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# IMPACT ASSESSMENT OF WORKPLACE ENVIRONMENT FOR DEVELOPMENT OF AN INTEGRATED SAFETY MANAGEMENT IN PHARMACEUTICAL INDUSTRIES

[1]Ashraf Saeed, [2]Gihan Hosny

[1]**Ashraf Saeed**, PhD Candidate and Integrated Management Systems Researcher
[2]**Gihan Hosny**, Professor of Public Health and Occupational Medicine
[1,2]Institute of Graduate Studies and Research, Alexandria University, Alexandria, Egypt

***Abstract:*** Pharmaceutical industry has a progressively multifaceted and energetic environment with some differences in the current years and this probably tends to continue for maximizing use of resources with highest levels of investments. Integrated management systems enhance organizations' performance through the management philosophy that allows the processes to be managed successfully and attain the desired results. The current study aimed to investigate the impact of workplace environment on development of integrated safety management system in pharmaceutical industries, review the key elements of integrated safety management system and describe benefits of implementation. The method used in this study was descriptive method making a simple random sampling conducted through gap analysis feasible to describe the actual requirements based on ISO 9001:2015, ISO 14001:2015, ISO 45001:2018 and cGMP for seven pharmaceutical companies from industrial zone in Alexandria, Egypt. The results revealed that the integrated management system has a constructive impact on production, employees, market, management, environment and occupational health & safety procedures. Gap analysis showed fluctuation over implementation of elements of the integrated management system. Also, the study illustrated that the developing management philosophy be situated internalized by executive managers and other employees has positive impact on sustainable development in addition to provide many benefits to organization. Thus, it can be concluded that integrated management systems (IMS) of quality, environment, and safety can pose significant competitive advantages for the companies. The main benefits of these types of systems are improvement for performance, also reduction of costs and time for implementation. The resistance to change is the greatest difficulty for these firms. These difficulties are resistance from employees and lack of top management commitment, and understanding of international standards.

***Keywords:*** *Safety, Workplace Environment, Pharmaceutical Industries, Integrated Safety Management, Integrated Management System*

## 1. Introduction

The pharmaceutical industry is an important sector of the healthcare structure conducts marketing, research and manufacturing of medicinal devices and biological and pharmaceuticals products intended for the treatment and diagnosis of diseases (Remington, 2006). Pharmaceutical organizations meet several new challenges to confirm efficient business processes. Project management has stayed a well-known utensil and well-established method outside the pharmaceutical industries several decades. The project management become a significant portion of the pharmaceutical industries in current situation (Müller *et al.*, 2013).

Organizations have to sell extra every day and aim to preserve or increase their existing market share necessary to familiarize laws such as consumer protection and occupational health & safety. Altering prospects of

consumers and stakeholders should be considered. The management carries a full commitment to environment, safety, and quality through the implementation of an integrated management system (IMS) based on ISO 14001, ISO 45001, and ISO 9001 standards and the GMP guide. Liability in linking with quality, environment, occupational health and safety are important for the competitiveness and helpful image of organizations. The organization's level of accountability and consideration for stakeholder interactions is demonstrated by the certification of its management systems in these areas (Darabont *et al.*, 2019).

ISO 9001 explains the requirements for improving customers satisfaction by implementing the requirements of customers and legal obligations. The standard has general provisions are authority, duties, organizational chart and liabilities, effective use of processes interrelationship, resources, service or product design, customer satisfaction, development works, internal audit, documentation and continuous improvement. The quality of pharmaceutical products has continuously stayed a main concern for the regulatory organizations in the world (Tsim *et al.*, 2015). ISO 14001 currently, with resources increasingly damaged in an irreparable process and all fundamentals to make the environment are further down risk. It is now believed by the entire world that the danger is not regional or local, but global. Both written and seeable broadcasting, there are a portion of environment-oriented tidings and message (Campos *et al.*, 2015). ISO 45001 is an internationally recognized standard defined as Occupational Health & Safety (OH&S) Management Systems that evaluates probable hazards that may arise throughout the workflow for a worker through risk analysis; its chief purpose is to make a better environment for working with the health and safety of workers (Morgado *et al.*, 2019).

The system of quality in the pharmaceutical manufacturing consistent of implementation the best management system of quality inside the manufacturing. However, International Council for Harmonization recently introduced a guide recognized as ICH Q10 that is basis both standard of ISO 9001 and Good Manufacturing Practices known as GMP. Pharmaceutical organizations are found in a special zone. In response to the market's demands, which impose ISO standards as a control mechanism, they must also respond to legal requirements requiring them to apply GMPs. Good practices provide specific responses to the requirements and enforce them as the only ones that are acceptable, whereas ISO standards provide businesses some latitude in meeting requirements and leave it to them to figure out the solutions on their own (Bekčić *et al.*, 2013).

The principal reason for focusing on these standards for studies conduct on IMSs defined as integrated management systems is environmental magnitude, quality and human health have developed an integral portion of current life. All standards can be applied in all the organizations disregarding of activity size, type, and number of personnel in organizations. These integrated standards also cover different cultural, social conditions and geographical (Nunhes *et al.*, 2019).

The aim of this study is to review the key elements of integrated management systems (IMSs) for pharmaceutical enterprises, develop an integrated management system (IMS) in terms of the upcoming revision of ISO 9001:2015, ISO 14001:2015, ISO 45001:2018 and cGMP, as well as to describe the benefits of implementation of such systems. Specific objectives were implemented: (Determine the current level of safety project management and perform gap analysis in some pharmaceutical companies; apply integrated safety project management in product manufacturing; analyze the key elements in project management in some pharmaceutical companies, identify its dimensions, and propose the consequences of integrated management system; and provide evidence about the factors that should be enforced to improve performance and integrate system in safety project management).

## 2. Materials and Methods

### 2.1. Study Methods

A cross sectional study was carried out in seven pharmaceutical companies representing vital sector of market share in Alexandria, Egypt. Verbal consent from study subjects to participate in the study was obtained before the start of work with assurance of confidentiality and anonymity of the data. Approval of the administrative authority of each company was obtained. Also, the study protocol was approved by Ethical Research Committee of Institute of Graduate Studies and Research, Alexandria University.

The sampling design was simple random sampling, in which every element in the population has equal chance of been selected as a sample, it has least bias and offer the most generalizability (Sekaran & Bougie, 2016). The population of the study is the entire internal auditors at companies. The data were administered and collected through internal auditors employed so that to facilitate quick retrieval of completed study gap analysis checklist and equally to provide high response rate (Hair *et al.*, 2010).

The study method used in this study is the descriptive method, which is a study to make improvements to the current conditions that are deemed necessary to be improved. The current condition data is obtained by performing an internal audit checklist according to ISO 9001:2015, ISO 14001:2015, ISO 45001:2018, and cGMP for the selected pharmaceutical companies. Including the head of the company, vice head of the company, and human resources working committee. Data on the condition is also obtained by performing direct

observation of the quality, environmental, occupational health and safety management system, and manufacturing practices documents made by the company.

### 2.2. Study tools:

A gap analysis checklist sheet was pre-designed in "English" language for high level of education. The structure of the gap analysis checklist was designed to cover the all variables in all standards. Gap analysis covering variables on quality management systems were 7 variables, environmental management systems were 7 variables, Occupational health and safety management systems were 7 variables, and good manufacturing practices were 12 variables. Respondents were asked to give their preference and spaces were provided beside each question to mark their preference on the 5-point scale.

Checklist assessment by respondents based on the current condition of each organization or company. The respondents chosen were the respondents who had enough competence (Picard *et al.*, 2016). Each item in the structured gap analysis checklist was measured on a 5-point Likert scale to measure validity of the item. The assessment is done by scoring system as follows:

- **1=Non-Compliance:** If the organization or the company does not understand what is required and does not do it.
- **2=Major N/C (Major Non-Conformance):** If an organization or company understand the importance of the activity but does not do it.
- **3=Minor N/C (Minor Non-Conformance):** (If the organization or the company have the documents but have not implemented or have implemented but not recorded).
- **4= OFI (Opportunities for Improvement):** If an organization or company does the activity but is not consistent.
- **5= Compliant:** If an organization or company do the activity consistently.

Gap assessment aimed to recognize how large a gap there was in the company. Percentage value was obtained by summing the scores of each variable and dividing it by the maximum value in the variable. The smaller the gap, the better. To measure preparedness, the obtained value of percentage corresponds to the preparedness of company in implementation (Bakhtiar & Purwanggono, 2009). The obtained data then weighted with a score of 1-5 with each percentage score presenting specified range of readiness of the company. The results then became a base to improve the readiness of the company in facing the Certification of ISO 9001:2015, ISO 14001:2015, ISO 45001:2018 and cGMP and prioritized according to lowest percentage, level of ease and the scope of effect produced. The percentage range of the gap value was as follows: (**90%–100%**) for work procedures and requirements that are well executed; (**75%–89%**) for work procedures and requirements that are run but are not consistent and have opportunities for improvement; (**64%–74%**) for some work procedures have not been executed but other requirements are well executed; (**50%–63%**) for many work procedures have not been executed but some requirements that do not require working procedures have been applied; (**< 50%**) for very poor implementation, and companies need to understand and review the implementation because it is still far from the requirements.

### 2.3. Standards and requirements variables

Study variables used in this study is taken from the clauses included in ISO 9001:2015 Quality Management System (International Organization for Standardization [IOS], 2015a), ISO 14001:2015 Environmental Management Systems (IOS, 2015b) and ISO 45001:2018 Occupational Health and Safety (IOS, 2018) the clauses that become a variable is only clause 4 to clause 10. As the following: (Context of the organization, Leadership, Planning, Support, Operation, Performance Evaluation and Improvement).

Also, study variables used in the study taken from the cGMP parameters observed in the current Good Manufacturing Practices (cGMP). The clauses that become variables is the following (WHO, 2014): (General, Validation, Water System, Storage Area, Documentation, Non-Sterile Products, Sterile Products, Quality Control, Quality Assurance, Packaging, HVAC System and Personnel).

### 2.4. Data management

#### 2.4.1. Data collection

The study used a gap analysis checklist for data collection. The gap analysis checklist examined the concerned the requirements for each standard was conducted among the internal auditors of pharmaceutical companies. Data was collected from the selected pharmaceutical companies in Alexandria between the March, 2022 to April, 2023. The gap analysis checklist was filled through interviews with internal auditors to the companies to get the perception from all standards to analyze the extent to which companies comply with the necessary requirements in the specifications (ISO 9001, ISO 14001, ISO 45001and cGMP).

### 2.4.2. Data analysis

After data were collected, data were revised, coded and fed to statistical software IBM SPSS version 27. Data entry and analysis was performed using Microsoft Excel. The given tables were constructed using Microsoft excel software (version 2019).

All statistical analysis was done using two tailed tests and alpha error of 0.05. P value less than or equal to 0.05 was considered to be statistically significant. Each respondent's overall scores were calculated by adding the scores for each measurement, which were obtained by adding the ratings for each individual statement. The internal consistency of each of the seven questionnaire dimensions was tested by calculating Cronbach's alpha coefficients (coefficients of reliability). ANOVA, Pearson's chi square test and Factor Analysis were utilized to assess and analyze the data.

The consistency reliability of the study was determined by the use of Cronbach's Coefficient Alpha that is used to test internal consistency. The alpha provided a coefficient to estimate consistency of scores on a gap analysis checklist when the items were scored as continuous variables. While the reliability coefficient of 0.7 was acceptable the gap analysis checklist designed and tested to determine the reliability coefficient.

The data obtained was analyzed using SPSS version 27 and presented in the form of tables. Descriptive statistics such as frequencies, percentages, means, standard deviations, and Pearson product-moment correlation coefficient were used to analyze the data. Descriptive analysis was performed to describe the sample profile of respondent. Five-point Likert scale are motivations that led them to the assessment and the main advantages is remove barriers to its implementation perceived (Armstrong & Overton, 1977).

A set of tests compared respondents who participated the gap analysis checklist during the first administration and those who participate when the gap analysis was submitted for the second time after improvement. T-test comparisons performed between the means of the two groups to show the significant differences (p-value <0.1). Data of percentages; maximum and minimum values; mean +/- SD were calculated. This analysis enables to point out to the variables that directly influence the present status for the requirements of the standards. The data were analyzed using SPSS, hence descriptive statistic was carried out, factor analysis was equally carried out so that to reduce the items into more manageable number (Pallant, 2020) in which after the factor analysis, the items remain for each variable certified the requirement of factor analysis, such as KMO >0.5, Bartlett's test of Sphericity p< 0.05 or smaller, communalities >0.5, factor loading above >0.5 (Murtagh & Heck, 2012), correlation matrix has been carried out and lastly, simple regression analysis was then conduct.

This study adopted descriptive and analysis to examine the gap analysis checklist in selected pharmaceutical companies. noted that descriptive and correlation methods basic designs of quantitative methods of study the correlation was intended to interaction between variables in analysis of gap for the requirements of the standards.

## 3. Results

### 3.1. Reliability Analysis

The Alpha Cronbach's coefficient was 0.999, 0.997, 0.998 and 0.998 for gap analysis checklist ISO 900:2015, ISO 14001:2015, ISO 45001:2018 and cGMP respectively. The value of the coefficient is higher than the statistically accepted 60%, reflecting a high degree of consistency and credibility in the data, and indicating that the data collected can be relied upon to complete the post-statistical examinations and hypotheses tests.

### 3.2. Profile of the Respondents:

### 3.2.1. Gap analysis result for ISO 9001:2015

Gap analysis checklist data is obtained through observation on field. In this research checklist data is in the form of system observation and audit checklist ISO 9001:2015 which are made to understand the condition of company readiness for certification. Data processing at this stage is to calculate the scores obtained from the gap analysis checklist. The results of score calculation will then be used as the basis for identifying level of readiness of the company in facing the certification of ISO 9001:2015. The total score for each company from the results of the checklist in order from the highest value of readiness level for certification to the lowest value of readiness level for certification are Company E (95.50%), Company F (92.55%), Company C (91.34%), Company D (89.19%), Company B (73.36%), Company G (63.69%) and Company A (49.46%), shown in table 1.

### 3.2.2. Gap analysis result for ISO 14001:2015

Gap analysis checklist data is obtained through observation on field. In this research checklist data is in the form of system observation and audit checklist ISO 14001:2015 which are made to understand the condition of company readiness for certification. Data processing at this stage is to calculate the scores obtained from the gap analysis checklist. The results of score calculation will then be used as the basis for identifying level of readiness of the company in facing the certification of ISO 14001:2015. The total score for each company from the results of the checklist in order from the highest value of readiness level for certification to the lowest value

of readiness level for certification are Company F (91.19%), Company C (90.24%), Company E (89.88%), Company D (87.50%), Company B (68.57%), Company G (65.24%) and Company A (48.21%), shown in table 1.

### 3.2.3. Gap analysis result for ISO 45001:2018

Gap analysis checklist data is obtained through observation on field. In this research checklist data is in the form of system observation and audit checklist ISO 45001:2018 which are made to understand the condition of company readiness for certification. Data processing at this stage is to calculate the scores obtained from the gap analysis checklist. The results of score calculation will then be used as the basis for identifying level of readiness of the company in facing the certification of ISO 45001:2018. The total score for each company from the results of the checklist in order from the highest value of readiness level for certification to the lowest value of readiness level for certification are Company E (92.23%), Company F (91.08%), Company C (88.23%), Company D (86.69%), Company G (71.77%), Company B (70.54%) and Company A (47.69%), shown in table 1.

### 3.2.4. Gap analysis result for cGMP

Gap analysis checklist data is obtained through observation on field. In this research checklist data is in the form of system observation and audit checklist cGMP which are made to understand the condition of company readiness for certification. Data processing at this stage is to calculate the scores obtained from the gap analysis checklist. The results of score calculation will then be used as the basis for identifying level of readiness of the company in facing the certification of cGMP. The total score for each company from the results of the checklist in order from the highest value of readiness level for certification to the lowest value of readiness level for certification are Company E (96.35%), Company F (93.20%), Company C (92.60%), Company D (89.95%), Company B (80.50%), Company G (78.94%) and Company A (75.04%), shown in table 1.

**Table 1: Companies ranking for gap analysis**

| Gap Analysis | Companies Ranking | Score | Percent | Readiness Level | Mean Rank[a] | Rank (1-7)[b] |
|---|---|---|---|---|---|---|
| ISO 9001:2015 | Company (E) | 1423 | 95.50 | Very High | 5.68 | 1 |
| | Company (F) | 1379 | 92.55 | Very High | 5.33 | 2 |
| | Company (C) | 1361 | 91.34 | Very High | 5.18 | 3 |
| | Company (D) | 1329 | 89.19 | High | 4.94 | 4 |
| | Company (B) | 1093 | 73.36 | Moderate | 3.24 | 5 |
| | Company (G) | 949 | 63.69 | Low | 2.15 | 6 |
| | Company (A) | 737 | 49.46 | Very Low | 1.47 | 7 |
| ISO 14001:2015 | Company (F) | 766 | 91.19 | Very High | 5.43 | 1 |
| | Company (C) | 758 | 90.24 | Very High | 5.41 | 2 |
| | Company (E) | 755 | 89.88 | High | 5.31 | 3 |
| | Company (D) | 735 | 87.50 | High | 5.02 | 4 |
| | Company (B) | 576 | 68.57 | Moderate | 2.90 | 5 |
| | Company (G) | 548 | 65.24 | Moderate | 2.47 | 6 |
| | Company (A) | 405 | 48.21 | Very Low | 1.46 | 7 |
| ISO 45001:2018 | Company (E) | 1199 | 92.23 | Very High | 5.45 | 1 |
| | Company (F) | 1184 | 91.08 | Very High | 5.39 | 2 |
| | Company (C) | 1147 | 88.23 | High | 4.96 | 3 |
| | Company (D) | 1127 | 86.69 | High | 4.74 | 4 |
| | Company (G) | 933 | 71.77 | Moderate | 3.17 | 5 |
| | Company (B) | 917 | 70.54 | Moderate | 2.95 | 6 |
| | Company (A) | 620 | 47.69 | Very Low | 1.33 | 7 |
| cGMP | Company (E) | 2722 | 96.35 | Very High | 5.46 | 1 |
| | Company (F) | 2633 | 93.20 | Very High | 4.96 | 2 |
| | Company (C) | 2616 | 92.60 | Very High | 4.89 | 3 |
| | Company (D) | 2541 | 89.95 | High | 4.46 | 4 |
| | Company (B) | 2274 | 80.50 | High | 2.96 | 5 |
| | Company (G) | 2230 | 78.94 | High | 2.83 | 6 |
| | Company (A) | 2120 | 75.04 | High | 2.44 | 7 |

***a***. *Mean Rank Calculated by Friedman Test*

***b***. *Rank from 1 (Most Mean Rank) to 7 (Least Mean Rank)*

***Note:***

***1***. *Total Items for ISO 9001:2015 gap analysis (298) with Maximum Score (1490).*

***2***. *Total Items for ISO 14001:2015 gap analysis (168) with Maximum Score (840).*

***3***. *Total Items for ISO 45001:2018 gap analysis (260) with Maximum Score (1300).*

***4***. *Total Question for cGMP gap analysis (565) with Maximum Score (2825).*

### 3.3. Assessment analysis:

The five points Likert scale was used in these gap analysis questions and the following weights have been allocated to the responses of the companies studied: (5) Compliant, (4) OFI, (3) Minor N/C, (2) Major N/C, (1) Non-Compliance. The following tables shows the analysis of the responses.

#### 3.3.1. Analysis of the responses for the gap analysis result toward ISO 9001:2015 in the studied company

The descriptive statistics of the responses to the companies studied were calculated and analyzed using the One Sample T-test, and the results in the table 2 revealed that all variables have a mean greater than the default mean of the Likert scale which is equal to (3), which reflects the company have the documents but have not implemented or have implemented but not recorded in the companies studied. As illustrated, there was significant difference using t-test at $p \leq 0.05$ between good and poor implementation for ISO 9001:2015, which Company (A) has a less t-value (-8.547) and Company (E) has a high t-value (73.281).

In addition to Normality Test of the responses to the companies studied, and the results in the table 2 revealed that company (A) has a less value Kolmogorov-Smirnov Statistic (0.240) on the contrariwise it has a higher value Statistic Shapiro-Wilk (0.855) this statistical analysis refer that company very poor implementation for ISO 9001:2015. Company (A) need to understand and review the implementation because it is still far from the requirements.

#### 3.3.2. Analysis of the responses for the gap analysis result toward ISO 14001:2015 in the studied company

The descriptive statistics of the responses to the companies studied were calculated and analyzed using the One Sample T-test, and the results in the table 2 revealed that all variables have a mean greater than the default mean of the Likert scale which is equal to (3), which reflects the company have the documents but have not implemented or have implemented but not recorded in the companies studied. As illustrated, there was significant difference using t-test at $p \leq 0.05$ between good and poor implementation for ISO 14001:2015, which Company (C) has a high t-value (35.822) followed by Company (F) has an t-value (30.913) then Company (E) has an t-value (29.912) then Company (D) has an t-value (27.651) then Company (B) has an t-value (7.438) then Company (G) has an t-value (5.463) then Company (A) has a less t-value (-7.186).

In addition to Normality Test of the responses to the companies studied, and the results in the table 2 revealed that company (A) has a less value Kolmogorov-Smirnov Statistic (0.204) on the contrariwise it has a higher value Statistic Shapiro-Wilk (0.867) this statistical analysis refer that company very poor implementation for ISO 14001:2015. Company (A) need to understand and review the implementation because it is still far from the requirements.

#### 3.3.3. Analysis of the responses for the gap analysis result toward ISO 45001:2018 in the studied company

The descriptive statistics of the responses to the companies studied were calculated and analyzed using the One Sample T-test, and the results in the table 2 revealed that all variables have a mean greater than the default mean of the Likert scale which is equal to (3), which reflects the company have the documents but have not implemented or have implemented but not recorded in the companies studied. As illustrated, there was significant difference using t-test at $p \leq 0.05$ between good and poor implementation for ISO 45001:2018, which Company (A) has a less t-value (-10.191) and Company (F) has a high t-value (38.403).

In addition to Normality Test of the responses to the companies studied, and the results in the table 2 revealed that company (A) has a less value Kolmogorov-Smirnov Statistic (0.200) on the contrariwise it has a higher value Statistic Shapiro-Wilk (0.878) this statistical analysis refer that company very poor implementation for ISO 45001:2018. Company (A) need to understand and review the implementation because it is still far from the requirements.

#### 3.3.4. Analysis of the responses for the gap analysis result toward cGMP in the studied company

The descriptive statistics of the responses to the companies studied were calculated and analyzed using the One Sample T-test, and the results in the table 2 revealed that all variables have a mean greater than the default mean of the Likert scale which is equal to (3), which reflects the company have the documents but have not implemented or have implemented but not recorded in the companies studied. As illustrated, there was significant difference using t-test at $p \leq 0.05$ between good and poor implementation for cGMP, which Company (A) has a less t-value (21.197) and Company (E) has a high t-value (88.567).

In addition to Normality Test of the responses to the companies studied, and the results in the table 2 revealed that company (A) has a less value Kolmogorov-Smirnov Statistic (0.342) on the contrariwise it has a higher value Statistic Shapiro-Wilk (0.735) this statistical analysis refer that company very poor implementation for cGMP. Company (A) a perform work procedures and requirements are run but not consistent and have opportunities for improvement.

**Table 2: Descriptive analysis for the gap analysis result**

| Gap Analysis | Audit Findings | N | Mean* | Standard Deviation | Standard Error | One-Sample Test | | Tests of Normality | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Kolmogorov-Smirnova | | Shapiro-Wilk | |
| | | | | | | t | Sig. (2-tailed)[b] | Statistic | Sig. | Statistic | Sig. |
| ISO 9001:2015 | Company (A) | 298 | 2.47 | 1.064 | 0.062 | -8.547 | 0.000 | 0.240 | 0.000 | 0.855 | 0.000 |
| | Company (B) | 298 | 3.67 | 0.752 | 0.044 | 15.322 | 0.000 | 0.295 | 0.000 | 0.842 | 0.000 |
| | Company (C) | 298 | 4.57 | 0.496 | 0.029 | 54.508 | 0.000 | 0.376 | 0.000 | 0.630 | 0.000 |
| | Company (D) | 298 | 4.46 | 0.499 | 0.029 | 50.477 | 0.000 | 0.362 | 0.000 | 0.634 | 0.000 |
| | Company (E) | 298 | 4.78 | 0.418 | 0.024 | 73.281 | 0.000 | 0.480 | 0.000 | 0.515 | 0.000 |
| | Company (F) | 298 | 4.63 | 0.549 | 0.032 | 51.136 | 0.000 | 0.412 | 0.000 | 0.645 | 0.000 |
| | Company (G) | 298 | 3.18 | 0.627 | 0.036 | 5.079 | 0.000 | 0.310 | 0.000 | 0.775 | 0.000 |
| ISO 14001:2015 | Company (A) | 168 | 2.41 | 1.063 | 0.082 | -7.186 | 0.000 | 0.204 | 0.000 | 0.867 | 0.000 |
| | Company (B) | 168 | 3.43 | 0.747 | 0.058 | 7.438 | 0.000 | 0.326 | 0.000 | 0.784 | 0.000 |
| | Company (C) | 168 | 4.51 | 0.547 | 0.042 | 35.822 | 0.000 | 0.350 | 0.000 | 0.692 | 0.000 |
| | Company (D) | 168 | 4.38 | 0.645 | 0.050 | 27.651 | 0.000 | 0.298 | 0.000 | 0.756 | 0.000 |
| | Company (E) | 168 | 4.49 | 0.647 | 0.050 | 29.912 | 0.000 | 0.360 | 0.000 | 0.712 | 0.000 |
| | Company (F) | 168 | 4.56 | 0.654 | 0.050 | 30.913 | 0.000 | 0.399 | 0.000 | 0.666 | 0.000 |
| | Company (G) | 168 | 3.26 | 0.621 | 0.048 | 5.463 | 0.000 | 0.306 | 0.000 | 0.766 | 0.000 |
| ISO 45001:2018 | Company (A) | 260 | 2.38 | 0.060 | 0.974 | -10.191 | 0.000 | 0.200 | 0.000 | 0.878 | 0.000 |
| | Company (B) | 260 | 3.53 | 0.052 | 0.836 | 10.169 | 0.000 | 0.249 | 0.000 | 0.868 | 0.000 |
| | Company (C) | 260 | 4.41 | 0.043 | 0.700 | 32.508 | 0.000 | 0.334 | 0.000 | 0.740 | 0.000 |
| | Company (D) | 260 | 4.33 | 0.043 | 0.686 | 31.370 | 0.000 | 0.292 | 0.000 | 0.768 | 0.000 |
| | Company (E) | 260 | 4.61 | 0.043 | 0.697 | 37.290 | 0.000 | 0.446 | 0.000 | 0.584 | 0.000 |
| | Company (F) | 260 | 4.55 | 0.040 | 0.652 | 38.403 | 0.000 | 0.395 | 0.000 | 0.671 | 0.000 |
| | Company (G) | 260 | 3.59 | 0.041 | 0.666 | 14.242 | 0.000 | 0.285 | 0.000 | 0.800 | 0.000 |
| cGMP | Company (A) | 565 | 3.75 | 0.035 | 0.844 | 21.197 | 0.000 | 0.342 | 0.000 | 0.735 | 0.000 |
| | Company (B) | 565 | 4.02 | 0.024 | 0.580 | 42.006 | 0.000 | 0.380 | 0.000 | 0.664 | 0.000 |
| | Company (C) | 565 | 4.63 | 0.024 | 0.568 | 68.267 | 0.000 | 0.396 | 0.000 | 0.582 | 0.000 |
| | Company (D) | 565 | 4.50 | 0.027 | 0.649 | 54.876 | 0.000 | 0.354 | 0.000 | 0.685 | 0.000 |
| | Company (E) | 565 | 4.82 | 0.021 | 0.488 | 88.567 | 0.000 | 0.486 | 0.000 | 0.395 | 0.000 |
| | Company (F) | 565 | 4.66 | 0.024 | 0.560 | 70.491 | 0.000 | 0.411 | 0.000 | 0.563 | 0.000 |
| | Company (G) | 565 | 3.95 | 0.031 | 0.727 | 30.943 | 0.000 | 0.389 | 0.000 | 0.710 | 0.000 |

** The mean score based on the audit finding of gap analysis which each five points Likert scale*
*a. Lilliefors Significance Correction*
*b. Statistically significant differences value by t-test at p≤0.05*

### 3.4. Critical Success for Effective Integrated Safety Management Implementation:

Table 3 present the result reveals that 86.65% of the audit findings are cGMP while 79.35% of the audit findings are ISO 9001:2015; this implies that the cGMP audit findings outweigh the ISO 9001:2015 audit findings. Descriptive statistic result indicates that 78.45% of the audit findings are the ISO 45001:2018 which implies that the majority of audit findings are within the effective integrated safety management implementation which their audit findings can equally be fair. With regard to ISO 14001:2015, the result shows that majority of the audit findings which represent 77.26%. The present study suggested possible integrated safety management implementation levels and asked participants to rate the extent to which level has helped the studied organizations the most.

The results are shown in table 3. By examining table 3, it was clear that the most helpful level the participants cited in the effective implementation of integrated safety management are Current Good Manufacturing Practice (cGMP). Current Good Manufacturing Practice (cGMP) was regarded as the most important level in implementing integrated safety management in Egypt and this is supported further with the current findings of the fact that top management were the contributing for the effective Current Good Manufacturing Practice (cGMP) implementation this is due to an essential factor, which is that cGMP is essential for organizations to obtain an operating license from the Egyptian Drug Authority (EDA). The second most important cited factor was the marketing share, whether local or export. The process of implementing integrated safety management in organizations requires the availability of resources that should be provided by top management, and this stresses the importance of their support. The second most important cited level was Quality Management Systems (ISO 9001:2015), followed by Occupational Health and Safety Management Systems (ISO 45001:2018), followed by Environmental Management Systems (ISO 14001:2015).

Table 4 presented the correlation coefficient between ISO 9001:2015 gap analysis and cGMP gap analysis, ISO 45001:2018 gap analysis and ISO 14001:2015 gap analysis showed that is rated between 0.971 and 0.991 with a p-value less than 0.01, which shows that there is high correlation. The result shows that there is significant relationship between cGMP gap analysis and ISO 9001:2015 gap analysis with the Pearson correlation of 0.971 with a p-value less than 0.01, which shows that there is high correlation. The findings indicate that ISO 14001:2015 gap analysis and cGMP gap analysis are related with influences the coefficient of correlation of 0.964 with a p-value less than 0.01; the findings shows also that there is significant relationship between ISO 45001:2018 gap analysis and ISO 14001:2015 gap analysis with the Pearson Correlation of 0.985 with a p-value less than 0.01, this shows that there is high correlation, finally it shows that there is significant relationship

between cGMP gap analysis and ISO 14001:2015 gap analysis with the Pearson correlation of 0.941, which shows that there is high correlation.

Table 5 displayed the result of regression analysis on the relationship of cooperation between cGMP gap analysis and the others gap analysis. Cooperation between cGMP gap analysis has significant positive relationship with ISO 9001:2015 gap analysis (β = 0.814, t = 0.785, p = 0.490); Cooperation between cGMP gap analysis has positive relationship with ISO 14001:2015 gap analysis (β = 0.381, t = 0.274, p = 0.802); Cooperation between cGMP gap analysis has significant negative relationship with ISO 45001:2018 gap analysis (β = - 0.227, t = - 0.283, p = 0.795)

Table 6 shows a comparative analysis of discernment for market share of three sectors for the seven studied companies of integrated safety management implementation. Analysis revealed that the highest mean percent values was for exporting outside the country sector compared to of export planned and local market sectors (statistically significant differences at p≤0.05).

**Table 3: Descriptive Statistic for Integrated Safety Management Implementation**

| Audit Findings | ISO 9001:2015 | ISO 14001:2015 | ISO 45001:2018 | cGMP |
|---|---|---|---|---|
| **Company (A)** | 49.46 | 48.21 | 48.00 | 75.04 |
| **Company (B)** | 73.36 | 68.57 | 70.54 | 80.50 |
| **Company (C)** | 91.34 | 90.24 | 88.23 | 92.60 |
| **Company (D)** | 89.53 | 87.50 | 86.69 | 89.95 |
| **Company (E)** | 95.50 | 89.88 | 92.23 | 96.35 |
| **Company (F)** | 92.55 | 91.19 | 91.38 | 93.20 |
| **Company (G)** | 63.69 | 65.24 | 72.08 | 78.94 |
| **Mean** | 79.35 | 77.26 | 78.45 | 86.65 |
| **Standard Deviation** | 17.593 | 16.786 | 16.078 | 8.320 |
| **Standard Error** | 6.649 | 6.344 | 6.077 | 3.145 |
| **Minimum** | 49.46 | 48.21 | 48.00 | 75.04 |
| **Maximum** | 95.50 | 91.19 | 92.23 | 96.35 |
| **Mean Rank[a]** | 2.71 | 1.57 | 1.71 | 4.00 |
| **Importance Level[b]** | 2 | 4 | 3 | 1 |

*a. Mean Rank Calculated by Friedman Test*

*b. Importance Level from 1 (Most Mean Rank) to 4 (Least Mean Rank)*

**Table 4: Correlation Matrix for Integrated Safety Management Implementation**

| | | ISO 9001:2015 | ISO 14001:2015 | ISO 45001:2018 | cGMP |
|---|---|---|---|---|---|
| **ISO 9001:2015** | **Pearson Correlation** | 1 | .991** | .973** | .971** |
| | **Sig. (2-tailed)** | | 0.000 | 0.000 | 0.000 |
| **ISO 14001:2015** | **Pearson Correlation** | .991** | 1 | .985** | .964** |
| | **Sig. (2-tailed)** | 0.000 | | 0.000 | 0.000 |
| **ISO 45001:2018** | **Pearson Correlation** | .973** | .985** | 1 | .941** |
| | **Sig. (2-tailed)** | 0.000 | 0.000 | | 0.002 |
| **cGMP** | **Pearson Correlation** | .971** | .964** | .941** | 1 |
| | **Sig. (2-tailed)** | 0.000 | 0.000 | 0.002 | |

********. *Correlation is significant at the 0.01 level (2-tailed).*

**Table 5: Simple Regression Analysis Results for Integrated Safety Management Implementation**

| Model Summary | | | | | | |
|---|---|---|---|---|---|---|
| **Model** | **R** | **R Square** | **Adjusted R Square** | | **Std. Error of the Estimate** | |
| 1 | .972[a] | 0.944 | 0.889 | | 2.77640 | |
| **ANOVA[b]** | | | | | | |
| **Model** | | **Sum of Squares** | **df** | **Mean Square** | **F** | **Sig.** |
| 1 | Regression | 392.218 | 3 | 130.739 | 16.961 | .022[a] |
| | Residual | 23.125 | 3 | 7.708 | | |
| | Total | 415.344 | 6 | | | |
| **Coefficients[b]** | | | | | | |
| **Model** | | **Unstandardized Coefficients** | | **Standardized Coefficients** | **t** | **Sig.** |
| | | B | Std. Error | Beta | | |
| 1 | (Constant) | 50.727 | 5.790 | | 8.762 | 0.003 |
| | ISO 9001:2015 | 0.385 | 0.491 | 0.814 | 0.785 | 0.490 |
| | ISO 14001:2015 | 0.189 | 0.689 | 0.381 | 0.274 | 0.802 |
| | ISO 45001:2018 | -0.118 | 0.415 | -0.227 | -0.283 | 0.795 |

***a***. *Predictors: (Constant), ISO 9001:2015, ISO 14001:2015, ISO 45001:2018*
***b***. *Dependent Variable: cGMP*

**Table 6: Corporative analysis of discernment for market share**

| **General Question (02)** | **Is the company exporting outside the country?** | | | | | | **F (p)** |
|---|---|---|---|---|---|---|---|
| | **Yes** | | **Planned** | | **No** | | |
| **Gap Analysis** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | |
| **ISO 9001:2015** | 93.13 | 2.141 | 81.44 | 11.437 | 56.58[d] | 10.061 | 0.001* |
| **ISO 14001:2015** | 90.44 | 0.677 | 78.04 | 13.385 | 56.73[d] | 12.038 | 0.001* |
| **ISO 45001:2018** | 90.62 | 2.108 | 78.62 | 11.422 | 60.04[d] | 17.025 | 0.001* |
| **cGMP** | 94.05 | 2.015 | 85.22 | 6.683 | 76.99[d] | 2.753 | 0.001* |

***F**: One Way ANOVA* ***d**: Significantly different group* ****** $p < 0.05$ *(significant)*

## 4. Discussion

The objective of arranging an integrated management system of a pharmaceutical enterprise is creation of joint documented subsystems for quality management, risk management, product safety, environment safety, occupational health and safety, project management, etc., as well as their adjustment in terms of corporate management of the enterprise. To meet the legal and market requirements, pharmaceutical companies around the world are forced to implement several management systems simultaneously. Efficiently integrated management system becomes the basis for improvement of performance of the enterprise, allows to work successfully in the future, unites all stakeholders with a common goal, and ultimately, the company operates effectively in a tough competitive environment (Domokos, 2021).

### 4.1. Performance of the implementation for specifications

For this study, in seven cases are from the pharmaceutical sector in Alexandria; Gap analysis checklist has been applied to all companies according to the following specifications:

#### 4.1.1. ISO 9001:2015 - Quality management systems

The quality is attributed to products, focusing on aspects such as customer satisfaction, standardization, and control processes. Thus, according Natarajan (2017), the quality represents competitive advantage through improved organizational performance. Companies must implement a system to satisfy stakeholders' and consumers' expectations, stop non-compliance, and look for solutions for their websites when they become available in order to build and preserve quality. This will start the process of continuous improvement. Companies must implement a system to satisfy stakeholders' and consumers' expectations, stop non-compliance, and look for solutions for their websites when they become available in order to build and preserve quality. This will start the process of continuous improvement (Solomon *et al.*, 2017). The quality management systems have among its aims to implement and their requirements while minimizing costs, with monitoring and control, as can be seen in the case of company (A), and the items that were not implemented. For the success of the QMS in a company, that's necessary the commitment of senior management and all employees, in addition to providing financial resources, and adequate infrastructure (Pimentel & Afonso, 2019). It became clear to us

in this study that the Quality management systems changed in the performance of implementation, where all the improvement is always for the company (E). Although it is larger in volume for commercial transactions in different markets.

#### 4.1.2. ISO 14001:2015 - Environmental management systems

With the inherited culture of the industrial revolution, the world was absolutely focused on strictly financial enrichment, by promoting the production of an environmentally unacceptable level, where the environment was not part of the priorities. This culture has resulted in environmental degradation that reaches its limit. In this context, society, the pharmaceutical sector and the governmental and non-governmental spheres, seek to act to suit the environmentally responsible development (Krishna *et al.*, 2017). The company (E) includes only the control of documents, records, the process of prevention, and corrective actions regarding nonconformities. The case of company (A), as can be seen, implemented a number of parts, and poor conditions of their management systems, which would not be conducive to proper functioning of the environmental management systems, although he claimed not only the implementation of aspects not related to systems management.

According to Latan *et al.* (2018), development must be based on three points: economic, social and environmental policy that can be sustained and above all balanced, as shown in this study. Thus, the environmental management shows up as a strategy to manage the environment internalizing it to other political, social and economic that is, also characterize the environment as a priority within the context of strategic decisions. The company (F) had implemented important indicators of environmental management systems that can increase the efficiency of its monitoring by the development continual improvement. It was also observed for the company (C), a satisfactory implementation of their training, thus promoting global awareness of their management systems.

#### 4.1.3. ISO 45001:2018 - Occupational Health and Safety management systems

The concept of safety and health can be defined, according to ISO 45001 - Occupational Health and Safety Management Systems, as the set of factors that could affect the safety, and health of staff, employees, and visitors outsourced of an organization. In this context, the management system of safety and health (OHSMS) is defined as a system of management responsible for safety and health of employees and people who are part of the organization (Morgado *et al.*, 2019). One of the guiding rules for the implementation of OHSMS in organizations is the ISO 45001 (Darabont *et al.*, 2019). According to Purwanto (2020), the OHSMS promotes several benefits to companies, some of them: improved corporate image, increased competitiveness, open markets, prevent risks and accidents, increased productivity, and improved quality of life of employees, and co-related. It was shown in both companies (E) and (F) and those that implemented the requirements in a very excellent manner, the implementation can be noted that the companies have implemented the scope and management manuals, measurement, control, and monitoring of documents and processes, contribution and critical analysis of top management, recognition and treatment of non-compliance, communication, internal audit, and continuous improvement processes.

There are challenges associated with implementing an OHSMS in companies, including inconsistent deployment practices, resistance to change, a lack of commitment from management, employee churn, and low employee involvement (Beisseyev *et al.*, 2020). Additionally, none of the employees in company (A) implemented occupational health and safety management systems at the same time; rather, they all hired outside consultants to build. The fact that organizations still require outside supervision for their performance and implementation even after they have gotten the certificate of occupational health and safety management system indicates that the deployment of management systems is still a relatively recent practice. This case company (E) had a satisfactory implementation of the occupational health and safety management systems, as observing increased productivity to decrease accidents, which demonstrations the competence of OHSMS.

#### 4.1.4. cGMP - Good Manufacturing Practice

The system of good manufacturing practices (cGMP) promotes several benefits to organizations, as can be highlighted: services, processes, and improved products; increased customer satisfaction; improved corporate image; competitive advantage. However, there are still issues with its implementation, chief among them being senior management's lack of participation, the lack of involvement of middle managers, resistance to change, little knowledge about the requirements of the rule by the officials, and resistance to investment in its implementation (Sarvari *et al.*, 2020).

Although the results of the study demonstrated high levels of implementation, this is because it is an authorized requirement from the government and egyptian drug agency for grant licenses to companies. The company (A) is still in place, and they have implemented their subpar management indicators and addressed the surface-level components of good manufacturing practice. The training's implementation can be deemed satisfactory as it fosters awareness of their practice on a global scale.

It is still considered a company (E), a company (F) and a company (C) that is the highest even in implementation good manufacturing practice requirements, which shows the extent of companies' efficiency in application and

the keenness of these companies to reach international ranks. It is also clear that the motivation for this is the external market and the extent of their keenness to reach the top of this market.

These have less to do with the real challenges of other management systems and more to do with the anticipated outcomes of the pharmaceutical industry. It was anticipated that the integration would offer the secret to improving the level of dedication and organizational performance in the certified areas.

### 4.2. Effective Integrated Safety Management Implementation

The Integrated Management System (IMS) includes management systems focused on quality (QMS - ISO 9001), environmental (EMS - ISO 14001), health and safety (ISO 45001), as well as adding aspects of manufacturing practice (cGMP) certified by certification bodies (Korčok *et al.*, 2020).

The result of regression analysis on the relationship of cooperation between cGMP gap analysis and the others gap analysis. Cooperation between cGMP gap analysis has significant positive relationship with ISO 9001:2015 gap analysis; Cooperation between cGMP gap analysis has positive relationship with ISO 14001:2015 gap analysis; Cooperation between cGMP gap analysis has significant negative relationship with ISO 45001:2018 gap analysis this implied that cooperation between cGMP gap analysis and ISO 9001:2015 gap analysis is the key success for effective integrated safety management implementation. Similarly, this finding is in line with the literature argument of Korčok *et al.* (2020) who argued that, it is important every gap analysis to understand the key role that cooperation play in the effective integrated safety management implementation in order to improve the operations of the organization toward objective achievement.

According Muthusamy *et al.* (2018), it is necessary to integrate certified management systems at the same time. According to Talapatra *et al.* (2019), IMS may derive important benefits to organizations, benefits including higher output, enhanced brand recognition for the business, lower deployment and certification costs for management systems, potential for synergy in the integration, and simpler management. The management handbooks and policies, document and record control, senior management review, internal audit, training, and work instructions have already been incorporated by the company (E). The company (E) utilized the IMS in a manner akin to that of the company (F), successfully integrating certain areas of its management systems, particularly those that dealt with integration-related issues. However, the management manuals were excluded. The management systems are influenced by both external and internal influences. As these systems address various management systems, their integration and impacts become ever more pronounced. As a result, it is crucial to incorporate in an interactive way, taking into account management goals, policies, and standards in addition to legal needs and unique circumstances. Senior management's advance preparation and the agreement of every employee in the company make this practice feasible and guarantee the overall integration of all departments (Souza & Alves, 2018). The manual management systems were the only ones incorporated by the corporation A. It is evident that the company (A) did not fully utilize the IMS to inform the integration of the few components of their management systems. For the example company (A), the integration of management indicators was likewise inadequate. The training was not integrated.

The company (B) has integrated systems for managing policies, document control, communications, process improvement, internal audit, training, and senior management review. Although not to the same extent as company (E), this case has integrated significant portions of their management systems. company (B) used the IMS efficiently to link some of the elements that were excluded because they are all special requirements for each management system. Because the management systems' indicators encompass the tracking of the main indices, take note of their adequate integration. Additionally, the training was satisfactorily integrated, enabling the promotion of broader systems management capacity.

A range of challenges encountered by companies has been noted; these can be attributed to variations in the integration procedures of management systems as well as enterprise characteristics. However, there are significant challenges that are comparable to those faced by certain companies, including employee resistance, a lack of dedication from upper management, exorbitant expenses, and a lack of comprehension of standards and integration.

### 4.3. Export

Customers, employees, shareholders and the community are also concerned about integrated safety management systems matters and creating a principle that meets customer expectations can help to improve market share. Management standards and systems as ISO 9001, ISO 14001 and ISO 45001 have been developed and introduced to address these needs, but dealing with separate management systems covering quality, environment, safety, and good manufacturing practice, and ensuring that they align with the organization's strategy, has proved difficult. The case for integrated management systems (IMS) is now starting to be made in the literature and an IMS is increasingly seen as part of the organization's management portfolio (Balogh *et al.*, 2020). Consequently, it can be observed that these are all companies with high market capture and high incomes, whereas companies (C), (E), and (F) rely on export. Also, companies (A), (B), (D) and (G) do not export. These

characteristics indicate that integrating systems for certified management is a practice by large organizations; in other words, it is noted that companies use this practice to ascend to a competitive market.

## 5. Conclusion

The qualitative method has been well used in this study because it showed five companies with integrated management systems, and its main features, allowing proper analysis, and interpretation. It is noteworthy to limit your search because it is seven companies among a large sphere of enterprises with integrated management systems, also the data collection was limited to information provided by companies, and review your documents. Although study has shown diversity in some benefits and difficulties for the integration of management systems, there is similarity among some, such as improving internal processes and its products, increasing customer satisfaction, decrease in number of non-compliance and returns, increase productivity and profits, improved management of resources, enhance the image of their market, systematic processes and management systems and reduction of costs and time to the integration of management systems. The difficulties it stresses: resistance from employees, lack of top management commitment, and understanding of low standards, and the integration of management systems. It highlights the lack of understanding of integrated systems, which significantly influences the integration and monitoring of the management systems in industry. It can see that in general, companies do not yet have a real interpretation of management systems, as do the integration and monitoring of their management systems in various ways, and often inefficiently.

It is recommended that all organizations operating in the pharmaceutical sector need new approaches to meet customer expectations, while differentiating from their competitors and succeeding in the market especially exporting products abroad. Moreover, approaches that can meet the expectations of all stakeholders have gained importance. Organization should not be ignored common values such as environment, social responsibility, and human resources, which should be protected as they may be regarded as a company's assets. We also suggest that governments consider implementing integration between different management systems alongside of good manufacturing practices as an essential aspect of granting operating licenses to companies.

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