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Original Article

Quality risk management during pharmaceutical 'good distribution practices' – A plausible solution

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ABSTRACT

Quality of medicinal product is an important facet throughout lifecycle owing to its importance as acceptance criteria at customer's end. Drugs regulatory agencies have issued guidelines for quality risk evaluation, mitigation and review management. Quality risk management has become an integral part of quality management system at manufacturing plants. Procedures for deviation control, change control, investigations of market complaints and batch failures are dealt with the principle of quality risk management at the manufacturing facility. The exploratory study shows a dearth of research on quality risk management during supply chain operation, however, a few study has been carried out by keeping financial risk into account. This study addresses the gap in literature on quality risk management during supply chain operations. There are cases of unresolved customer complaints and batch failures originated due to inadequacies during distribution of pharmaceutical products. In absence of established quality risk management system during product shipment, there is no effective preventive plan related to risk factors. A corollary of manufacturing quality risk management has been drawn to the distribution of pharmaceutical products through this study. The quality risk management during pharmaceutical distribution may be useful to avoid market complaints, drug recalls, and regulatory actions. This study produces one unique model solution for industry professionals and policymakers opening a scope to reduce the product rejection thereby paving the way for substantial business growth.

1. Introduction

The distribution operation of pharmaceutical products has a fundamental obligation to maintain quality till shelf life and deliver a safe product to patients. An understanding of quality risk associated with the product shall enable supply chain managers to handle the pharmaceutical distribution more effectively. Pharmaceutical companies, during supply chain, face much quality risk. The risk disrupts the distribution of medicine in many ways such as their quantity and quality product delivery at the right time. Therefore, quality risk management during the distribution process of pharmaceutical products is highly recommended. Risk management principles are utilized in many areas of business including finance, manufacturing, insurance, occupational safety, public health, pharmacovigilance, and by agencies regulating these industries. Although there are some examples of the use of quality risk management in the pharmaceutical industry today, they do not represent the holistic approach that risk management has to offer across the supply chain network. It has been observed that the majority of risks during operations of the pharmaceutical supply chain are internal risks due to processes, people, and functions mismanagement which could be managed by suitable mitigation strategies [1].

The Quality risk management (QRM) is a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product. Further, QRM concept depends upon the understanding of terms 'Quality' and 'Risk'. The term Quality means "The degree to which a set of inherent properties of a product, system or process fulfills requirements" (ICHQ9) and as per ISO/IEC Guide 51, the term Risk means "The combination of the probability of occurrence of harm and the severity of that harm" [2]. The quality risk management process involves:

a. Hazards (sources of harm) that can adversely influence drug quality characteristics
b. Extent of harm
c. Sub processes critical for quality

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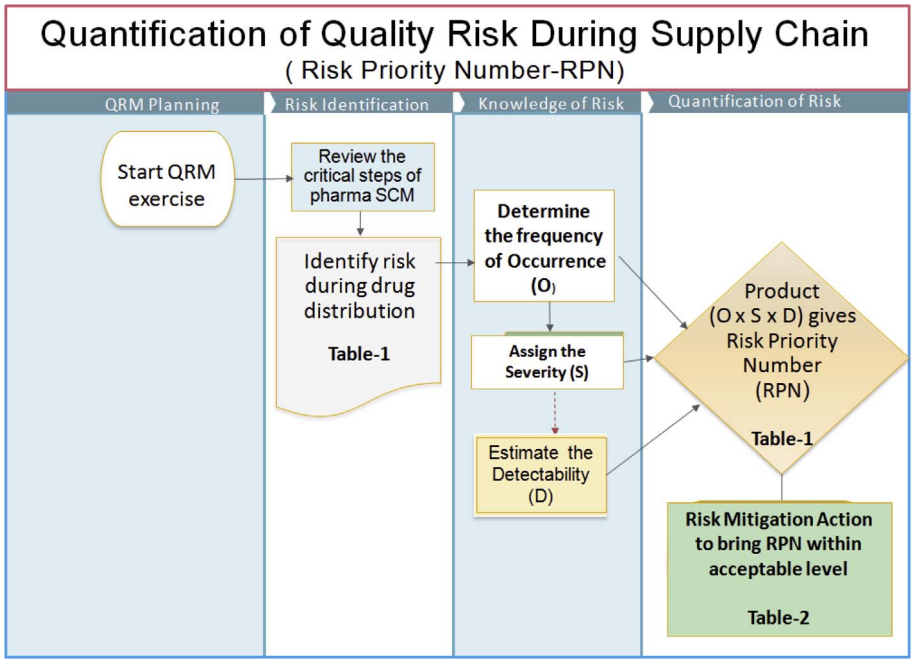

Fig. 1. Scheme for quality risk management.

Use', also known as ICH is an international agency which has issued guidance for the healthcare industry. ICH has described 'Quality Risk Management' in section Q9. The guidance ICH Q9 explains a process and methodology for QRM to add value. US Food & Drug Administration (FDA) has issued an identical guidance paper that serves as a foundation or resource document that supports other ICH Quality documents and complements existing quality guidelines within the pharmaceutical industry and regulatory environment [3,14]. According to corollary drawn from quality management principle there are two primary principles of quality risk management: (i) The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and (ii) The action and documentation of the quality risk management process should commensurate with the level of risk.

A scheme for quality risk management is outlined in the diagram (Fig. 1). The emphasis on each component of the QRM framework might differ from case to case but a robust process will incorporate consideration of all the elements of quality risk.

1.1. Literature review

The quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug product across the product lifecycle [2]. This is a proclaimed understanding amongst drugs manufacturers that Pharmaceutical supply chain should deliver medicines in the correct quantity, with the specified quality but the currently available literature have hardly discussed the quality aspects during pharmaceutical distribution management [1].

During the course of study of Mexican pharmaceutical industry Lutz Kaufmann (2005) has stated that An expansion of direct sales to pharmacy chains is certainly an appropriate measure to make the supply chain shorter and more transparent, however, the quality crisis arising due to improper cargo has been grossly overlooked in this study [18]. The quality of pharmaceutical product shall further deteriorate if the risk of temperature excursion is not handled appropriately [7]. As a key role of wholesalers in pharmaceutical products circulation, wholesalers are experiencing the dramatic change in market Macao. Wong (2012) aimed to improve the service of wholesalers and researched the functions of pharmaceutical wholesalers [19]. This indicates that Quality of pharmaceutical products is at higher risk if mitigation is not effectively ascertained [8]. The acceptable risk level can be decided by the manufacturer and its business unit, formulation and research development wings based on the standalone case and risk factor [10].

America based think-tank organization Product Quality Research Institute (PQRI) involves FDA's Center for Drug Evaluation and Research (CDER), industry, and academia in various case studies [21]. One working group was formed under the aegis of PQRI who studied the industry case studies for the purpose of improving and application of ICH: Q9 during 2008 and year 2011 [22,23]. This group comprised of eight experts from leading pharmaceutical manufacturers and US drug regulator. risk management working group of PQRI provided a summary of common risk management principles and best practices, several working tools to nurture consistency about the use of ICH Q9 in risk management process and a series of examples of risk management applications in use by major pharmaceutical multinational companies.

The working paper on drug quality and safety issues in India by Maulik Chokshi [5] observed that there are approximately 20% of pharmaceutical products have serious issues originated during supply chain operation such as:

a. Spurious drugs
b. Falsely labelled drugs
c. Counterfeit drugs

However, the above risk is due to administrative reasons rather than quality system aspects and hence have been considered out of the purview of this study. The issues raised here are perceived from the criminal angle and the quality perspective have been grossly excluded from this study.

1.2. Research gap

Quality risk management (QRM) is practiced by quality professionals of the pharmaceutical manufacturing plant, whereas the concept is not diligently practiced during pharmaceutical distribution operation [4]. Based on inference from review data and survey data, it is observed that there is need of enhanced awareness about the quality of the pharmaceutical product during pharmaceutical goods distribution

handled by supply chain managers.

Ironically none of the existing study paper and regulatory literature has discussed quality risk aspect of pharmaceutical product distribution or supply chain management, leaving the scope of study on QRM during supply chain operation [17].

Since there is a different kind of quality risk associated with pharmaceutical distribution, so there is need of study to enlighten the quality risk during supply chain management [6]. To validate the necessity of this study, an exhaustive search has been attempted through search engines with key phrase 'quality risk management during pharmaceutical distribution' and found that most of the studies are away from quality risk aspects during distribution operation [12]. The existing study is more focused on the general principle of quality risk management and there is lack of comprehensive illustrations during pharmaceutical distribution [13,16].

The literature review shows the lack of parity amongst available pieces of literature that lies between quality risk during manufacturing and that during distribution operations. Even the concept of quality by design (QbD) has been conceptualized by keeping manufacturing process quality risk in contemplation [26]. The disparity in the current literature between manufacturing and distribution approach for managing risk creates unresolved quality issues.

1.3. Objectives of study

In view of the gap observed in existing research papers, the study of quality risk aspect during pharmaceutical supply chain management is needed. This study shall be helpful to the pharmaceutical supply chain managers to protect the product and prevent rejections due to deteriorated quality. The objective of this research study is to:

a. Identify the various components of quality risk during pharmaceutical supply chain management and
b. Propose a model for illustration of quality risk management process during supply chain operations

This research details about the way to handle quality risk management during supply chain unit operations like transportation, shipping, replenishment handling and distribution. The study is limited to the quality perspective of pharmaceutical products and the risk arising due to criminal aspects like spurious, counterfeiting and falsification of products. Nirmal et al. have concluded that a significant number of pharmaceutical quality complaints are originated due to inadequacies in supply chain management [9,24].

1.4. Barriers before achieving the study objective

The major obstruction before producing the model solution for quality risk management during pharmaceutical good distribution practices is the unavailability of sufficient database of industrial losses due to quality defects generated during transportation and storage in the marketplace. There is literature available to describe financial risk during supply chain management, however; there is a dearth of literature effectively describing quality risk during distribution. This has imposed a limitation towards availability of secondary data related to losses due to quality defects that could be avoided with help of quality risk management.

2. Material and methods

The research is inductive because theory emerged from the review of material in the form of literature, data collection, and analysis. The secondary and primary data drawn from literature and survey conducted amongst the pharmaceutical professionals. The study uses a combination of descriptive and exploratory methods. Based on exploratory analysis for evaluating the status of Quality Risk Management (QRM) during distribution operation, the gap between available standards and application of drug regulatory guidance have been established. An interpretive conclusion shall be drawn based on this study. The materials from search engines have been collected analyzed and the relevant information has been drawn according to exclusion method.

The keywords used for review of literature survey available in the search engine (Google) were the terms such as Guidelines on Good Distribution Practices, GMP-GDP integration, Gap between GMP and GDP. The data displayed on the first page of Google against each browser hit were included in the study database. The information irrelevant to the study has been omitted as per consent of both authors. The following instruments were used for data generation for the study:

a. Primary data obtained from the survey among the pharmaceutical professionals were considered to assess the quality aspects of the distribution operation. The survey data was used to prioritize the quality risk during distribution process on Likert's scale i.e. Summated scale.
b. An exploratory study carried out to identify the quality risk associated with pharmaceutical good distribution operation. Regulatory guidance papers and related literature databases were searched for pharmaceutical supply chain risk management studies. Searching through databases in Google was done with different keywords: supply chain risk, good distribution practices, and quality risk management. Searching in each database was adapted to databases characteristics and additionally pharmaceutical risk. The results were screened and exclusion process was based on a consensus of both the authors:
   i. Resulting titles were reviewed and non-relevant articles were excluded by outcome of researcher boundaries of study
   ii. A few of the literature were found in different database and also, they were duplicated via different groups of keywords, hence duplicated references were eliminated
   iii. After screening the articles, abstracts of all remained articles were reviewed and the articles out of the purview of study and were not considered.
   iv. The full content of articles was read and a few of them were excluded by the outcome of interest.

3. Calculation – data and analysis

A survey design was used for the research, which provided a quantitative description of trends, attitudes, and opinions of the pharmaceutical professionals. Precaution was taken to avoid any sampling and non-sampling errors. The stimuli were selected from each of the various categories of the pharmaceutical industry, namely personnel from manufacturing plant operations and pharmaceutical supply chain management. Further, to select the sample respondents from these fields, the technique of convenience sampling (N = 260) under non-probability sampling was used. The results survey respondents were evaluated to study the opinion of pharmaceutical professionals in different companies catering pharmaceutical product requirement in international regulatory market engaged in business with US, EU, and Asia Pacific nations.

3.1. Data collection

A questionnaire with five sections was developed according to the research framework to measure five latent variables. Respondents were administered with the questionnaire consisting of items related to awareness, motivations and knowledge characteristics having linkage with quality risk during pharmaceutical supply chain management. The questions related to quality aspects of pharmaceutical products during supply chain operations which are managed with principles laid down under good distribution practices (GDP).

3.2. Data analysis

The participants could rate the detectability status of quality defects generated during the course of distribution operation on Likert's summated scale.

The reliability of test scores has been estimated by calculating Cronbach's alpha [24]. The reliability coefficient has been found to be 0.25 hence the test score is reliable.

4. Result – Estimation of quality risk during pharmaceutical distribution

The quality risk management requires quantification of risk with help of risk priority number (RPN) which is obtained by multiplying the three indices, namely detectability, occurrence, and severity. Survey data has been used to determine the detectability score (D) and occurrence score (O) each on the arbitrary scale of 1 to 5. The third-factor severity score (S) depends upon the pharmacological action of specific drug product and hazard associated thereto. The survey results amongst pharmaceutical professionals reveal five common quality risks during pharmaceutical transportation and handling [6].

4.1. Review of detectability score

These quality risks were identified and their detectability value was assigned based on the ranking of risk scores obtained through the survey among pharmaceutical professionals. The higher the detectability lesser shall be risk hence the detectability score (D) appears in reveres order from 5 to 1 (See Table 1).

4.2. Review of occurrence score

The frequency of occurrence (O) of quality defects during pharmaceutical distribution operation was determined on the basis of indices (scores) on summated scale of 1–5 and found that the probability of occurrence of defect – Label scratching or ink smudging shall cause illegible product information is the highest and defect like smell and taste is least probable (See Table 2).

4.3. Review of severity score

The severity index value against the quality risks identified has been assigned based on medical and pathological consequences on the scale of 1–5. This process is called impact assessment of severity.

It is observed that due to the breach of seal integrity there is the potential harm of microbial contamination and shall cause adverse drug reaction if such medicines are consumed. In view of this dire consequence and lethal drug effect the highest severity index has been marked 5 on the scale of '1 to 5'. (See Table 3)Table 4.

This depends upon a technical outlook of the drug manufacturer to design such a sealing pattern in medicinal product pack that shall sustain in case of mishandling. The exposure beyond specified environmental conditions such as higher temperature shall reduce the efficacy [25]. Hence the hazardous impact, in this case, is 4, on the higher side of scale '1 to 5'.

A comparative evaluation of severity impact between the two cases, seal break *vs.* environmental excursion reveals that the former shall cause microbial attack if impacted medicine is consumed by patient, whereas the temperature excursion reduces the efficacy.

4.4. Calculation of quantity of quality risk during pharmaceutical good distribution operations

The quality risk is quantified through a parametric number termed as Risk priority number (RPN). This is calculated by multiplication of, Detectability risk (D), Occurrence risk noticed (O) and 'Severity of potential hazard (S)' i.e. RPN = D × O × S

ICH: Q9 suggests the way to quantify the quality risk through calculation of risk priority number (See Fig. 2). Calculation of quality risk priority number (RPN) involves following steps:

Step-1: Identification and listing down of quality risk
Step-2: Assigning detectability score (D), occurrence risk (O) and severity score (S)
Step-3: Multiplication as detectability score (D) x occurrence score (O) x severity score (S)

Quality risk management comprises of three important components, risk identification, risk evaluation and risk mitigation. To mitigate these risks, it's important to understand the existing status of the pharmaceutical industry and potential quality risk. The challenge is not only assessing risk for an individual part or service but also to quantify the risk during good distribution practices by assigning the risk priority number (RPN). From the referred table, it is found that RPN is highest in case of risk due to 'environmental exposure beyond specified temperature causing product degradation, which is indicated in quality risk matrix (Fig. 3).

After the risk identification stage, the organization should plan to effectively reduce the risk to bring up to an acceptable level [15]. After risk mitigation strategy is established the respective action points are implemented to bring down the quality risk up to an acceptable level. The specimen risk mitigation strategies for good distribution practice have been cited in Table 5.

5. Discussion – A plausible model for good distribution quality risk management

The literature survey indicated that a principle of quality risk management (QRM) is exercised well during pharmaceutical good manufacturing practices (GMP), whereas the same principles are not diligently followed during good distribution practices (GDP). Therefore, there is a need for a model for QRM during pharmaceutical distribution operation. The model shall be shall be helpful to mitigate the risk arising from pharmaceutical good distribution through supply chain network. The model for quality risk management during pharmaceutical drug distribution has been discussed as under:

Table 1
Survey data on Likert scale.

S. No	Star (1 Star – Strongly Disagree; 2 Star – Disagree; 3 Star – Neutral; 4 Star – Agree; 5 Star – Strongly Agree)	1 Star	2 Star	3 Star	4 Star	5 Star	Population Strongly Agree and Agree	Inference about comparative Detectability
Q1	Exposure beyond specified temperature shall cause degradation	0.0%	0.0%	3.9%	25.0%	71.2%	96%	1
Q2	Seal break shall cause microbial contamination	1.9%	3.9%	5.8%	19.2%	69.2%	88%	2
Q3	Mishandling shall cause defect related to product integrity	0.0%	3.9%	9.6%	25.0%	61.5%	87%	3
Q4	Label scratching or ink smudging shall cause illegible product information	3.9%	5.8%	9.6%	19.2%	61.5%	81%	4
Q5	Transit in common cargo (eg shared with paint/cement etc) shall cause bad smell and taste	3.9%	9.6%	19.2%	23.1%	44.2%	67%	5

Table 2
Estimation of detectability score (D) and occurrence score (O).

S. No	S. No	Defect during distribution	Detectability	Detectability score (D)	Occurrence score (O)
Q1	1.	Exposure beyond specified temperature cause degradation	1	5	4
Q2	2.	Seal break shall cause microbial contamination	2	4	2
Q3	3.	Mishandling shall cause defect related to product integrity	3	3	3
Q4	4.	Label scratching or ink smudging shall cause illegible product information	5	2	5
Q5	5.	Transit in common cargo (eg shared with paint/cement etc) shall cause bad smell and taste	4	1	1

5.1. Scope of the model

This model provides principles & examples of tools of quality risk management that can be applied to distinct aspects of pharmaceutical quality. These aspects include the creation of post-manufacturing finished good transfer note (FGTN), despatch, transfer to warehouse, distribution, and the inspection and submission/review processes throughout the distribution of drug (medicinal) products. A systematic approach to facilitate and improve science-based decision making with respect to risk to the quality of pharmaceutical products during distribution operations is the foundation of successful quality risk management.

5.2. Principles of supply chain quality risk management

The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient's health. The level of effort, formality, and documentation of the quality risk management process should be commensurate with the level of risk.

5.3. Step of supply chain quality risk management

The quality risk identification starts with listing down each activity associated with various components of supply chain management and calculating the risk priority number with each of them. The team of senior management from the organization led by quality personnel shall decide the acceptable level of risk. The most vital action item in supply chain quality management is to define the corrective and preventive action (CAPA) plans in response to identified sources of risk throughout the lifecycle of the product including that during supply chain network [9]. The schematic process flow of supply chain quality risk management is envisaged as under:

a. Identify the processes and sub-processes during distribution such as transportation, replenishment during shipping, risk environment, storage, and handling.
b. Generate ideas and probable sources of risk by involving representatives from all sub-processes.
c. Identify the risks
d. Quantify the risk in terms of RPN
e. Define the acceptance level of RPN
f. Assign roles for mitigating the risks
g. Mitigate the risk with help of product knowledge acquired from the manufacturer, controls techniques, better infrastructure for handling of pharmaceutical products and the suitable environment during storage of the product.
h. Periodic review to maintain the risk control plans in place

5.4. Guiding values of quality risk mitigation

Adapt the quality risk management with help of concerned involved across all levels of supply chain. The risk control aspects are:

a. Decision-making activity
b. Residual Risk
c. Risk Reduction
d. Risk Acceptance

5.5. Continually explore new factors posing quality risks

The cause-effect diagram is used to depict the cause-effect relationship between risk and its contributing factors collected through brainstorming sessions. The various risk causing factors are listed down as a part of the brainstorming exercise. The quality risk may be originated man, material, method, machine etc and can be categorized as following factors:

- System Risk (facility & personnel)
  – e.g. operators risk, resource components such as equipment, automated design elements
- System Risk (organization)
  – e.g. policies, controls, measurements, documentation, regulatory compliance
- Process Risk (methods & procedure)
  – e.g. process operations and quality parameters
- Product Risk (safety & efficacy)

e.g. quality attributes, specifications

5.6. Risk mitigation and acceptance review

Against each of the quality risk contributing factor, suitable risk mitigation plan should be applied to bring down the residual risk to an acceptable level [11].

The tool like FMEA (Failure Mode Effect Analysis) should be used for evaluation of processes failures and its impact on the product to list down the failure modes and their effects (See Table 6). Ultimately all reasons possible failures should be brought up to an acceptable risk level with help of stringent controls during storage and transportation of dug products [20].

Table 3
Estimation of severity score (S).

S. No	S. No	Defect during distribution	Potential Consequences	Severity index (S)
Q1	1	Exposure beyond specified temperature that shall cause degradation	Lack of drug efficacy	4
Q2	2	Seal break shall cause microbial contamination	Adverse drug reactions	5
Q3	3	Mishandling shall cause defect related to product integrity	Loss of product	2
Q4	5	Label scratching or ink smudging shall cause illegible product information	Confusion about manufacturing date	3
Q5	4	Transit in common cargo (eg shared with paint/cement etc) shall cause bad smell and taste	Aesthetic impact	1

Table 4
Calculation of risk priority number (RPN).

S. No	S. No	Risk during distribution	D	O x S	Risk Priority Number (RPN = S × O × D)
Q1	1	Exposure beyond specified temperature that shall cause degradation	5	16	80
Q2	2	Seal break shall cause microbial contamination	4	10	40
Q3	3	Mishandling shall cause defect related to product integrity	3	6	18
Q4	5	Label scratching or ink smudging shall cause illegible product information	2	15	30
Q5	4	Transit in common cargo (eg shared with paint/cement etc) shall cause bad smell and taste	1	1	1

Abbreviations – S: Severity, O – Occurrence, D – Detectability, RPN – Risk Priority Number.

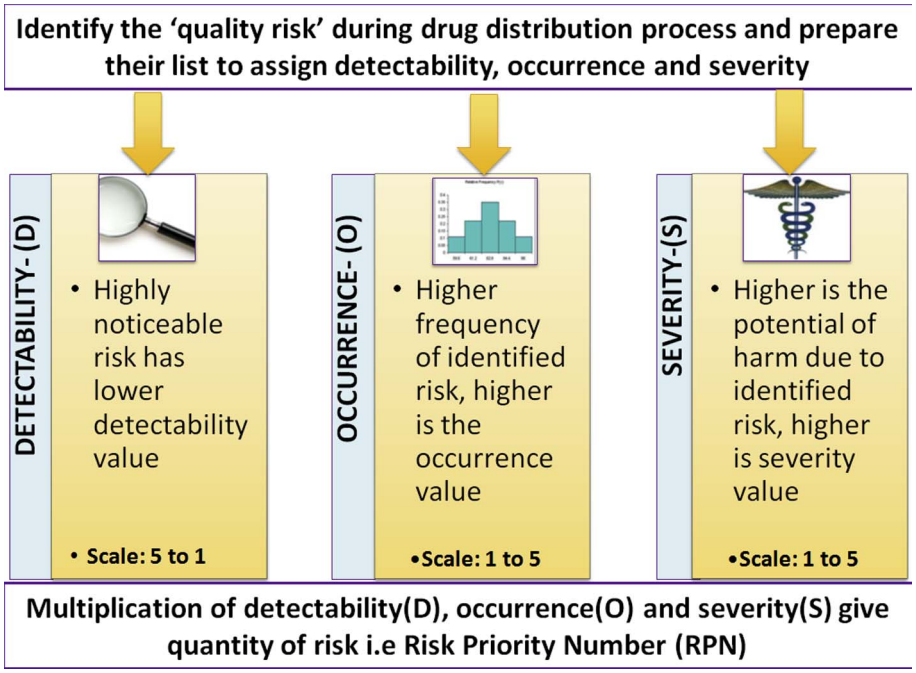

Fig. 2. Scheme for quality risk priority number quantification.

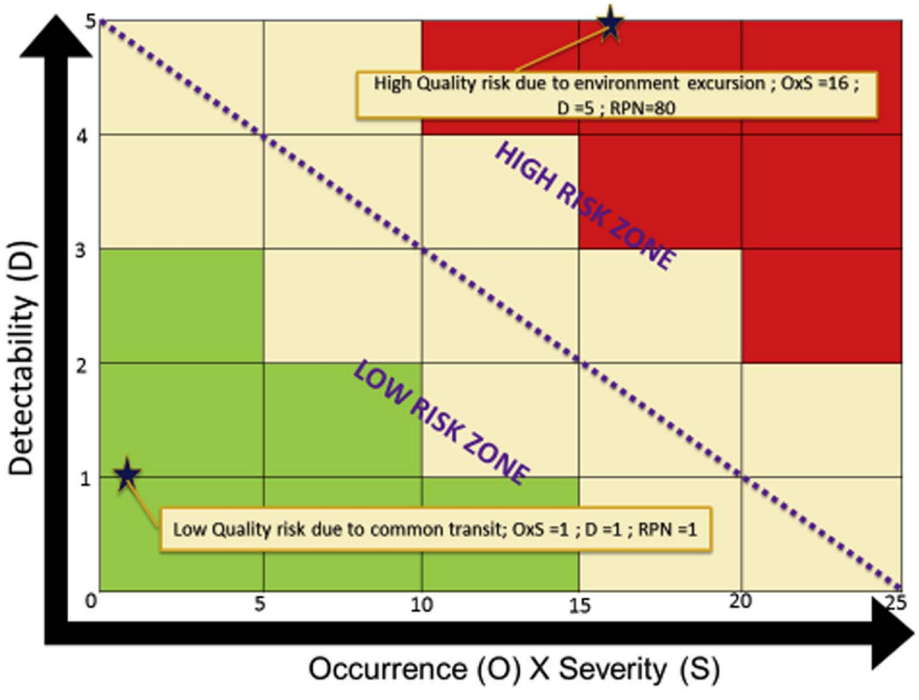

Fig. 3. Quality risk matrix before quality risk mitigation.

Table 5
Specimen risk mitigation plan proposed to reduce RPN.

S. No	Defect during distribution	Risk mitigation strategy
Q1	Exposure beyond specified temperature that shall cause degradation	– Endorsing environmental storage conditions in transport agreements, – Display of instructions on product packs, – Digital data loggers (temperature measuring devices), – SMS alert for temperature excursions. – Investigation of cases reporting the environmental excursion during distribution and transportation – Effective control of temperature excursions through adequate corrective and preventive actions.
Q2	Seal break shall cause microbial contamination	Robust seal design which shall pass the stringent leak test In process testing of sealing process during packing operation
Q3	Mishandling shall cause defect related to product integrity	Caution notes Training to logistics personnel
Q4	Transit in common cargo (eg shared with paint/cement etc) shall cause bad smell and taste	Agreement with shipment agencies to ensure that pharmaceutical products shall not be transported with non-pharmaceutical (contaminating) materials Caution note for drivers to keep the medicines isolated from smelling products
Q5	Label scratching or ink smudging shall cause illegible product information	Water proof labels on product packs Secured handling procedure

The success of a strategy depends upon the effectiveness of mitigation strategy that shall substantially reduce the Risk Priority Number (RPN).

The potential failure modes should be identified along with their associated risks and controls on the basis of particular supply chain function. After successful mitigation strategy, the supply chain quality risk is bound to come down to an acceptable level (See Fig. 4).

The pharmaceutical industry and regulators assess and manage risk using recognized risk management tools and/ or internal standard operating procedures. The non-exhaustive examples of some of these tools used for mitigation of quality risks are FMEA, FMECA, FTA, PHA and risk ranking (See Table 7).

6. Scope of future study

The principles of quality risk management have the prophecy to identify, mitigate and periodically review the various risk within compass, thereby helping business to control the potential losses. The application of QRM is at wide acceptance level during pharmaceutical manufacturing operations. The pharmaceutical industry has been benefitted with considerable use of quality risk management to control deviations, complaints and recalls originated from the manufacturing site. The deployment of quality risk management tools in pharmaceutical good distribution practices shall help the industry to further strengthen the cause. Based on this study there is a scope available to produce and integrated framework of quality risk management (QRM) starting from good manufacturing practices (GMP) with good distribution practices(GDP) to propagate a holistic concept.

7. Conclusion and recommendations

The quality risk management (QRM) is an activity that integrates identification of quality risk, risk analysis, risk assessment, developing strategies to manage them. Some traditional QRM exercises are focused on pharmaceutical manufacturing only, however, the ignorance of quality risk during distribution poses business challenges finally leading to market complaints, recall, rejections, and regulatory actions. A model way to deal quality risk during distribution operation provides

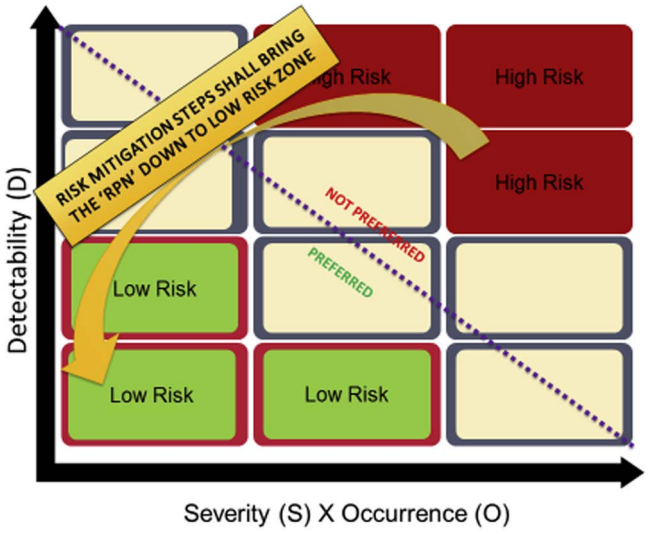

Fig. 4. Quality risk mitigation steps shall bring down RPN from elevated risk to low-risk zone.

Table 7
Quality risk mitigation tools.

S. No	QRM Tools	Summary of Steps involved
1	Failure Mode Effects Analysis (FMEA)	Break down large complex processes into manageable steps and evaluating the risk
2	Failure Mode Effects and Criticality Analysis (FMECA)	FMEA & links severity probability & detectability to criticality
3	Fault Tree Analysis (FTA)	Tree of failure modes combinations with logical operators
4	Preliminary Hazard Analysis (PHA)	Possibilities that the risk event happens
5	Risk ranking and filtering	Compare and prioritize risks with factors for each risk

Table 6
Template for FMEA and risk mitigation.

Sl. No.	Potential Failure Mode (Hazards)	Potential Effects (Consequences)	RPN = SxOxD (Before Control Measures)	Potential Causes	Application of Control Measures	RPN = SxOxD	Acceptable (Yes/No)
1	Example-Consignment kept lying on port for longer time	Example-Product storage conditions (eg Temperature) not be maintained	(Say RPN = 125)	Example-Use of unqualified cargo	Example-Qualification of cargo through capability evaluation and SOP review	(Say RPN = 20)	Yes

Abbreviations S: Severity, O – Occurrence, D – Detectability, RPN – Risk Priority Number, FMEA: Failure Mode Effect Analysis.

more insight to supply chain strategy. This also helps to develop the understanding of the quality risk of supply chain management that facilitates logic-based risk control decisions for overall business growth through entrusted quality brand creation.

The quality risk management during pharmaceutical good distribution practices helps effective management of quality risks to ensure supply continuity is a significant challenge has following key steps:

i. Make quality and risk management as key elements during supply chain
ii. Identify the supply chain quality risk through holistic approach
iii. Establish risk mitigation tools during supply network
iv. Ensure that supplier risk management is an on-going activity, not one-time action
v. Enhance communication about risk elements and controls exercised across the supply chain
vi. Maintain comprehensive procedure, task and responsibility metrics

It is recommended that companies involved in pharmaceutical supply chain operation should adopt the concept of quality risk management for the goal of business accomplishment by reducing the losses and rejections due to poor quality. Each pharmaceutical organization must establish a mechanism for quality risk management during pharmaceutical distribution to accomplish the goals of patient's safety and customer satisfaction without apprehension of drug regulatory actions due to quality risk.

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