RESEARCH ARTICLE

An Appraisal of Adoption Status of "Quality By Design" Approach in Pharmaceutical Industries in Himachal Pradesh, India

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ABSTRACT

The present study aimed to evaluate the current status and adoption of the quality by design (QbD) approach in the pharmaceutical industries of Himachal Pradesh. The study was conducted by distributing a well-designed questionnaire survey, and data were collected electronically. In the study, the status of QbD adoption among pharmaceutical industries of Himachal Pradesh was investigated and also aimed to evaluate the factors influencing the QbD adoption. A total of 112 pharmaceutical units were enrolled initially for the study, but finally, 100 units participated in this study. A total of 97 responses were received and analyzed by Statistical Package for Social Sciences (SPSS) to derive the inferences related to QbD adoption status and the factors influencing QbD adoption. The results revealed a significant degree of QbD adoption among the participant pharmaceutical units. A total of 14 factors had been identified with 57 indicators. It has been observed that the key area where the adoption of QbD influences the industry output are 'Risk Assessment and efficient management of the unit' with the highest eigen-value at maximum variance and highest factor loading. This identified factor (F1) was found to be a crucial element in QbD adoption. The study indicated the identification of several factors for a successful QbD adoption and implementation in pharmaceutical manufacturing and the regulatory authority should inspire, be aware and support the companies by organizing consistent workshops, seminars, and pre-designed training programs.

Keywords: Pharmaceutical manufacturing, Pharmaceutical Quality, QTPP, Quality by Design (QbD), Risk Assessment, Risk Management.

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INTRODUCTION

Quality has become the utmost important norm laid by all regulatory bodies for pharmaceutical products[1] and Indian regulators have been constantly revising the guidelines to pave the way for adoption and implementation of a quality driven approach. Quality denotes customer satisfaction via consistency in terms of service, product, and process. Quality and related activities have become the trend for success in every aspect for excelling in local and global markets.[1] Customer satisfaction has evolved to new height demanding superior quality products and services at low cost with consistency and timely schedule. Various product parameters are involved in maintaining a satisfied customer pool, including cost, product performance, serviceability, robustness, ease of application, and trustworthiness.[2] Generally, products are tested for quality control and assurance. But, just analysis of final product will not ensure the quality of the product; rather the quality should be designed into entire process and the product. The emphasis must be on precaution rather than on just testing followed by correction of quality problems. The quality by testing has become an obsolete concept in present day scenario. The various quality related product features must be built into the product and the manufacturing process should be such that the product is free from all kind of deficiencies. This concept of building quality into product paved the QbD approach, which has become a driving strategy in present day world.[3,4]

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Well-known quality expert, Joseph Moses Juran first described the concept of QbD approach[5] and believed that mostly all quality problems arise due to issues from initial product planning steps. He believed that quality can be planned and built into the product, provided proper optimized panning is done first. The principles of QbD have been applied to improve the product and process quality in every industry.[3]

Cost and clinically effective drugs with high safety profiles are the need of the hour for the pharmaceutical industry. They are investing a fortune to achieve the same in the drug discovery and development process, endeavoring to design quality products with consistency in the manufacturing process to deliver the product's intended performance. A plethora of gathered pharmaceutical knowledge and information related to manufacturing, provides a basic framework for logical and scientific understanding of process variables to prop up a design space, manufacturing controls, and control of materials. The knowledge of pharmaceutical development can help to make protocols for risk management for quality arena.[6] The data relating to manufacturing alongside the data from lifecycle management forms a basis for the design space.[7] This design space is planned initially and can be submitted for regulatory audit and assessment following approval. The audited design space can be explored while manufacturing or processing to ensure no failure in quality norms.[8] However, any operation out of this design space is considered a change and needs to be audited and addressed as a post approval regulatory change.[9] There are various parameters related to drug development and manufacturing, such as active pharmaceutical ingredients, excipients, container closure systems, processes involved in manufacturing, and quality control tests,[10] which are critical to finished product quality. These can be designed and planned for an optimized quality product. The QbD approach can lead to a state of industrial art standard which ultimately equips the industries to manufacture quality products with superior acceptability and financial gains. Therefore, the present study aimed to investigate the status of the adoption of QbD and indicators influencing the QbD adoption by the pharmaceutical units in Himachal Pradesh.

METHODS

Study Design

We conducted a survey of Pharmaceutical Industries in state of Himachal Pradesh for exploring the status of adoption of QbD approach.

Study Area

The area for the present study was the state of Himachal Pradesh. Himachal Pradesh is considered a pharmaceutical manufacturing hub in India and all categories of pharmaceutical manufacturing industries based upon their annual turnover viz; large scale, medium scale and small-scale pharmaceutical units exist in Himachal Pradesh. Himachal Pradesh comprises of twelve districts: Bilaspur, Chamba, Hamirpur, Kangra, Kinnaur, Kullu, Lahaul and Spiti, Mandi, Shimla, Sirmaur, Solan, and Una. The pharmaceutical industries are present in seven districts; Bilsapur, Kangra, Mandi, Shimla, Sirmour, Solan and Una. The study population comprised of all the manufacturing units which responded to the survey invitation

Sample Size

The study is descriptive and utilized a pre-structured questionnaire for performing the survey. At the time of review, 558 pharmaceutical companies were operating in different state locations as per the data available from the office of the Drug Controller of Himachal Pradesh. The companies were divided into large, medium and small-scale industries based on their annual turnovers. Sample size for the present study was 112 based on stratified proportionate random sampling.

Participants

Respondents for this study were either quality assurance heads or quality control heads or a person holding both responsibilities in the participant companies.

Procedure

A comprehensive review of the existing literature and regulatory guidelines on quality by design approach was performed to construct a relevant and effective measurement scale. While constructing the questionnaire, due consideration was given to keep it simple and easy to understand. QbD adoption and indicators influencing QbD adoption were selected based upon literature review. The organization demographic factors considered in this study included, position of the respondent, his/her department, education, the experience of the respondent in the company, age of the company, number of employees, type of products, quality management trainings, approvals, certifications, awards, and awareness. The QbD adoption and its indicators were considered for evaluation, followed by extracting significant factors using SPSS. The organizational variables were also studied, and descriptive statistical analysis was performed to derive insight into the organization's status in the quality context. An attempt was made to understand QbD adoption and its influencing indicators in the context of organizational and other pre-framed factors. The questionnaire comprised of general question like the organizational demographic profile of the manufacturers along with details about the respondents. The questionnaire also comprised of questions related to quality and QbD approach. The questionnaire was sent to 112 representatives of pharmaceutical companies across Himachal Pradesh. Out of 112, 12 companies were observed to be closed and a response to the survey was sought from 100 companies. A time frame of one month was allotted to each participant for filling up the survey. The survey was constructed and distributed via Google forms. A rather high response rate of 97% was received with 97 out of 100 companies approached for the survey responding in the given time frame. This can be attributed to the frequent follow-ups and the online mode of the survey. As certain data, especially about ongoing development projects, is kept confidential by pharmaceutical companies, some of the contacted individuals were reluctant to participate to avoid handing out any confidential data. This

issue was known beforehand and addressed with great care. It was ensured that the survey was completely anonymous, and the questionnaire was designed in a way to avoid any sensitive information and leave the possibility to enter blank data through open-ended questions. Yet, some questions were still perceived to ask for semi- or full-sensitive data which drove many potential participants to halt participation.

Measurements

The 5 points Likert's scale categorized under the interval scale was utilized to measure the respondents opinions by specifying by what range they agree or disagree to the statement in the questionnaire i.e. range between strongly disagree (1) to strongly Agree (5). Another 5point modified Likert's scale was also utilized to measure the respondents knowledge/ perception by specifying by what point they agree or disagree to the statement i.e. range between never (1) to always (5).[11,12]

Statistical Analyses

The data were analyzed using SPSS version 20.0 (IBM Corp. Released 2011, IBM SPSS Statistics for Windows, and Version 20.0. Armonk, NY: IBM Corp.). Participants with more than one missing value within a scale were excluded. A *p*-value of ≤0.05 was considered statistically significant. Coefficients between 0 and 0.30 were defined as a weak correlation, from 0.30 to 0.50 as moderate, and 0.50 or higher, as a strong correlation. Factor analyses were performed to extract the factors.[12]

RESULTS AND DISCUSSION

Organizational Demography: Findings About the Pharmaceutical Industry

In total, 97 responses were received representing 97 unique manufacturing units. Out of the responses received, 43.2% were from Quality Control department (QC Head), 48.4% from Quality Assurance department (QA Head), and 8.4% were from the person holding both QC Head and QA Head positions. Participating units were based in the following zones: BBN (Baddi, Brotiwala and Nalagarh) 54.5%, Sirmour20.2%, Solan (except BBN) 15.1%, Kangra 3%, Una3% and others 2%.WHO GMP Certified units comprised 32% of participants, whereas 2.1% were MHRA approved and 1% is USFDA approved units. Out of 97 units, 33.3% of participants deal with their brands as well as third-party manufacturing, 27.3% are only third part manufacturers, 18.2% are dealing with all possible kind of business dealings, 13.1% manufacturer only their brands, 5.1% are exporting their brands and 1% are exporting as third-party manufacturers. It is noteworthy that all participating units were engaged in continuous manufacturing activities. The respondents' experience in their current positions ranged from less than one to over sixteen years. While 34.3% of respondents had 0-5 years of experience, 27.3% had 6 to 10 years, 17.2% had 11 to 15 years, 16.5% had over 16 years of experience, and 7% of respondents did not answer this question. The frequency and percent data from the organizational demography are presented in Table 1. The sample contained all different kinds of units:

Table 1: Organizational demographic findings of the surveyed pharmaceutical industries

Organizational Demographic Parameters	*Frequency*	*Percent*
The position of the respondent		
QC Head	41	42.27
QA Head	46	47.42
Both	8	8.25
Not answered	2	2.06
Qualification of the respondent		
PhD	4	4.13
Master degree	53	54.64
Bachelor degree	40	41.24
Background of the respondent		
Engineering	2	2.06
Business	3	3.09
Science	68	70.10
Pharmacy	22	22.68
Science and pharmacy	2	2.06
Experience of the respondent		
0-5 years	32	32.99
6-10 years	27	27.84
11-15 years	17	17.53
16 years and above	16	16.50
Not answered	5	5.15
Quality Improvement Training of the respondent		
Yes	40	41.24
No	57	58.76
Number of employees	*Frequency*	*Percent*
Below 50	25	25.77
Between 50-100	20	20.62
Between 101-250	14	14.43
Above 250	9	9.28
Not answered	29	29.90
Age of the company		
Below 5 years	5	5.15
Between 6-10 years	25	25.77
Above 10 years	41	42.27
Not answered	26	26.80
Year of Establishment		
Between 1980 and 1990	2	2.06
Between 1991 and 2000	4	4.12
Between 2001 and 2010	56	57.73
After 2010	10	10.31
Not answered	25	25.77
Dealings (Trade Type)		
Own brand	13	13.40
Third party	27	27.84
Own brand and third party	18	18.56

Organizational Demographic Parameters	*Frequency*	*Percent*
Own brand and export	33	34.02
Third party and export	5	5.15
Own brand and third party and export	1	1.03
Turnover (2016-2017)	*Frequency*	*Percent*
Below 10 cr	30	30.93
10-50 cr	36	37.11
51-100 cr	9	9.28
101-200 cr	5	5.15`
201-500 cr	8	8.25
501-1000 cr	4	4.12`
Above 1000 cr	3	3.09
Not answered	2	2.06
Approvals		
USFDA approved	1	1.03
MHRA approved	2	2.06
WHO GMP certified	31	31.96
None of these	63	64.95
Schedule M Compliance		
Complied	97	100
Not Complied	0	0
ISO Certification		
IS0 9001	11	11.34
ISO 9001:2000	5	5.15
ISO 9001:2008	43	44.33
No ISO Certification	38	39.18
Certificate of International Quality Assurance System		
Certified	11	11.34
Not Certified	70	72.16
Cannot Say	16	16.49

from small, medium and rather local up to large scale units and from highly specialized to very broadly operating units. Also in terms of popular manufacturing brands, most major manufacturers (India) were represented. Additionally, there were participants from two departments (e.g. Quality control and quality assurance) with different experience levels. Based on the demographics of the respondents, the sample appears to be a good representation of the pharmaceutical industry in India and can, therefore, be used to derive inferences about the current state of the pharmaceutical industry.

Factor Extraction: Adoption of QbD in the Pharmaceutical Industries

Data analysis was performed using SPSS for analysis and evaluation of data from organizational demography and adoption parameters. The factor analysis was carried out on SPSS version 20.0 as a dimension reduction test. Since the present study variables are multi-dimensional concepts, there was a need to examine the dimensionality of each main variable and define the number of dimensions that constitute the variable. Factor extraction becomes handy for analyzing and evaluating the interactions and correlations between parameters based on statistical relevance. Principal component analysis was used as an extraction method in the factor analysis followed by Varimax rotation with Kaiser normalization. Based on the Eigen-values and rotation component matrix, 14 factors were extracted from the adoption section.

Table 2: Total variance Explained: Factor extraction

Total Variance Explained			
	Rotation Sums of Squared Loadings		
Component	*Total*	*% of Variance*	*Cumulative %*
1	6.371	11.176	11.176
2	4.817	8.451	19.627
3	4.656	8.169	27.796
4	4.177	7.329	35.125
5	3.302	5.792	40.918
6	3.249	5.701	46.618
7	3.070	5.387	52.005
8	2.680	4.702	56.707
9	2.301	4.036	60.743
10	2.150	3.772	64.514
11	1.786	3.133	67.647
12	1.762	3.091	70.738
13	1.575	2.764	73.502
14	1.426	2.501	76.003

Extraction Method: Principal Component Analysis.

Elucidation of the Extracted Factors

F1: Risk Assessment and Efficient Management: Out of the 14 factors extracted, it is the first factor. It has the maximum Eigen-value of 6.371 and accounted for 11.176% of the total variance. The indicator of supportive statistical tools has the highest factor loading of 0.741. This suggests that Risk Assessment and efficient management factor explained most of the variance and was the most important factor in determining the overall QbD adoption in the study area. There were 10 indicators associated with Risk Assessment and Efficient Management. Among these, the indicator 'supportive statistical tools' were highly correlated with 'Risk Assessment and Efficient Management followed by Failure Mode', 'Effects & Criticality Analysis (FMECA)', 'Fault Tree Analysis (FTA)', 'Preliminary Hazard Analysis (PHA)', 'Failure Mode Effect Analysis (FMA) as a risk management tool', 'Hazard Analysis & Critical Control Points (HACCP)', 'company policy to assess risks, Risk Ranking & Filtering', 'Basic risk management facilitation methods (Flow charts, check sheets etc)', and 'Setting up of appropriate calibration and maintenance schedules' (Table 2).

F2: Effective company policy to ensure quality: It became the second most important factor in the analysis. This factor comprises of 8 indicators. They together exhibit 8.451% variance and have Eigen value of 4.817. The indicator 'regular internal and external auditing/inspections' has the highest factor loading of 0.801 followed by 'Risk minimization steps', 'Hygiene aspects', 'The process control strategies', 'periodically

conduct Internal and External auditing/inspections', 'Internal and External auditing/inspections', 'periodical review of Quality policy and timely feedback' respectively.

F3: Good documentation practice in terms of implementing company policy and control strategy: This shows 8.169% variance with Eigen value of 4.656. The indicator 'documentation prepared or not before commencing production' was found to be highly correlated with this factor having the highest factor loading of 0.873 followed by 'quality policy' is communicated with 0.779 loading; 'structured approach for implementing corrective and preventive actions' with, 0.761; 'monitoring critical process parameters', 0.601; 'data management and statistical tools', 0.537; 'process flow diagrams prepared', 0.454; and 'Rationale for selection of container closure system', 0.422.

F4: QTPP (Quality Target Product Profile): Six indicators viz 'documentation prepared (respect to **r**oute of administration, dosage form and delivery system)', 'documentation prepared (concerning factors affecting pharmacokinetics)', 'documentation prepared (respect to intended use)', 'documentation prepared (related to factors affecting release of therapeutic moiety/moieties)', 'appropriate Control Strategy (Chemical properties) and appropriate Control Strategy (Physical properties)' were found to be associated with the factor name 'QTPP (quality target product profile)'. This factor explained 7.329% variance with Eigen value of 4.177. The indicator 'documentation prepared (respect to the route of administration, dosage form and delivery system)' had the highest factor loading of 0.805 as compared to other indicators.

F5: Continuous improvement: This is the fifth factor obtained from the analysis and exhibited 5.792% of the variance with Eigen value of 3.302. The indicator having the highest factor loading of 0.743 was 'designed/installed aspects such as the flow of materials and personnel' followed by 'contamination minimization aspects', 'dedicated facilities and dedicate equipment', 'appropriate resources/training to the employees' and 'open vs. close equipment.

F6: Effective company policy to ensure quality: This factor is comprised of five indicators namely 'Material analysis and equipment monitoring', 'sharing information related to identified risk', 'identification of Sources of variations affecting process performance and product quality', 'ensured improvement', and 'periodical review of Information and data about product quality and manufacturing experience'. This extracted factor explained 5.701% of the total variance with an Eigen value of 3.249 and the highest factor loading of 0.785 for 'Material analysis and equipment monitoring'.

F7: Calibration of instruments and revision of SOPs at a pre-determined schedule: This factor explained 5.387% of the variance with Eigen value of 3.070. The indicator 'Regular and periodical maintenance of the facility, 'utilities and equipment' was found to be highly correlated with this factor with the highest factor loading of 0.766 followed by 'implementation of necessary steps to ensure prevention of mix-ups',0.613; and 'Scrutiny of intra-batch as well as inter-batch variation' 0.590 respectively.

F8: Effective company policy to ensure quality (AMV, PDR and vigilance): This came out to be the eighth important factor in the analysis. This factor comprises of 3 indicators. They together exhibit 4.702% of the variance and have Eigen value of 2.680. The indicator 'documentation (AMV/PDR)' had the highest factor loading of 0.698 followed by 'Responsible senior management for effective pharmaceutical quality system', 0.559; and 'Manufacturing process validation', 0.473.

F9: QTPP (documentation about primary & secondary packaging, stability studies and quality testing): The factor' QTPP' explained 4.036% of the variance with Eigen value of 2.301. The indicator 'documentation prepared (respect to **c**ontainer closure system)' was highly correlated with this factor having the highest factor loading of 0.843; followed by 'documentation prepared (respect to factors about drug product quality criteria)' with 0.653.

F10: Effective company policy to ensure effective risk assessment and to update regulatory authority on time: This factor is comprised of 3 indicators, namely 'sharing information related to identified risk with other companies', 'sharing information related to identified risk with the regulators' and 'company policy for sharing risk assessment report within the company'. This extracted factor explained 3.772% of the variance with Eigen value of 2.150 and factor loadings of 0.726, 0.700 and 0.487, respectively.

F11: Effective quality assurance protocol and in-process quality control strategy: This is the eleventh factor obtained from the analysis and exhibits 3.133% of the variance with Eigen value of 1.786 and factor loading of 0.803 and 0.392, respectively.

F12: Risk management: Risk management comprises one indicator, namely 'Literature reviews including Historical data/ literature/theoretical analysis/informed opinions etc for risk identification'. This extracted factor explained 3.091% of the variance with Eigen value of 1.762 and factor loading of 0.613.

F13: Audit readiness: It comprises one indicator namely 'regular Internal and External auditing/inspections' to ensure 100% compliance to SOPs. This extracted factor explained 2.764% of the variance with Eigen value of 1.575 and factor loading of 0.742.

F14: Interaction of QA/QC people with production: The factor 'Interaction of QA/QC people with production' comprises one indicator, namely 'company policy to ensure the interaction of QA/QC people with production staff' periodically. This extracted factor explained 2.501% of the variance with Eigen value of 1.426 and factor loading of 0.568 (Table 3).

The findings of the study relate to QbD adoption by the pharmaceutical manufacturers in Himachal Pradesh. A total of 14 factors with 57 variables were considered in the questionnaire. Basedown of the Factor Analysis, fourteen new factors were identified. It is imperative that the new factors obtained after applying factor analysis can serve as an important tool to understand QbD adoption by the pharmaceutical units. First factor obtained was 'risk assessment and efficient management' with indicators like 'supportive statistical tools', 'Failure Mode, Effects and Criticality Analysis

(FMECA)', 'fault tree analysis (FTA)', 'preliminary hazard analysis (PHA)', 'failure mode effect analysis (FMA) as a risk management tool', 'Hazard Analysis and Critical Control Points (HACCP)', 'company policy to assess risks', 'Risk Ranking & Filtering', 'Basic risk management facilitation methods (Flow charts, check sheets etc)', and 'Setting up of appropriate calibration and maintenance schedules'. These indicators were strongly associated with the first factor. Second factor obtained was 'effective company policy to ensure quality' and the indicators involved were 'regular internal and external auditing/inspections', 'Risk minimization steps', 'Hygiene aspects', 'The process control strategies', 'periodically conduct Internal and External auditing/inspections', 'Internal and External auditing/inspections', and 'periodical review of quality policy and timely feedback'. Third factor obtained was 'good documentation practice in terms implementing company policy and control strategy', which comprises of the indicators like, 'documentation prepared or not before commencing production', 'quality policy is communicated', 'structured approach for implementing corrective and preventive actions', 'monitoring critical process parameters', 'Data management and statistical tools', 'Process flow diagrams prepared' and 'Rationale for selection of container closure system'. Fourth factor obtained was 'Quality Target Product Profile (QTPP)', which involved indicators like, 'documentation prepared (respect to **r**oute of administration, dosage form and delivery system)', 'documentation prepared (concerning factors affecting pharmacokinetics)', 'documentation prepared (respect to intended use)', 'documentation prepared (related to factors affecting release of therapeutic moiety/moieties)', 'appropriate

Table 3: Component Transformation Matrix: Factor extraction

Component Transformation Matrix							
Component	*1*	*2*	*3*	*4*	*5*	*6*	*7*
1	.530	.340	.386	.329	.271	.277	.253
2		.621	.075			.288	.076
3		.539		.147	.332		
4	.447					.162	
5			.168		.650	.114	
6	.262				.302		.552
7	.195	.313	.085	.257			
8		.068		.256	.155		.270
9				.137	.110	.692	
10				.413	.055	.145	.080
11			.120				
12		.073		.137		.176	.334
13		.149	.023	.210	.086		
14			.141	.101			
Component Transformation Matrix (Continued..)							
Component	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1	.232	.147	.176	.089	.043	.072	.105
2	.238					.051	
3		.378			.207	.103	
4	.336		.274	.144	.065	.127	.041
5			.047	.395	.052	.320	.081
6				.282			
7				.209			.048
8	.037		.349			.364	.284
9		.386	.128				
10	.480			.214			.092
11	.302	.484	.209	.243		.103	.382
12		.045	.134	.572	.302	.341	.004
13	.155		.448	.297	.018		
14	.244		.083	.038		.359	

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

control Strategy (Chemical properties)' and 'appropriate control Strategy (Physical properties)'. The fifth factor obtained was a continuous improvement having indicators like, 'designed/installed aspects such as the flow of materials & personnel' followed by 'contamination minimization aspects', 'dedicated facilities and dedicated equipment', 'appropriate resources/training to the employees' and 'Open Vs Close Equipment'. Sixth factor obtained was 'effective company policy to ensure quality' containing indicators like, 'Material analysis and equipment monitoring', 'sharing information related to identified risk', 'identification of sources of variations affecting process performance and product quality', 'ensured improvement', and 'periodical review of Information and data about product quality and manufacturing experience'. The seventh factor obtained was 'calibration of instruments and revision of SOPs at a pre-determined schedule'. It contained indicators like, 'Regular and periodical maintenance of the facility', 'utilities and equipment' followed by 'implementation of necessary steps to ensure prevention of mix-ups' and 'Scrutiny of intra-batch as well as inter-batch variation'. The eighth factor obtained was 'effective company policy to ensure quality (AMV, PDR and vigilance)' involves indicators, 'documentation (AMV/PDR)' followed by 'Responsible Senior Management for effective Pharmaceutical Quality System and Manufacturing process validation'. Ninth factor obtained was 'QTPP (documentation pertaining to primary & secondary packaging', stability studies and quality testing)' containing indicators like, 'documentation prepared (respect to **c**ontainer closure system)' followed by 'documentation prepared (respect to factors pertaining to drug product quality criteria)'.Tenth factor obtained was 'effective company policy to ensure effective risk assessment and to update regulatory authority in a timely manner' including indicators, 'sharing information related to identified risk with other companies', 'sharing information related to identified risk with the regulators' and 'company policy for sharing risk assessment report within the company'. Eleventh factor obtained was 'effective quality assurance protocol and in-process quality control strategy including indicators, Pest Control measures, and monitoring the manufacturing process. The factor twelve obtained was 'risk management including indicator, 'Literature reviews including Historical data/literature/theoretical analysis/ informed opinions etc for risk identification'. Thirteenth factor obtained was 'audit readiness including indicator, 'regular Internal and External auditing/inspections to ensure 100% compliance to SOPs'. Lastly, factor 14 was obtained as the 'interaction of QA/QC people with production' having only indicator, 'company policy to ensure the interaction of QA/ QC people with production staff periodically'. Each of the indicators mentioned in the above paragraph showed a strong correlation for the factors they were mapped to.

CONCLUSION

The present study focused on understanding the status of adoption of QbD and the factors which influence QbD adoption among pharmaceutical manufacturing units of Himachal Pradesh. The status of QbD adoption and factors influencing QbD adoption in the pharmaceutical manufacturing units were studied using 57 variables about QbD adoption. The study has classified these 57 variables into 14 factors using factor analysis. The outcome of this present study demonstrated that the pharmaceutical manufacturing units are approaching a better-quality orientated protocol by adopting and implementing various quality norms about the QbD concept. It has been observed that the key area where the adoption of QbD influences the industry output are 'Risk Assessment and efficient management of the unit' with the highest Eigen value at maximum variance and highest factor loading which explains the importance of factor F1. F1 is a crucial element in QbD adoption. Therefore, pharmaceutical manufacturers aiming at QbD adoption must involve and practice 'FMECA', 'FTA', 'PHA', 'FMA as a risk management tool', 'HACCP', 'company policy to assess risks', 'Risk Ranking and Filtering', 'Basic risk management facilitation methods (Flow charts, check sheets etc)', and 'Setting up of appropriate calibration and maintenance schedules for achievement of quality'. Other factors like 'Effective company policy to ensure quality', 'Good Documentation Practice in terms of implementing company policy and Control strategy', 'QTPP', 'Continuous improvement', 'Effective company policy to ensure quality', which were further identified as important factors based on Eigen value, variance and factor loading which disclose that organizations need a solid company policy and control strategy towards making their product quality consistent. Organizations need to focus on these factors to adopt QbD for achieving maximum benefits in terms of product quality and company growth.

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