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A REVIEW: ROOT CAUSE ANALYSIS IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

A methodical approach to identifying the underlying root causes of our process problems is called root cause analysis (RCA). In order to perform the proper improvement action and make sure that improvements are maintained over time, RCA is helpful in identifying the cause(s) of variation. Improvement actions that are not focused on the primary cause will not be effective, or at least will not last long, therefore in order to sustain the improvement over time, the fundamental causes must be identified and addressed. The main goal of corrective action and preventative action (CAPA) in any pharmaceutical or medical device company is to identify any weaknesses, deviations, or failures and to conduct a review and take the necessary corrective action to prevent a recurrence of those issues. CAPA is another approach in which preventive actions are conducted instantaneously to avoid any incidence from occurring. It is a prerequisite for a pharmaceutical company's regulatory framework and a component of the overall Quality Management System (QMS).

KEYWORDS: Root cause, corrective action and preventive action (CAPA), Pareto Charts, Failure Mode and Effect Analysis (FMEA), 5 Whys, Ishikawa Fishbone Diagram, DMAIC template.

INTRODUCTION

Root cause analysis

One of the seven basic Quality Control Tools, or graphical techniques used to troubleshoot quality-related problems, the root cause analysis (RCA) is a systematic problem-solving tool

used to determine the root cause of any fault or problems.[1] The term "root cause" refers to the underlying or fundamental cause of a non-conformance, flaw, or failure. Additionally, the phrase "root cause" can also be used to describe the precise point in the causal chain at which implementing an appropriate measure or intervention will stop the non-conformance from recurring.[2] It aims for the root of a problem implementing a series of particular procedures and techniques to determine the main contributing factor.[3] Root cause assessment relates to failure to adequately investigate deviations, out of specification (OOS) results, invalidated OOS and customer complaints.[4]

Principles of root cause analysis

The primary focus of root cause analysis is to determine what triggers an issue so that it may be corrected and the processes that produced it can be changed. However, in order for this to function, the root cause analysis must be carried out in a methodical manner.[5]

1. Analyze why, how, and when the incident occurred.
2. Concentrate on the fundamental reasons rather than the symptoms.
3. When applying RCA to solve problems, consider preventive.
4. The first time, do it correctly.[6]

Basic types of root causes

When a problem or incident occurs, organizations conduct root cause analysis, however there are a variety of problems that call for an RCA.

Physical cause: When real-world materials or equipment fail in some way (for example, a desktop computer stops working or a component from a third-party vendor performs poorly).[7]

Human causes: May be carried on by mistakes made by individuals or by a lack of ability or experience to complete a task.[8]

Organizational causes: As the name suggests, an organizational cause is one that results from organizations. Organizations are sometimes able to also be held accountable for systemic issues. Not every choice made by the organization has to be accurate. A choice may be inappropriate or incorrect.[9]

Root cause analysis categories

The methodology of root cause analysis is not uniform. In actuality, it is carried out using a wide range of different equipment, procedures, and approaches.

Most RCA principles fall into one of five broad groups, according to the National Association of State Mental Health Program Directors:

1. **Safety-based RCA:** This procedure is used for searching and highlight the causes of any failures in safety compliance, accident investigation, or other aspects of work-related health and safety.
2. **Production-based RCA:** This is frequently done in the area of quality control for manufacturing to look into the reasons why particular defects exist in the production process or the final product.
3. **Failure-based RCA:** is based on the failure analysis concept, which is often utilized in engineering and maintenance.
4. **Systems-based RCA:** This method integrates two or more RCA techniques and incorporates concepts from change management, risk management, and systems analysis.[8]

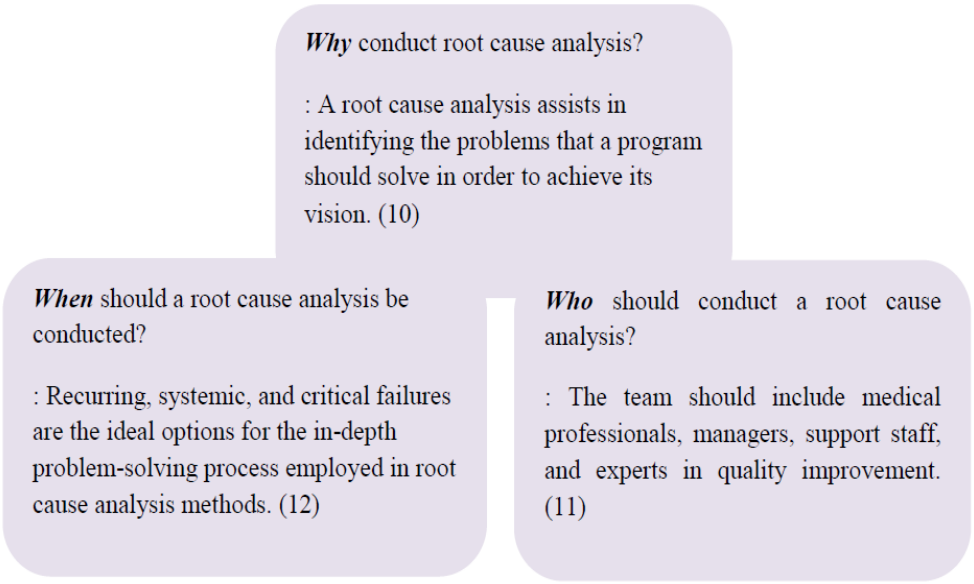

Fig. 1: 3W's of RCA.

Advantages of RCA

- RCA enables to intervene immediately to resolve an issue and prevent it from creating widespread damage. The decision-making process should be improved and accelerated.[13]

- By recognizing the fundamental cause, one can find a permanent solution to it, reducing or eliminating the potential of its recurrence in the future.[14]

Disadvantages of RCA

- A thorough evaluation necessitates considerable effort, including data collecting, interviews, documentation, and analysis. This procedure can be time-consuming, especially when dealing with complicated issues or large-scale occurrences.[15]
- The fundamental issue with RCA is that it only assumes and focuses on one root cause of an issue. In fact, however, the situation may be more complicated. There could be multiple underlying causes of a fault. As a result, one must concentrate on all parts of the fault and consider all underlying causes of the defect.[14]

Classification of "causes" of problems

Process-wise, "causes" of problems classify in two types: Common Causes or Special Causes.[6]

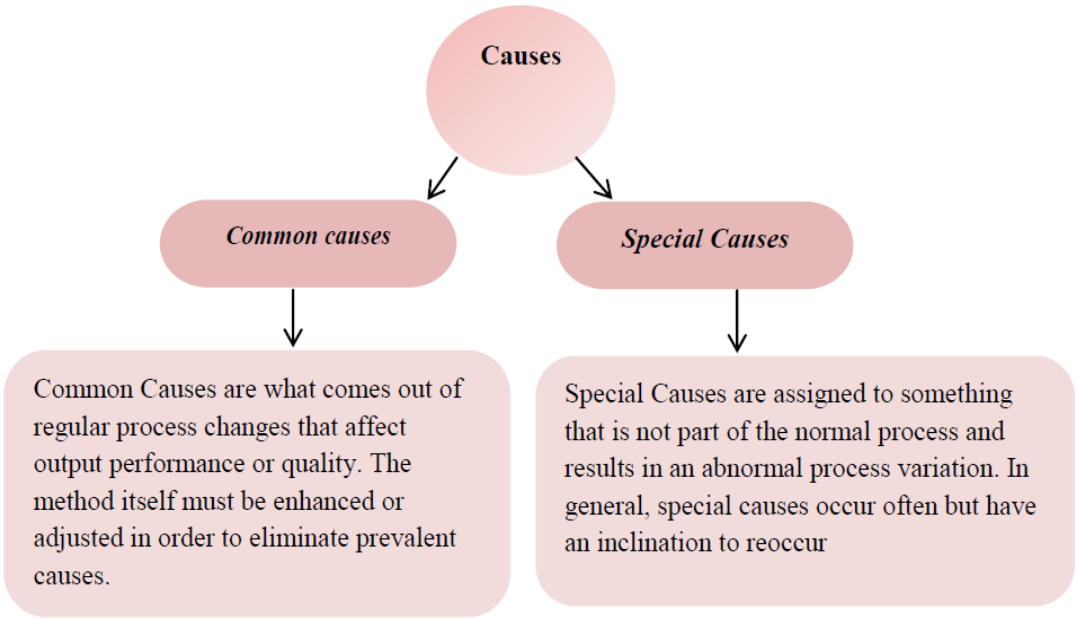

Fig. 2: Classification of "causes" of problems.[16]

Process of conducting the root causes analysis

To determine the fundamental causes of occurrences or trends of events, RCA is carried out using a variety of approaches and methodologies. It looks past the superficial aspects to identify where systems or procedures were ineffective or contributed to the initial problem.[17]

Step 1 Define the Fault/Incident

Members of the root cause analysis team must first determine what went wrong. At this stage, it is beneficial to gather as much information about the defect or incident as possible, i.e., a summary of what went wrong, including as much as possible the sequence of events and what has been done so far in terms of crucial corrective action and incident management. This information serves as circumstances for the team, allowing everyone to understand the incident situation.

Step 2 Collect Data

Following that, it is critical to gather further, more thorough information that will aid in evaluating the situation. This could involve, for example, the following:

- Product testing outcomes.
- Lists of items or procedures that have been involved.
- Raw material lists linked to implicated goods and processes
- Material lists for packaging
- Monitoring findings encompassing suspected dates and times (the sample(s) should be large enough to catch all relevant data surrounding the suspect dates, allowing for a margin of error).
- Corrective action documents covering the dates and hours suspected of being involved.
- Records of engineering and maintenance
- Records of pest management.
- Customer contact details and complaint records.
- Any additional relevant details, such as staff interview information, etc.

Brainstorming will be an effective strategy for identifying all of the relevant information sources, after which members of the team will be assigned specific records to gather and examine on a preliminary basis.

Step 3 Evaluate Data and Identify Possible Causal Factors

To identify potential causal factors, must examine and discuss all of the data have gathered currently, as well as identify any further information that is required. This is best accomplished by the team discussing the information discovered and bringing in additional personnel as needed to help understand the situation, such as factory floor staff who are familiar with the ongoing processing situation and additional experts (possibly external) who

can advise on specific issues. Further debate and brainstorming will aid in understanding the potential cause elements, which must all be recorded by the group or its designated secretary/scribe.

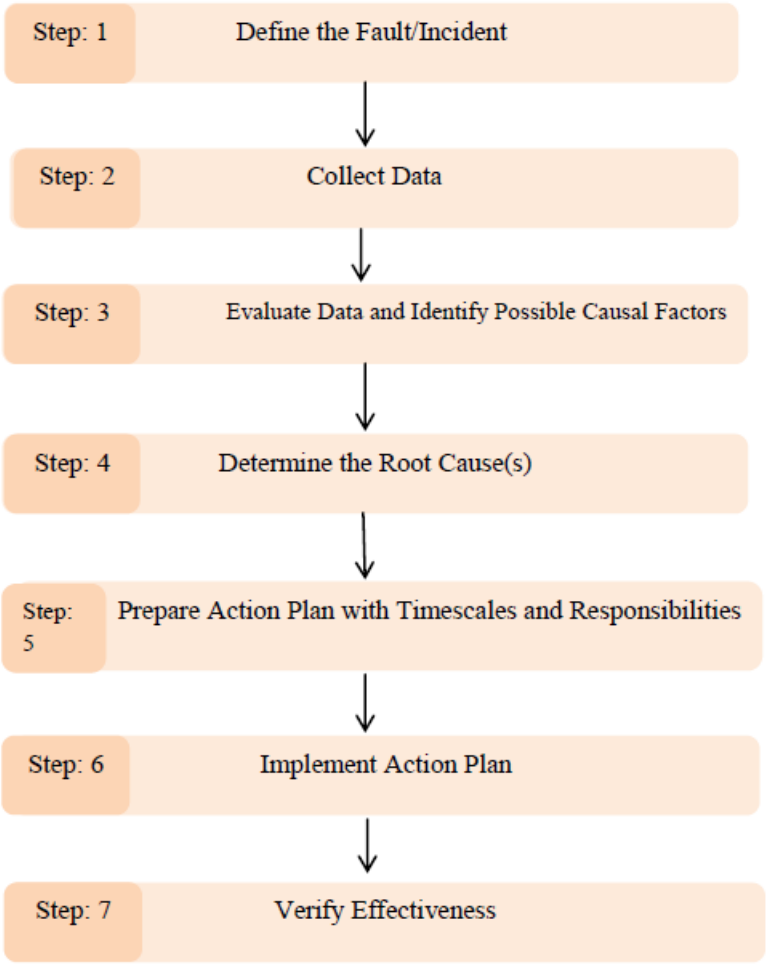

Fig. 3: The seven-step process of root cause analysis.[18]

Step 4 Determine the Root Cause(s)

The team must investigate the list of possible causes further, considering how each one may have contributed to the problem. The use of tools from the root cause analysis toolbox (see section Root Cause Analysis Toolbox) will assist the team in understanding how the potential reasons may be interconnected and in tracking backward to the root cause(s). In this context, grouping techniques like the Ishikawa Cause and Effect Analysis and questioning techniques like the 5-Whys are especially useful, though teams may also find some of the other tools useful in ranking likely causes from their list.

The team must get an agreement on the root cause or causes (especially if there are multiple gaps or causal elements involved in an incident). The conversation might then focus to what needs to be done to address the underlying cause(s). At this step, other techniques from the root cause analysis toolkit, such as the FMEA, which examines present controls and then identifies recommended new controls for each cause of failure, can be useful.

Step 5 Prepare Action Plan with Timescales and Responsibilities.

The team's proposals for new staff, infrastructure, systems, controls, and timetables for completion and implementation must be incorporated into an action plan. Each action point should have the appropriate responsibility from the management hierarchy identified, and staff members should be informed accordingly.

Step 6 Implement Action Plan

The action plan's individual steps must be carried out and verified as effective. This will require securely management to ensure the plan stays on track and can be lead by members of the root cause analysis team depending on the nature of the actions and the timeframes involved.

Step 7 Verify Effectiveness

The final stage in the root cause analysis process is to verify that the essential adjustments specified in the action plan are actually working in practice and are effective at resolving the fundamental cause of the problem. It is also critical at this stage to ensure that the improvements have not introduced any unexpected problems. Verification can be done using audit techniques, and after verification, the organization will most likely want to adopt additional monitoring around the modifications in addition to the regular planned monitoring activities.[18]

Root cause analysis tools for problem solving

Root cause analysis (RCA) is a technique for discovering and resolving the underlying issues that lead to faults, mistakes, or system failures in a process or system. RCA aids in the prevention of recurrence, the improvement of quality, and the enhancement of customer satisfaction. There are numerous RCA tools and approaches, but the following are some of the most common: *Pareto Charts, Failure Mode and Effect Analysis (FMEA), 5 Whys, Ishikawa Fishbone Diagram, Fault Tree Analysis, 8D report template checklist, DMAIC template, scatter diagram, corrective action and preventive action.*[19]

A. Corrective Action and Preventive action.

CAPA is the cornerstone of a quality management system, particularly the backbone of the pharmaceutical industry, and of quality improvement. CAPA assists the Quality System in organizing, documenting, and prosecuting firm, processes, strategies, and business. After determining the proper and actual root cause, the research is concluded, and CAPA is implemented.[20]

Why CAPA?

Regulatory requirement: Both the FDA and ISO consider an active CAPA program to be an essential component of a quality system. Customer satisfaction: the ability to rectify an existing problem or apply a control to prevent a potential problem, both of which are required for current customer satisfaction. Good business practice: a lack of quality can have a major financial impact on a company.[21] Corrective Action Preventive Action (CAPA) is an approach used to investigate and resolve quality issues along with identifying their causes. It was introduced as a result of Food and Drug Administration's (FDA) requirement under FDA 21 CFR 820.100.[22] Proper documentation of CAPA is usually required by ISO 9000 and other related standards such as the AS9100.[23]

CAPA - seven steps for an effective process

1. ***Identify the potential or actual problem-*** The first stage in implementing a CAPA program is to clearly characterize the possible or current problem, whether it's a non-conformance or a system failure. This necessitates a clear description of the problem and available evidence that the problem exists, as well as an accurate and complete consideration of the exact source of the information that prompted the action.

An external or internal source of information, such as a customer complaint, service request, risk assessment, or internal quality audit, can be used. The problem description should be brief yet comprehensive enough to guarantee that the problem is easily recognized when read. It's also critical to include any accessible information that shows the problem exists, such as continuously growing downtime, which may suggest a potential equipment problem.

2. ***Evaluate the potential impact and risk level-*** After the problem has been defined and documented, it should be analyzed to establish the need for action and the duration of action required. This entails assessing the possible impact of the problem as well as the actual hazards to the organization and its consumers.

A description of why the problem is of concern, such as its potential influence on pricing, product quality, safety, or reliability, is part of the review. The outcome of this impact assessment should be utilized to determine the severity of the situation. The risk level associated with the problem may influence the priority of activities conducted; for example, a problem that poses a major risk to a product's function or safety may be assigned a high priority and necessitate quick corrective action.

3. ***Develop an investigation procedure-*** It is essential to create a procedure for examining the problem after assessing the potential impact and danger of the situation. A documented plan should include at least the following parts in order to assure that the investigation is complete and nothing is overlooked: a purpose for the activities to be taken; the investigative technique and dates to be followed; and the responsibilities and resources required.

The written plan's objective should clearly indicate the desired CAPA result, along with detailed guidance on how to identify the problem's contributing and underlying causes. The inquiry process must include a thorough assessment and analysis of all the relevant circumstances. In accordance with the established timeframe, the method should also allocate tasks to those involved in the inquiry and identify and record any additional resources that might be required.

4. ***Analyze the problem using available information-*** The problem's root cause should be looked into using the newly developed investigation process. Analysis is gathering pertinent data, looking into all potential sources of the issue, and using the facts at issue to identify the main issue.

The maker must compile a list of all potential reasons and utilize it as the foundation for gathering pertinent data, test results, etc. It is important to organize and document the data collection's findings, which may incorporate test results as well as a review of documents, procedures, etc. The generated documentation should cover all previously identified potential reasons because it will be utilized to identify the problem's underlying cause. The failure mode and effects analysis (FMEA), the five whys, and fishbone diagrams are just a few of the various instruments that may be used to identify root causes. To decide what corrective and/or preventive measures should be implemented, it is crucial to identify and record the root cause.

5. ***Create an action plan using the analysis-*** The study' findings should be put to use in creating an action plan for fixing and/or preventing the issue. Tasks to be accomplished, revisions to documents, specifications, processes, etc., persons accountable for each task, staff training, and an anticipated completion date should all be included in a CAPA action plan. The manufacturer should mention any documentation that will be revised in the action plan and describe the planned adaptations in general terms. If modifications are to be made to processes, procedures, or systems, they should be stated in sufficient detail so that it is clear what must be done, as well as the expected effect of the changes. Employee training is a crucial component of any change and, as such, must be included in the action plan.

6. ***Implement and Document action plan tasks-*** Once the CAPA action plan has been prepared and is ready for implementation, the actions mentioned and specified in the plan should be started, completed, and documented. The significance of good documentation in the implementation of the action plan cannot be overstated. To generate an implementation summary, list and summarize all activities carried out in accordance with the action plan's requirements, establishing a thorough record of steps taken to remedy and prevent the problem from recurring. This includes, among other things, modifications, preventive measures, process controls, and training.

7. ***Verify completion and effectiveness of actions-*** The CAPA process requires a detailed analysis of the activities done immediately the plan has been implemented. This follow-up has two main objectives: making sure that all tasks have been completed and that they were successful. All changes, controls, training, etc., should be implemented, completed, and the verification of these actions' completion should be documented. Additionally, a thorough evaluation should be performed to confirm the effectiveness of the actions taken and ensure the following: the problem's root cause has been fixed; any resulting secondary situations have been corrected; appropriate controls have been established; sufficient monitoring of the situation is in place; and any unfavorable effects of the actions taken have been addressed.[24]

1) Initiation of Capa[25]

1. To initiate a CAPA, the appropriate department head must send the source document to QA (Quality Assurance).
2. The QA manager will determine whether CAPA is required.

3. The department head must acquire a CAPA form from QA. Before forwarding the form to the appropriate department, QA must write the name and number of the source document on it.
4. Department heads must complete the following CAPA form:

a. When CAPA was founded.
b. Estimated completion date.
c. Select the applicable system that will be impacted and check the box next to it.
d. Select "Not Applicable" if none of the printed systems are affected. If any additional systems other than those specified are involved, write the impacted system in the areas provided.
e. Describe the CAPA from the source document in detail, as well as the specifics of the corrective and preventive action.
f. After properly signing, the department head must sign their names and provide a date.

5. The CAPA form must be sent to QA by the department the individual in charge.
6. QA must assign the CAPA form a reference number and record the pertinent information in the CAPA log. After that, QA will send the CAPA form to the relevant department.

Difference: Corrective Action and Preventive action

Table 1: Difference between corrective Action and Preventive action.

Sr. No.	Corrective action	Preventive action.
1	After a problem occurs in the process	Before a problem arise.[23]
2	Include the assessment of root cause and plan to prevent recurrence	Replace by risk based thinking and improvement, rather than a formal process
3	Prevent from recurrence the non-conformity.	Prevent from occurrence the non-conformity.
4	Reactive activity- happens after the fact.	Proactive activity- takes an action when the risk identified.[26]

2) Pareto charts

The Pareto Principle, which claims that "80% of the effects come from 20% of the causes," is the foundation for Pareto charts. A Pareto chart is a bar chart and line graph that shows a frequency distribution.[23] A Pareto chart is a graph that shows the cumulative effect of flaws as well as their frequency. Pareto charts are helpful in identifying which problems should be fixed first to see the highest overall improvement.[28]

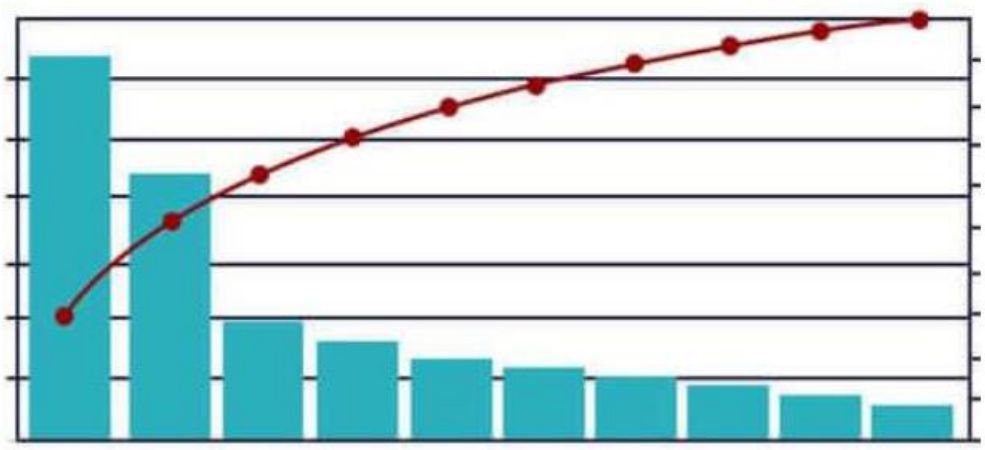

Fig. 4: Pareto Charts.[19]

3) Failure Mode and Effect Analysis (FMEA)

Failure modes and effects analysis (FMEA), first developed by the U.S. military in the 1940s, is a step-by-step methodology for detecting all potential problems in a design, a manufacturing or assembly process, a product or service. It is a frequently used process analysis tool.

"Failure modes" refers to the potential failure modes or ways. Failures can be possible or Actual and Include any mistakes or flaws, especially those that negatively impact customers.

- The term "effects analysis" describes the investigation of such failures' effects.

Failures are classified according to the severity of their effects are, how frequently they happen, and how simple it is to spot them. By starting with the failures that are most critical the FMEA aims to eliminate or reduce failures. For use in ongoing improvement, failure modes and effects analysis also documents the most recent information and steps about failure risks. To avoid failures, FMEA is utilized during the design process. Later, both before and throughout the process' continuous operation, it is employed for control. FMEA should ideally start during the early conceptual design stages and continue throughout the product's life.[29]

Types of FMEA analyses

There are three main types of failure mode and effects analysis.

1. FMEA design (DFMEA) -This focuses on possible system, product, or process failures and how to prevent or mitigate them. DFMEA is used to identify probable failures, estimate their severity and identify mitigation and prevention measures. This method aids engineers in identifying problems before they become costly to fix.

2. Process FMEA (PFMEA) - This focuses on identifying potential hazards to process PFMEA assists businesses in understanding potential risks for each process step as early as possible by identifying process functions, failure modes, and impacts.
3. Functional FMEA (FFMEA) - This technique concentrates on preventing potential failures before remedial actions are required. Using FFMEA, feasible functional failure modes are identified and evaluated.[30]

4) Whys

The 5 Whys technique was developed by Sakich Toyoda, the inventor and industrialist who founded Toyota Industries.[31] When using the 5 Whys method, your goal is to identify the root of the issue before addressing it. Actually, the answers to the five whys questions may indicate that the problem's origin is somewhat unexpected. Frequently, what develop to be technological challenges turn out to be human and process issues. This is why identifying and removing the root cause is critical if want to minimize failure iteration.[32]

As an illustration, suppose the operator of a compression machine suddenly stops the machine while it is compressing. It is important to determine the problem's underlying cause. The following conclusions result from applying the five whys.

a) What caused the compression device to abruptly stop?

: Human mistake took place.

b) What led to this human error?

: The operator depressed the stop/emergency button.

c) Why was this button pressed by the operator?

: The button's label was illegible.

d) Why wasn't the label more obvious?

: The dirt obscured the labels.

e) Why were the labels covered with mud?

: The machine wasn't thoroughly cleaned.

Because the compression machine was not cleaned well and the operator was unable to recognize the stop button, we were able to identify the root cause of the unexpected halt of the compression machine using the 5 Why tool. Effective implementation of remedial and preventive measures is also aided by root cause analysis.[33]

Fig. 5: Whys.[34]

As an illustration, suppose the operator of a compression machine suddenly stops the machine while it is compressing. It is important to determine the problem's underlying cause. The following conclusions result from applying the five whys.

f) What caused the compression device to abruptly stop?

: Human mistake took place.

g) What led to this human error?

: The operator depressed the stop/emergency button.

h) Why was this button pressed by the operator?

: The button's label was illegible.

i) Why wasn't the label more obvious?

: The dirt obscured the labels.

j) Why were the labels covered with mud?

: The machine wasn't thoroughly cleaned.

Because the compression machine was not cleaned well and the operator was unable to recognize the stop button, we were able to identify the root cause of the unexpected halt of the compression machine using the 5 Why tool. Effective implementation of remedial and preventive measures is also aided by root cause analysis.[34]

5) Ishikawa diagram

The fishbone diagram, often called the Ishikawa diagram after its developer Kaoru Ishikawa, is one of the more widely used tools in process improvement. It was created in the 1960s.[34] An effective tool for determining the cause(s) of flaws, variances, or failures in a process is

the fishbone diagram. Put differently, it aids in dissecting root reasons that may contribute to an outcome in a series of layers. A fishbone diagram is one of the essential tools used in a root cause analysis. It is also referred to as an Ishikawa diagram or a cause-and-effect study.

As the name implies, a fishbone diagram resembles the skeleton of a fish. The causes stretch to the left as the skeleton's bones; the ribs branch off the back and indicate significant causes, while sub-branches branch off of the causes and indicate root causes. The underlying issue is represented by the fish's head, which is facing right. These factors resemble the fish skeleton's bony structure. To find the root causes of the issue, the fishbone structure can branch off to as many levels as necessary. As the name implies, a fishbone diagram looks like a fish skeleton. The ribs branch off the back and indicate primary reasons, while sub-branches branch off of the causes and indicate root causes. The underlying issue is represented by the fish's head (facing right), and the causes extend to the left as the skeleton's bones. These conditions look like the fish skeleton's bones. The fishbone diagram can be extended to as many levels as necessary to identify the root causes of the issue.[36]

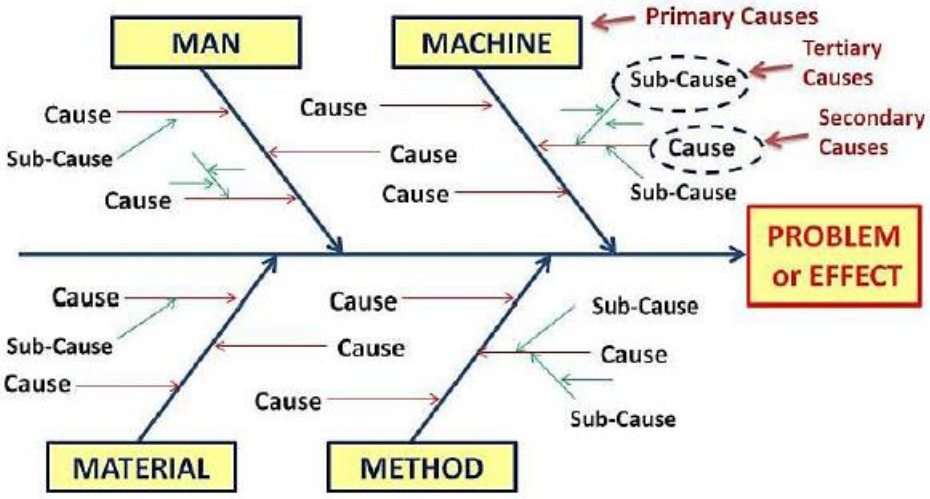

Fig. 6: Fishbone Diagram/ Ishikawa Diagram/ Cause & Effect Diagram.[37]

Identifying the variables that lead to changes within a process is one of the first steps in making a fishbone diagram. The *6 Ms* of manufacturing, according to Ishikawa, are man, machine, method, material, measurement, and Mother Nature. These 6 *Ms* are the first six major "bones" of your fishbone, influencing variance in all processes.

- ***Manpowe***r - manpower is the operational and/or functional labor performed by those involved in the product's development and delivery. This is regarded as a somewhat

uncommon "cause" of a certain issue. When manpower is shown to be a contributing element in an unfavorable outcome, it is often another 6 M.

- ***Method -*** A production process and the supporting service delivery processes comprise a method. Processes are often discovered to contain excessive steps, signoffs, and other non-value-adding or non-contributing activities. Processes can become complicated and challenging to follow if they are not standardized, streamlined, and simplified.
- ***Machine*** - Machines are the buildings, machinery, systems, and tools employed in production. Due to technical or maintenance problems, equipment, tools, and facilities, together with the underlying support systems, are frequently mismanaged or unable to produce the desired output.
- ***Material***- the components, raw materials, and consumables required to make a desired final product. Materials are frequently mishandled due to a variety of reasons, including inaccurate labeling, faulty specification, inappropriate storage, and wear and tear.
- ***Mother nature (Environment)-*** Unpredictable and uncontrollable environmental factors like the weather, floods, earthquakes, fires, etc. Certain environmental conditions are essential and for which some facilities discover they are unprepared, even if many of them are predictable and hence controlled.
- ***Measurement-*** physical measurements (distance, volume, temperature, pressure, etc.) and manual or automatic inspections. When measurements are inconsistent, it might be challenging to draw conclusions that can be repeated in order to identify a recurring cause.[36]

6) Fault tree analysis

The fault tree is a technique for identifying and resolving faults in any system or process. It is also useful in determining the fundamental cause of any incident. Based on their defects, errors, or difficulties, an organization or firm may have multiple fault trees. A fault tree has a structure similar to that of a fishbone tool, with tree roots. Root branches suggest potential sources of flaws or difficulties. In some faults or difficulties, the "5 Why" tool does not operate, and you are unable to determine the root cause of the problem. This tool works in conjunction with the "5 Why" tool; if you are preparing a fault tree and want to find the root cause of a problem; you must ask a "Why". Actually, if there are multiple probable reasons of a complex occurrence, the "5 Why" technique will confuse you in determining the root cause of the problem. A fault tree diagram can help you more quickly pinpoint the root cause of these issues.[37]

7) Fault tree diagramming

A fault tree is a technique for identifying the points at which mistakes can occur. The National Aeronautics and Space Administration (NASA) of the United States of America developed this technique to assess the safety of spacecraft (Vesely et al., 2002). Conventional event tree analysis may depict the stages that lead to food-borne illnesses from farm to fork and determine the likelihood of sickness by multiplying the probabilities of the detected steps. However, due to the complexity and unpredictability of informal value chains, an event tree may not be appropriate. A fault-tree analysis begins with an unintended result - food borne disease. The analysis seeks the direct cause(s) of the problem and traces the causes backwards at each stage.

In the case of staphylococcal food poisoning caused by milk consumption, for example, the preceding requirements are that the person is vulnerable to staphylococcal enterotoxin (SE) 'and' that the milk contained SE. The fault tree then searches for direct causes or essential conditions, such as milk containing enough Staphylococcus Aureus to form SE. Milk must be contaminated either during milk handling or during the manufacturing process for this to occur.

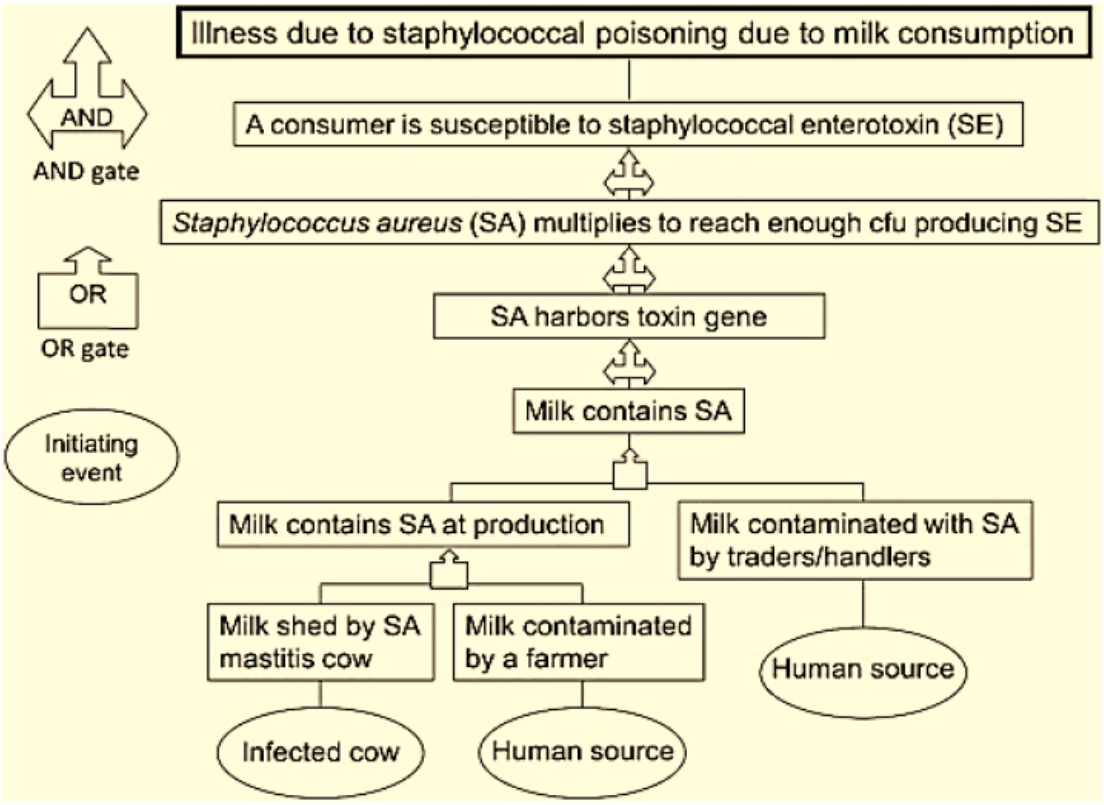

Fig. 7: A fault tree to identify logic of illness for staphylococcal food poisoning.[38]

It discovers human or animal (mastitis cows) sources by tracing back till the source of contamination. A fault tree, like an event tree, can be used to directly determine the probability of disease. It also applies to non-linear and complex informal value networks. This method is beneficial for hazard detection and characterization. Fault tree can additionally assist in the planning of a field survey or collecting of published data, which becomes exposure assessment. It is best to undertake participatory risk analysis for informal value chains with both scientific professionals and local value chain actors.[38]

8) D report template checklist

The 8D method is a problem-solving approach that finds, corrects, and eliminates reoccurring issues. It can be used as strategy to design a permanent corrective action and prevent repeating issues by finding the root causes of a problem. The 8D technique, developed by Ford, provides a systematic means of recognizing an issue and its solution, making it ideal for organizational learning. This strategy is used in a variety of fields to aid with product and process improvement.[39]

There are numerous advantages to applying the 8D ideas to identify actual answers to workplace difficulties. To begin, the system is focused on determining the core cause of problems, which is required to resolve difficulties now and prevent them from recurring in the future. It is also beneficial since it examines "Escape Points" to improve the ability to detect failure in the event that something goes wrong again in the future. This system's prevention loop aids in the elimination of the factors that led to the failure in the first place.[40]

Table 2: 8D method uses eight steps to deal with issues.[40]

D0: Plan	Spending the time required to devise a strategy for determining and resolving a problem. This will entail defining the prerequisites and information needed to discover answers quickly
D1: Use a Team	In virtually all cases, having a team in place will result in greater results. It is vital to properly establish the team.
D2: Describe the Problem	It is critical to accurately describe the situation. Check that the explanation employs clear terminology and answers the questions "who, what, when, where, why, how, and how many."
D3: Create a Containment Plan in Transitional	Establishing an indefinite containment plan that can isolate the issue so that it does not impact the customer, even in the event that treatment is not successful, is often an excellent idea.

D4: Determine and Verify Root Causes and Escape Points	Identifying all of the core reasons of the problem and why they were not discovered earlier. Identifying the underlying reason is crucial for D8 problem solutions.
D5: Verify Permanent Corrections for the Problem	Determine whether recommended corrective activities will result in a long-term solution to the problem in question through a set of tests and analysis.
D6: Define and Implement Corrective Options	Choose the suggested corrective measures that will yield the desired outcomes and put them into effect.
D7: Prevent Recurrence	To avoid the issue from occurring again, make sure all management, training, records, and other facility-related aspects are up to date.
D8 Congratulate Main Contributors	It will promote people to participate in the problem-solving process going forward if you take the time to thank those who contributed

9) DMAIC Analysis

DMAIC is a data-driven quality technique for process improvement. It is an essential component of a Six Sigma program, but it can also be used as a stand-alone quality improvement technique.[41] The DMAIC approach has numerous advantages. By assessing the process before applying any solution, DMAIC decreases the possibilities of resolving the wrong problem.[42]

Table 3: DMAIC Methodology and Phases.[43]

Phase	Define	Measure	Analyze	Improve	Control
Description	The project team simplifies the problem that leadership has assigned them in the first stage of the DMAIC process by interviewing both internal and external stakeholders to confirm that the	The project team begins examining the problem's current baseline performance during the measure phase, gathering and interpreting the available data on current performance. This frequently results in a	The third phase of the DMAIC technique is analyzed. During this phase, the project team collects and analyzes data to test theories about the problem's fundamental cause or causes. These root causes are referred to as 'Project Xs'. By the end of this phase, the	This is the point at which the project team moves on the corrective route and begins acting on what they discovered by making improvements. At this moment, the team will do the following: Create alternate alternatives. Create the solution	The fifth and final phase of the DMAIC technique, during which the project team ensures that the gains gathered during the improved phase are maintained and that the problem does not reoccur. To accomplish this, members of the team must: Determine the subjects who will serve as

	problem is, in actuality, real.	redefinition of the problem in order to focus on the most important or 'critical few concerns.'	team will have limited down their many hypotheses to a few key underlying causes to test and verify correct or untrue.	(including designs for culture and control). Demonstrate the solution's efficacy. Put the solution into action.	controls. Create a control measurement Establish performance benchmarks. Actual performance should be measured. In order to compare actual measured performance to standards. Take action on the gap
Tools	Stakeholder analysis Collection of the voice of the customer using the voice of the customer matrix Voice of the customer to critical to quality translation High-level process map (SIPOC diagram)	Juran's Pareto Analysis Data Collection Plan Detailed Process Mapping 6S Value Stream Maps	Calculating Sigma Level Graphs and Charts Brainstorming Stratification Histograms Box Plots Scatter Diagrams Cause and Effect Diagrams 5 Why Analysis Failure Mode and Effect Analysis Impact Control Matrix	Brainstorming Solution Matrix Barriers and Aids Chart Pilot Study Mistake Proofing Benchmarking Pugh Matrix	Process Control Plan Control Charts

10) Scatter diagram

In order to determine whether there is a relationship between two sets of numerical data, one variable is compared on each axis of the scatter diagram. If there is a correlation between the variables, the points will fall along a line or curve. The spots will be closer to the line the stronger the link. This method of cause analysis is one of the seven essential instruments for quality.[44] It is ordinary to apply a scatter diagram to support or refute cause-and-effect

connections. The visual shows relationships, but it does not prove that one variable causes another. Because of this, we can use a scatter diagram to look into hypotheses about cause-and-effect relationships and to identify the underlying causes of issues.[45]

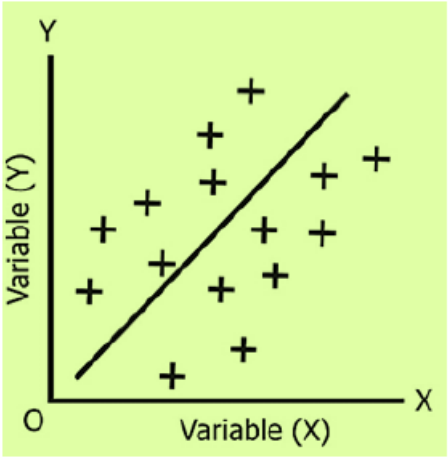

Fig. 8: Scatter diagram.[46]

11) Brainstorming technique

Brainstorming is an organized group technique designed to generate as many ideas as possible in as little time as feasible, such as one session, and to evoke both individual and collective creativity.

- Structured Brainstorming: Each member of the group contributes an idea in turn or passes until the next round.
- Unstructured Brainstorming: Everyone in the group contributes ideas as they arise.[47]

❖ **What FDA Regulations Address Root Cause Analysis Requirements?[48]**

Table 4: Root Cause Analysis Requirements by FDA.

What FDA Regulations Address Root Cause Analysis Requirements?	
Drugs	**Devices**
21 CFR 211.192 for Production record verification. Before a batch is issued or distributed, all drug product manufacturing and control records, including those for packing and labeling, must be examined and authorized by the quality control unit to ensure compliance with all established, approved written procedures. Any unexplained discrepancy (including a percentage of theoretical yield exceeding the maximum or minimum percentages	21 CFR 820.100 for Corrective and preventive action. Each manufacturer must develop and maintain procedures for corrective and preventative action. The procedures must include requirements for: a. investigating the cause of nonconformities relating to the product, processes, and the quality system; determining the action(s) required to correct and prevent the recurrence of nonconforming product and other quality problems; and Presenting appropriate information for

established in master production and control records) or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed, shall be thoroughly investigated.	management evaluation regarding detected quality issues, as well as corrective and preventive measures. All activities specified by this section, as well as their outcomes, must be documented.

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