The investigations, actions, implementations, etc. from the improvement processes

7.2 Management Review

The manufacturer has procedures for what is provided as input for the management review, including relevant information from the improvement processes, such as improvement actions (corrective actions, and/or preventive actions) as well as important corrections.

The manufacturer needs to define what meaningful data is to be reported for a management review. Data should be specific to the quality objectives of the manufacturer and be reported regularly. Merely providing the number of improvement actions or the number of how many improvement actions are opened or closed to the management review process are not sufficient in assessing the effectiveness of the processes.

Included in this review would be an assessment of any opportunities for improvement of the device, manufacturing process, QMS or the organization itself.

An outcome of the review could be the allocation of funding or personnel to a particular area, project or device that the review has identified as not meeting customer and regulatory safety and effectiveness expectations.

Annex A: Examples of Phase Activities

List of possible activities corresponding to the phases in Figure 1.

The following is an outline/aid memoir of the main points described in this document. It is not intended as a “box ticking” exercise and should not be used as such, but used purely to summarize and align the steps in the process described in this document. The activity numbers do not imply sequential steps – some steps may take place in parallel.

The references in this Annex refer to the sections in this document.

Phase	Activities
Planning	<ol style="list-style-type: none"> 1. Identify all data sources (internal/external) by product type (4.1) 2. Identify resources required and individual personnel responsibilities for measuring each data source (4.1) 3. Define the requirements for each data source and the data elements within each data source that will be measured and analysed (4.1) 4. Define requirements for escalation to the improvement phase (4.1) 5. Define requirements for monitoring the measurements in the data sources (5.1) 6. Establish data sources (4.2)
Measurement and Analysis within and across Data Sources	<ol style="list-style-type: none"> 7. Measure and analyse all data sources for nonconformities and potential nonconformities (5.0, 5.1 and 5.2) 8. Have reports of nonconformity or potential nonconformity come from more than one data source? 9. Is the nonconformity or potential nonconformity systemic?
Improvement	<ol style="list-style-type: none"> 10. Determine scope and required outcome of investigation (6.1) 11. Investigate nonconformity or potential nonconformity (6.1) 12. Analyse nonconformity or potential nonconformity for root cause(s) (6.2) 13. Identify actions (correction, corrective action or preventive action) (6.3) 14. Verify proposed actions before implementation (6.4) 15. Implement proposed actions (6.5) 16. Determine effectiveness of actions (validate if possible) (6.6)
Input to Management	<ol style="list-style-type: none"> 17. Report investigation and outcome to management (7.1) 18. Review investigation, analysis and outcome (6.6, 7.2) 19. If not satisfied return to step 10 20. If required, report to regulator (note: reporting may be required earlier depending on severity)* 21. Audit system at determined intervals* 22. If numbers of nonconformities or potential nonconformities exceeds targets, review all QMS processes*

*Steps 20 to 22 are not described in this document but are added as reminders of general management responsibilities in this area of the QMS.

Annex B: Examples of Data Sources and Data Elements

Examples of data sources and their data elements can be, but are not restricted to:

Data Sources	Data Elements
Regulatory Requirements	<ul style="list-style-type: none">▪ Result of a regulatory inspection▪ New or revised regulatory requirements
Management Review	<ul style="list-style-type: none">▪ Management review output
Supplier Performance/Controls	<ul style="list-style-type: none">▪ Number of batches received▪ Batch and/or shipment▪ Inspection and test records▪ Quantity of rejects or deviations▪ Reason for rejection▪ By supplier, if more than one supplier▪ Use in which product or service▪ Supplier problems
Complaint Handling	<ul style="list-style-type: none">▪ Quantity▪ By product family▪ By customer (physician, healthcare facility, patient, etc.)▪ Reason for complaint▪ Complaint codes▪ Severity▪ Component involved
Adverse Event Reporting	<ul style="list-style-type: none">▪ Event▪ Quantity▪ By product family▪ By customer (physician, healthcare facility, patient, etc.)▪ Type of event (death or serious injury, etc.)▪ Component involved
Process Controls	<ul style="list-style-type: none">▪ By product▪ Operator▪ Work shift▪ Equipment and/or instruments used▪ Inspection and test records▪ In-process control results▪ Process control parameters▪ Inspection process▪ Final acceptance▪ Rejects▪ Special process▪ Validation study results▪ Process monitoring observations
Finished Product	<ul style="list-style-type: none">▪ Inspection and test records
Quality Audits (internal/external)	<ul style="list-style-type: none">▪ Observations (number, category, corporate policy, regulatory requirements, significance, etc.)▪ Repeat observations (indicative of effectiveness)▪ Closure times▪ Overall acceptability of contractor or supplier▪ Compliance to audit schedule▪ Audit personnel

Data Sources	Data Elements
Product Recall	<ul style="list-style-type: none"> ▪ Timeliness of recall communication ▪ Classification of recall ▪ Recall effectiveness checks
Spare Parts Usage	<ul style="list-style-type: none"> ▪ Frequency of replacement ▪ Batch number of spare part ▪ By supplier of spare part, if more than one supplier ▪ By customer ▪ By location or area of customer
Service Reports	<ul style="list-style-type: none"> ▪ Installation ▪ First use of equipment ▪ Frequency of maintenance visits ▪ Types of repairs ▪ Frequency of repairs ▪ Usage frequency ▪ Parts replaced ▪ Service personnel
Returned Product	<ul style="list-style-type: none"> ▪ Quantity ▪ Reason for returning product ▪ By customer ▪ Types of defects identified on returned product
Market/Customer Surveys	<ul style="list-style-type: none"> ▪ Customer preferences ▪ Customer service response time ▪ Solicited information on new or modified products
Scientific Literature	<ul style="list-style-type: none"> ▪ Research papers
Media Sources	<ul style="list-style-type: none"> ▪ Articles in trade journals
Product Realization (Design, Purchasing, Production and Service and Customer information)	<ul style="list-style-type: none"> ▪ Design and development review results ▪ Design and development verification results ▪ Design and development validation results ▪ Design and development changes (reason or cause for change, effectiveness of change, etc.) ▪ Controls on purchased products or services (See above Supplier Performance/Controls) ▪ Verification results of purchased product ▪ Inspection and testing data of purchased product ▪ Production and Service processes- Cleaning operations of product and facilities ▪ Sterilization ▪ Installation results ▪ Servicing and Maintenance if required (See also: Service Reports) ▪ Verification and Validation results of processes used in production and service. Including approval of equipment and qualification of personnel ▪ Traceability Data ▪ Controls of monitoring and measuring devices ▪ Calibration and maintenance of equipment ▪ Customer Information- New or repeat customer ▪ Customer feedback maybe in other forms than complaints or returned product (Customer Service call data, repeat sales , delivery/distribution data)
Risk Management	<ul style="list-style-type: none"> ▪ Published reports/literature of failures of similar products ▪ Stakeholder concerns and generally accepted state of the art ▪ Risk acceptability criteria

Annex C: Examples of Contributing Factors

Examples of possible contributing factors to be considered when doing the root cause analysis:

Materials

- Defective raw material (does material meet specification?)
- Batch related problem
- Design problem (wrong material for product, wrong specifications)
- Supplier problem (lack of control at supplier, alternative supplier)
- Lack of raw material.

Machine / Equipment

- Incorrect tool selection – suitability
- Inadequate maintenance or design – calibration?
- Equipment used as intended by the manufacturer?
- Defective equipment or tool
- End of life?
- Human error – inadequate training?

Environment

- Orderly workplace
- Properly controlled – temperature, humidity, pressure, cleanliness
- Job design/layout of work

Management

- Inadequate management involvement
- Stress demands
- Human factors
- Hazards not properly guarded
- Were management informed / did they take action?

Methods

- Procedures not adequately defined
- Practice does not follow prescribed methodology
- Poor communications

Management system

- Training or education lacking
- Poor employee involvement
- Poor recognition of hazard
- Previous hazards not eliminated

Measurement, monitoring and improvement

- Inadequate measuring and improvement

Annex D: Examples for Documentation of the Improvement Processes

The table below includes guidance for documenting various requirements of the improvement processes.

	Guidance	Example Documentation
Problem Statement	<ul style="list-style-type: none"> Clearly defined problem statement. State how the issue was discovered. The process/procedure that was not followed. Provide evidence What, When, Who, Where and How much (as applicable) 	<p>During in-process testing of Product A finished product on [date], two devices out of 30 were found to be nonconforming per Design Document 123456, revision A. Note 2.1 in Design Document 123456 requires that the surface finish be 32 μinch maximum on all exterior surfaces. The two nonconforming devices had a surface finish above the maximum 32 μinch finish as follows:</p> <ul style="list-style-type: none"> Serial Number 54321 had a surface finish of 67 μinch Serial Number 65432 had a surface finish of up to 38 μinch
Correction	<p>General Examples</p> <ul style="list-style-type: none"> Containment, Stop of shipment/ supply Issuance of advisory notice Incident awareness / training Change or suspend production process 	<p>The supplier was notified of the issue on [date]. The supplier conducted an operator awareness training of the incident on [date].</p> <p>Initial extent of the issue is restricted to supplier lot #678. All unused components and product built with components from this lot were controlled on [date]. No product built with this lot had been distributed.</p>
Investigate	<ul style="list-style-type: none"> Clearly defined problem statement (update/refine if new information is determined) What information was gathered, reviewed and/or evaluated Results of the reviews/evaluations of the information Identification of cause(s) or contributing factors 	<p>See initial problem statement. Subsequent investigation confirmed that the issue was limited to lot #678. All additional available lots of this component were inspected with a 95/95 inspection plan and no additional lots were confirmed to have the issue.</p> <p>The incoming inspection process and component FMEA were reviewed and determined to be adequate and accurate, respectively.</p> <p>Review of finished product reject data over the past year revealed no other rejects for surface finish of this component.</p> <p>The following problem-solving tools and methods were used during the course of the investigation of the surface finish issue.</p> <ul style="list-style-type: none"> Fishbone analysis – see the attached file labeled ‘Surface Finish Analysis’. Conference calls and documentation reviews with the Supplier – see attached file which contains the minutes from the conference calls. <p>Results of the investigation were the following. Two different raw tubing lots were mixed at the Supplier’s finishing process. One raw tubing lot was intended for customer A’s products (Lot number 10000-100 requiring a surface finish of 32 μinch maximum) and the other was intended for customer B’s product which had a surface finish above the 32 μinch maximum.</p>

Identify Root Cause	<ul style="list-style-type: none"> The output of the root cause analysis should be a clear statement of the most fundamental cause(s) resulting in the nonconformity 	It has been concluded that the root cause of the tubing surface finish issue is inadequate line clearance procedures established at the supplier.
Planned actions	<p>Specify:</p> <ul style="list-style-type: none"> What the action is Who will do it When it should be done 	<p>Corrective action: Supplier to add line clearance requirements to documented procedures by [date].</p> <p>Preventive action: Not applicable.</p>
Verification of actions	<ul style="list-style-type: none"> Verification activities are to ensure that all the elements of the proposed action (documentation, training etc) will satisfy the requirements of the proposed action Validation activities generate data and information that confirm the likelihood of the effectiveness of the corrective action to eliminate the nonconformity or proposed nonconformity. 	<p>General examples are included below. Actual documentation would need to be more specific.</p> <ul style="list-style-type: none"> Review and approval of the procedural changes prior to use Conduct a pilot of new procedure on a specific project/department/time frame prior to full scale implementation Verification that the updated supplier procedure addresses the process that caused the nonconformity Verification that the training materials address the specific process that caused the nonconformity Comparing a new design specification with a similar proven design specification Performing calculations using an alternative method Perform validation of equipment, software, production processes, test method, component, etc. <p>Specific example: Review and approval of supplier procedure XXX by the supplier and the customer to ensure adequacy of the updated line clearance process.</p>
Verification of effectiveness	<p>Method or data for the determination of effectiveness with acceptance criteria.</p> <ul style="list-style-type: none"> The improvement goal The evidence (data sources) that will be used to support effectiveness (e.g., a data source could be where the problem was initially found) The time frame that effectiveness will be monitored (e.g., upon completion of actions or three months, six months as appropriate) <p>OR</p> <ul style="list-style-type: none"> Sample size required to demonstrate effectiveness 	<p>X months after implementation:</p> <ul style="list-style-type: none"> Conduct a query of the electronic manufacturing data system to verify there are zero surface finish rejects for this component at finished Product A final inspection. Supplier Quality Engineer to conduct on site review at the supplier of the action to confirm the procedures are in place, are known to the operators, and there is evidence that the procedures are being followed.